DOLENTIUM HOMINUM

No. 91 – year XXXI – No. 2, 2016

JOURNAL OF THE PONTIFICAL COUNCIL
FOR HEALTH CARE WORKERS
(FOR HEALTH PASTORAL CARE)

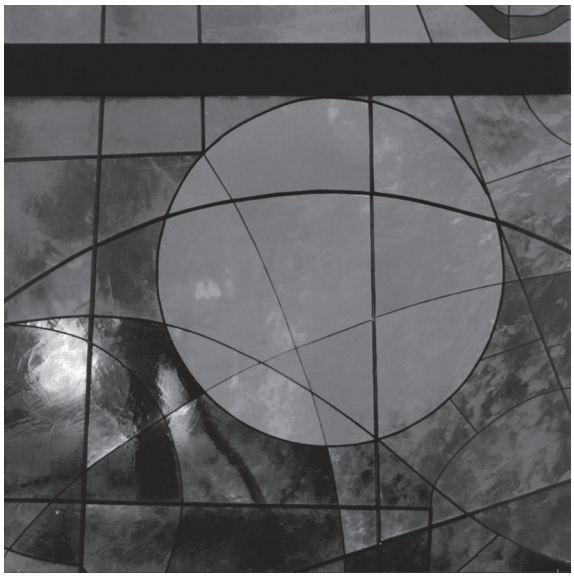
Proceedings of the XXXI International Conference

Organised by
the Pontifical Council
for Health Care Workers

Towards a Culture of Health that is Welcoming and Supportive at the Service of People with Rare and Neglected Diseases

10-11-12 November 2016

New Synod Hall
Vatican City



Editorial and Business Offices:
Pontifical Council for Health Care Workers (for Health Pastoral Care)
00120 Vatican City; Tel. 06.698.83138, 06.698.84720, 06.698.84799 - Fax: 06.698.83139
e-mail: **opersanit@hlthwork.va**
www.holyseeforhealth.net

Published three times a year. Subscription rate: 32 € postage included
Printed by Editrice VELAR, Gorle (BG)
Cover: Glass window Rev. Costantino Ruggeri
Poste Italiane s.p.a. Spedizione in Abbonamento Postale - D.L. 353/2003 (conv. In L. 27/02/2004 n° 46) art. 1, comma 2, DCB Roma

APOSTOLIC LETTER
ISSUED MOTU PROPRIO
BY THE SUPREME PONTIFF
FRANCIS
INSTITUTING THE

Dicastery for Promoting Integral Human Development

In all her being and actions, the Church is called to promote the integral development of the human person in the light of the Gospel. This development takes place by attending to the inestimable goods of justice, peace, and the care of creation. The Successor of the Apostle Peter, in his work of affirming these values, is continuously adapting the institutions which collaborate with him, so that they may better meet the needs of the men and women whom they are called to serve.

So that the Holy See may be solicitous in these areas, as well as in those regarding health and charitable works, I institute the Dicastery for Promoting Integral Human Development. This Dicastery will be competent particularly in issues regarding migrants, those in need, the sick, the excluded and marginalized, the imprisoned and the unemployed, as well as victims of armed conflict, natural disasters, and all forms of slavery and torture.

In the new Dicastery, governed by the Statutes that today I approve *ad experimentum*, the competences of the following Pontifical Councils will be merged, as of 1 January 2017: the Pontifical Council for Justice and Peace, the Pontifical Council *Cor Unum*, the Pontifical Council for the Pastoral Care of Migrants and Itinerant People, and the Pontifical Council for Health Care Workers. On that date these four Dicasteries will cease exercising their functions and will be suppressed, and articles 142-153 of the Apostolic Constitution *Pastor Bonus* will be abrogated.

I decree that what has been set out in this Apostolic Letter issued *Motu Proprio* have the force of law, notwithstanding anything to the contrary, even if worthy of special mention, and that it be promulgated by publication in *L'Osservatore Romano*, therefore published in the *Acta Apostolicae Sedis*, entering into force on 1 January 2017.

Given in Rome, at Saint Peter's, on 17 August 2016, the Jubilee Year of Mercy, the Fourth Year of my Pontificate.

FRANCIS

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SATURDAY 12 NOVEMBER

Message of His Holiness Pope Francis

To the Most Reverend Monsignor
Jean-Marie Mupendawatu
Secretary of the Pontifical Council for Health Care Workers

I wish to send my cordial greetings to those taking part in the thirty-first international conference on the subject 'Towards a Culture of Health that is Welcoming and Supportive, at the Service of People with Rare and Neglected Pathologies', organised by the Pontifical Council for Health Care Workers, which I thank for this initiative. I also address grateful thoughts to the memory of my much lamented brother in the episcopate, H.E. Msgr. Zygmunt Zimowski, the former President of the Pontifical Council, who returned to the House of the Father last July.

Qualified experts, from every part of the world, have come together to explore the subject of 'rare' pathologies and 'neglected' diseases in their various aspects: from the medical-epidemiological to the socio-political and from the economic to the juridical-ethical. The conference intends to engage in a survey of the present situation, as well as an identification and a re-launching of practicable guidelines for action in this special medical/health-care scenario; having as founding values respect for the lives, the dignity and the rights of patients, together with a welcoming and supportive approach; and producing strategies for care and treatment that are moved by a sincere love for the actual person who suffers – from a 'rare' or 'neglected' disease as well.

The data that are available on these two chapters of medicine are emblematic. The most recent calculations of the World Health Organisation indicate that 400 million people in the world as a whole suffer from diseases defined as 'rare'. The scenario of 'neglected' diseases is even more dramatic because they affect over a billion people. They are for the most part infectious diseases and they are widespread amongst the poorest populations of the world, often in countries where access to health-care services is insufficient to cover essential needs, above all in Africa and Latin America, in areas that have a tropical climate, with insecure drinking water and deficient hygienic/alimentary, housing and social conditions.

The challenge, from an epidemiological, scientific, clinical/care, hygienic and economic point of view is, therefore, enormous because it involves responsibilities and commitments on a global scale: international and national health-care and political authorities, health-care workers, the biomedical industry, associations of citizens/patients, and lay and religious volunteers.

This is an enormous challenge, but not an impossible one. Given the complexity of the subject, indeed, a multidisciplinary and joint approach is necessary; an effort that calls on all the human realities involved, whether institutional or otherwise. Amongst them there is also the Catholic Church which has always found a motivation and impulse in her Lord, Jesus Christ, who was crucified and rose again, the figure both of the patient ('*Christus patiens*') and the physician ('*Christus medicus*', the Good Samaritan).

At this point, I would like to offer some observations that can contribute to your reflections.

The first is that if the human person is the eminent value, it follows that each person, above all a person who suffers, because of a 'rare' or 'neglected' disease as well, without any hesitation deserves every kind of commitment in order to be welcomed, treated and, if possible, healed.

The effective addressing of entire chapters of illness, as is the case with 'rare' and 'neglected' diseases, requires not only qualified and diversified skills and abilities in health-care but also ones that are beyond health care – one may think of health-care managers, of administrative and political health-care authorities, and of health-care economists. An integrated approach, and careful assessments of contexts directed towards the planning and implementation of operational strategies, as well as the obtaining and management of the necessary sizeable resources, are required. At the base of every initiative, however, lies, first and foremost, free and courageous good will directed towards the solving of this major problem of global health: an authentic 'wisdom of the heart'. Together with scientific and technical study, the determination and wisdom of those who set themselves to work not only in the existential fringes of the world but also in its fringes at the level of care, as is of often the case with 'rare' and 'neglected' diseases, are, therefore, crucial.

Amongst the many who give of themselves generously, the Church, as well, has always been active in this field and will continue with this exacting and demanding pathway of nearness to, and the accompanying of, the person who suffers. It is no accident, therefore, that this thirty-first international conference wanted to adopt the following key words to communicate the sense – understood as meaning and direction – of the presence of the Church in this authentic work of mercy: *to inform*, in order to establish the state of present knowledge at a scientific and clinical/care level; *to care* for the life of patients in a better way in a welcoming and supportive approach; *to steward* the environment in which man lives.

The relationship between these diseases and the environment is decisive. Indeed, many diseases have genetic causes; in the case of others, environmental factors have a major importance. But even when the causes are genetic, a polluted environment acts as a multiplier of damage. And the greatest burden falls on the poorest populations. It is for this reason that I want once again to emphasise the absolute importance of respect for, and the stewardship of, the creation, our common home.

A second observation that I would like to bring to your attention is that it remains a priority of the Church to keep herself dynamically in a state of 'moving outwards', to bear witness at a concrete level to divine mercy, making herself a 'field hospital' for marginalised people who live in every existential, socio-economic, health-care, environmental and geographical fringe of the world.

The third and last observation relates to the subject of justice. Although it is true that care for a person with a 'rare' or 'neglected' disease is in large measure connected with the interpersonal relationship of the doctor and the patient, it is equally true that the approach, at a social level, to this health-care phenomenon requires a clear application of justice, in the sense of 'giving to each his or her due', that is to say equal access to effective care for equal health needs, independently of factors connected with socio-economic, geographical or cultural contexts. The reason for this rests on three fundamental principles of the social doctrine of the Church. The first is the principle of *sociality*, according to which the good of the person reverberates through the entire community. Therefore, care for health is not only a responsibility entrusted to the stewardship of the person himself or herself. It is also a social good, in the sense that the more individual health grows, the

more ‘collective health’ will benefit from this, not least at the level, as well, of the resources that are freed up for other chapters of illness that require demanding research and treatment. The second principle is that of *subsidiarity* which, on the one hand, supports, promotes and develops socially the capacity of each person in attaining fulfilment and his or her legitimate and good aspirations, and, on the other, comes to the aid of a person where he or she is not able on his or her own to overcome possible obstacles, as is the case, for example, with an illness. And the third principle, with which a health-care strategy should be marked, and which must take the person as a value and the common good into account, is that of *solidarity*.

On these three cornerstones, which I believe can be shared by anybody who holds dear the eminent value of the human being, one can identify realistic, courageous, generous and supportive solutions to addressing even more effectively, and to solving, the health-care emergency of ‘rare’ and ‘neglected’ diseases.

In the name of this love for man, for every man, above all for suffering man, I express to all of you, participants in the thirty-first international conference of the Pontifical Council for Health Care Workers, the wish that you will have a renewed impetus and generous dedication towards sick people, as well as a tireless drive towards the greatest common good in the health-care field.

Let us ask the Most Holy Mary, Health of the sick, to make the deliberations of this conference of yours bear fruit. To her we entrust the commitment to making increasingly human that service which, every day, the various professional figures of the world of health perform for suffering people. I bless from my heart all of you, your families, and your communities, as I do those whom you meet in hospitals and nursing homes. I pray for you; and you, please, pray for me.

From the Vatican, 12 November 2016

FRANCIS

OPENING OF THE XXXI INTERNATIONAL CONFERENCE

Towards a Welcoming and Supportive Culture of Health at the Service of People with Rare and Neglected Diseases

Speech by Cardinal Parolin

HIS EMINENCE CARDINAL PIETRO PAROLIN
Secretary of State of His Holiness, the Holy See

Your Eminences, Your Excellencies, Ladies and Gentlemen, from the many and important subjects worthy of attention, for this thirty-first international conference organised by the Pontifical Council for Health Care Workers the following subject was chosen: 'Towards a Welcoming and Supportive Culture of Health at the Service of People with Rare and Neglected Diseases'. This choice carries on from the subject that was recently addressed at the international meeting of 9-10 June 2016 which had the title 'Towards Holistic Care for People with Hansen's Disease Respectful of their Dignity'.

This new subject extends our gaze to two very broad chapters: that of rare diseases and that of neglected diseases. According to the geographical areas involved, these two fields are closely connected. Indeed, whereas even in countries with advanced medicine rare diseases constitute a field of care that can witness a low level of attention, in countries where the health-care service is deficient or totally insufficient, this lack of care concerns both rare diseases and very common tropical diseases.

Overall, these diseases afflict an enormous number of people. The figure is estimated at 350-400 million in the case of rare diseases and a billion people in the case of neglected tropical diseases.

This numerical fact in itself should alarm us and stimulate us to engage in an increasingly substantial commitment so that these people are not abandoned to a destiny of suffering and social marginalisation.

One of the topics that is most relevant to rare diseases is scientific-medical research which should understand their causes and identify possible therapies for them. The international pharmaceutical industry does not invest in a significant way in this kind of research and at times, although it has discovered effective medical products for such diseases, stops producing them because of a lack of profits.

The function of promoting research in this field is the task of governments. But during recent years we have witnessed a cutting back in systems of welfare and this does not allow, even in rich countries, a broad flow of investments for this kind of research. In this way, it is above all associations of family relatives, Catholic and non-Catholic non-governmental organisations, donor Foundations and organisations of volunteers that provide funds to finance research. Despite the efforts of all these bodies, research proceeds slowly and this remains one of the principal aspects to be considered in the context of action designed to achieve effective treatment of rare diseases.

As regards the field of neglected tropical diseases, we are certainly not at year one in terms of the commitment to provide treatment. In many cases, they are treated with medical products that are already in use and cheap or even donated by the pharmaceutical industries. For many years, the World Health Organisation has set in motion imposing programmes for the treatment of people with neglected diseases. These programmes have flanked the strong commitment of Catholic medical institutions, which are to be found in many countries that have high rates of neglected tropical diseases, and the programmes of a large number of international organisations of volunteers. But despite the efforts that have been made hitherto, only a part of sectors of the populations that are affected receive adequate care and treatment. In this case, the principal reason lies in the lack of networks of medical services involving prevention, diagnosis and treatment in those countries where these diseases are most widespread.

The Catholic Church, which has always seen care for sick people as an essential form of fraternal charity, feels herself strongly called upon by the condition of suffer-

ing of many millions of people. The Magisterium of Pope Francis never ceases to remind us that the duty of solidarity towards the suffering and the poor forms a part of the Christian vocation. On this point, we cannot forget the close tie that exists between many of the neglected tropical diseases and the condition of extreme poverty in which many populations live. Thus the subject of care is added to the subject of justice. The inequality of those who live in conditions of a certain prosperity and those who live in grave poverty cannot remain without answers.

It is clear to all those who work in this sector – medical doctors, social workers, priests, men and women religious, and volunteers – that tropical diseases often arise in a context of extreme poverty and in their turn generate further poverty, impeding any form of social progress on the part of patients and often also of their families. Thus health-care must be accompanied by programmes of help that foster access to drinking water, to decent housing, to the schooling of children, to the elimination of possible forms of stigma caused by illness, etc.

The Catholic Church works, and continues to work, for the achievement of these services for people with neglected tropical diseases, but on this pathway she wishes to find the company of all men and women of good will, who understand the needs of our brothers and sisters and also want to work to provide effective answers.

We should unite all the forces that are available to study the problems to the full, to assess the most promising actions that should be taken and then implement them at a practical level. In this undertaking we should not forget the necessary cooperation with States who are the first to be responsible for the health of their own citizens, but which often need to be helped to organise the network of their own health-care and welfare services.

For all of these reasons, we can easily understand how necessary it is to have an updated picture of the distribution of rare diseases and neglected diseases. This is a picture that should also include the current state of treatment and the most promising lines of research.

Of importance will also be dialogue between those who work in the field to compare and bring out best practices and encourage their spread.

Lastly, we cannot forget that it is important to call the attention of the mass media to this subject. In this way, those who are not experts in this area will also be able to become aware of the situations of suffering of very many people who call for understanding and support. This is a subject that touches upon the conscience of all men and women of good will and requires the cooperation of the largest number of people and precisely for this reason should be known about by as many people as possible.

To these objectives this thirty-first international conference on ‘Towards a Welcoming and Supportive Culture at the Service of People with Rare and Neglected Diseases’ wants to make a contribution, and on behalf of the Holy Father Francis I am happy to declare it open.

Thank you. ■

THURSDAY 10 NOVEMBER

Speech of Don Carmine Arice

DON CARMINE ARICE, SSC
Director of the National Office for Pastoral Care in Health, the Italian Bishops' Conference

I express my thanks for the invitation to take part in this international conference and with reverence and cordiality I greet His Eminence Cardinal Turkson, their Excellencies who are here with us, and Monsignor Mupendawatu, Father Chendi and all those here gathered here today.

The National Office for Pastoral Care in Health of the Italian Bishops' Conference welcomed the subject of the international conference of this year with especial favour, seeing in this decision a typically evangelical outlook: that is to say to look at, and to seek out, the last – those who are forgotten and expensive in the eyes of the world but precious in the eyes of God because 'where man has miserably fallen, there God has mercifully descended' (St. Bernard).

Experts will provide us with statistics, they will describe to us the state of the art of research and of health care for individuals, who, unfortunately, witness the right to health and treatment that is upheld by the Italian Constitution applied with difficulty. This a right that is still rather distant from being applied in real terms to everyone.

It may be useful to me and to you to remember, at the beginning of our deliberations, what the Magisterium of the Church tells us: 'the true measure of humanity', Benedict XVI wrote, 'is essentially determined in relationship to suffering and to the sufferer. This holds true both for the individual and for society. A society unable to accept its suffering members and incapable of helping to share their suffering and to bear it inwardly through "compassion" is a cruel and inhuman society'.

Yes, indeed. Sick people restore to us that humanity which at times the agitated rhythms of the world blow away: they remind us that people are more important than things; that being is more important than functioning.

Whereas science can increase the dissemination of knowledge within the human community, taking care of the suffering and the sick, specifically all sick people, beginning with the most neglected, as an act of justice before being an act of charity, can only make our society grow in humanity.

I am frightened when I hear it said that we must be careful about economic resources and in that in allocating them we must take into account what is available. And to fear is added anger when it is forgotten that 1% of the world's population possess wealth equal to that of the other 99% and that the sixty-two richest people on the planet have the same wealth as the poorest half of the world. The disciples of Jesus had much more than five loaves and a few fish to feed the multitude.

The various observers that our country possesses continue to tell us that health-care needs are on the increase and that with them health-care poverty is also increasing. Many people in Italy forgo the health care that they need because they cannot afford it. This is not something to which we can be indifferent. In the case of extraordinary care and treatment, the question becomes dramatic.

I will borrow the words of Pope Francis written in his apostolic letter *Evangelii gaudium* in order to express a hope to this highly qualified international conference: 'Today, we frequently hear of a "diagnostic overload" which is not always accompanied by improved and actually applicable methods of treatment' (*EG*, n. 50). Knowing about realities can only prepare the ground for discernment and discernment must lead to the setting in motion of virtuous processes. We hope that these days of deliberations, thought and dialogue will direct us towards suggesting concrete proposals for sick people and their families to the community of the Church, first of all, and then to civil society.

Lastly, we know that although we cannot always cure, we can always provide care and the first form of care is welcome and solidarity, or, as the Italian bishops have put it, enabling sick people to live in a 'hospitable community'.

The bishops of Italy wrote: 'Hospitality is the anthropological dimension that captures and connects the various forms of prevention, care and rehabilitation…It is the face, voice, gesture and speech that is able to generate care and at the same time to take care of people, above all when the illness turns out to be [complex]…responsibility is taken for accompanying incurable illnesses as well, in the rhythms of a period which, however tiring or painful it may be, can restore meaning to the whole of a person's existence' (*Predicate il Vangelo e curate i malati*, Rome, 2006, p. 23).

May the Lord give us witnesses to hope who are able to unite professional care and the comfort of the Spirit with compassion!

Speech of Greetings of Mariapia Garavaglia

PROF. MARIAPIA GARAVAGLIA
University lecturer on health-care systems, President of the Luigi Maria Monti Foundation IDI-IRCCS, Italy

Rare diseases: they are rare because of their percentages of incidence by cohorts of the population, but millions of people and their families are involved. Our meeting on this subject is an important one. The speakers will address the subject, bringing data and examples of success in their research as regards a goodly number of rare or neglected diseases. Unfortunately, a broad spectrum of diseases without a diagnosis still exists and this worsens the malaise and the suffering of families.

For us, involved as we are with our Catholic institutions, a further commitment is added to supporting research and health care and social care.

Through our activities we give form to the command 'go out and heal' and in our history we have made prophetic choices, acting where public and planned responses have not existed. Today, as well, we engage in activity that fills in gaps, even though in this way we operate at the level of state services.

We have the moral obligation to want to be present on the panorama of services that is offered to citizens with our own specific witness.

Often the founders of our institutions have been particularly farsighted. For example, over a hundred years ago the Blessed Luigi Maria Monti, starting with the treatment of patients with scabies, set up an institution dedicated to Our Lady and specialised in dermatology: the IDI (the Dermatopathic Institute of the Immaculate Mary). Today, as was the case then, almost every poor person has a 'neglected' disease (NTD, neglected tropical disease). The opposite is also the case: neglected diseases provoke poverty because they do not allow people to have a normal life with work activity. They are often neglected but not rare, and poor people who live amongst the rich are the most afflicted by neglected tropical diseases. In absolute terms, we can be happy that poverty is decreasing but inequalities are increasing.

Almost all our works seem to be in decline: perhaps we feel the malaise of not being up to the level of our predecessors and of ending initiatives and institutions that have had an impact in our society and in the Church. Our works involve many lay people whom we should not discourage and make lose confidence in us. Today, we must identify the most coherent role there is for us in order to be near to urgent needs; less substitution and more integration and cooperation with public services, but above all else 'prophecy': asking public institutions about forgotten urgent needs, because they allow us to be those Samaritans who act where technicians, experts and politicians neglect needs that are fundamental for human dignity. We have a task that cannot be put off and which precedes the organisation of services that should be provided: to form a culture of health that is welcoming and supportive.

Formation and information are very useful: without knowledge one cannot provide care and treatment. In particular, so-termed personalised medicine is advancing, precision medicine that corresponds to our personalist outlook, according to which we must dedicate ourselves to a person's health-care needs in a way that corresponds to that person's genetic profile. Genomics is very important and we must not be behind hand in our research. Indeed, we must not allow the 'geneconomy' to become the prey of speculation rather than precision medicine for everyone and not only for the wealthy. We must learn to make decisions in line with ethical priorities and, as the title of our international conference says, we must provide care in a way that respects the life and the dignity of the patient and the environment. It is therefore important – indeed this is a duty that cannot be put off – to educate all health-care workers at all levels, within our institutions as well, in the mission of 'going out and healing', as well as in the charisms on which those institutions were founded. This should become a criterion for our choices and for our proposals.

If in addition to being useful we are also indispensable within the framework of the organisation of health care, to assure the right to protection of health, our relationship with public institutions will not be one of subordination or that of 'mendicants' for authorisations, accreditations and agreements, but simply appreciated cooperation directed towards improving society as a whole.

Neglected Tropical Diseases: 21st Century Ancient Afflictions of the Poor and Vulnerable

PROF. PETER J HOTEZ MD PHD
President, Sabin Vaccine Institute;
Dean, National School of Tropical Medicine,
Baylor College of Medicine
U.S. Science Envoy
USA

I'm deeply appreciative of the honor to present here at the Vatican and to the Pontifical Council for Health Care Workers. I'm especially grateful to Msgr. Jean-Marie Mupendawatu, the Secretary of the Pontifical Council for Health Care workers for the invitation.

Today I am going to introduce a group of diseases I sometimes call "the most important diseases you have never heard of," what we first named back in the early 2000s as the 'neglected tropical diseases' or NTDs. These are diseases borne of poverty and conflict – two challenges at the heart of the social mission of the Catholic Church.

The concept of the NTDs was born out of the Millennium Development Goals (MDGs) first launched in 2000, when infectious diseases were highlighted as through Goal 6, "to combat AIDS, malaria, and other diseases". Whereas AIDS and malaria benefited from massive overseas development assistance, those called "other diseases" were ignored or neglected. In response, we created the framework of NTDs to embrace a group of 13-14 chronic and debilitating parasitic and related infections. NTDs are the most common diseases of the poor; one in six people in the world have at least one NTD.

Through the Global Burden of Disease Study we have now derived specific numbers for the prevalence of the world's NTDs, led by intestinal helminth infections, schistosomiasis, lymphatic filariasis, dengue, and foodborne trematode infections.

Why do we care so much about the NTDs? NTDs promote poverty. NTDs can cause blindness, horrible swelling of the limbs and even death. Schistosomiasis is the second largest parasitic killer after malaria, trachoma is the leading cause of preventable blindness. Lymphatic filariasis causes extreme, debilitating swelling of the legs and genitals. Intestinal worms such as ascariasis, hookworm and trichuriasis impede children's cognitive and physical development, and can make them too sick to attend school. Schistosomiasis and other NTDs disproportionately affect girls and women making them more susceptible to HIV/AIDS and other catastrophic infections. The stigma associated with some of the most disfiguring neglected tropical diseases isolates patients from their families and communities. These adverse health consequences translate to lost economic productivity and development opportunities, trapping families and communities in a cycle of disease and poverty.

NTDs are ancient afflictions described in the Bible and other ancient texts. Today, NTDs are having a horrific impact on the world's Christian populations living in poverty. Christian majority countries account for most of some of the highest disease burden NTDs such as Chagas disease, sleeping sickness, schistosomiasis, and others.

Many of the most common NTDs can be treated and prevented with existing drugs at an extremely low cost. A few, such as lymphatic filariasis and onchocerciasis, could be eliminated entirely if everyone at risk received treatment. Pharmaceutical companies have donated billions of doses of medication and have pledged to donate billions more, but increased investment is needed to expand treatment programs and ensure the delivery of these drugs to everyone at risk.

This global effort guided by the World Health Organization has scaled up NTD treatment programs in the last decade. This is now the largest public health program in the world. More than 978 million people were treated last year for NTDs. But that is still just half of people living in at risk communities who require medication. Treatment programs are underfunded, leaving hundreds of millions of people without access to these essential medicines, despite the low cost of treatment – just $0.50 per person, per year.

This global effort to control and eliminate NTDs has successfully reduced the prevalence of some NTDs such as lymphatic filariasis, onchocerciasis and trachoma. Just this year, four countries in the Western Pacific Region eliminated lymphatic filariasis. In the Americas, onchocerciasis has been eliminated from all but one region on the border of Venezuela and Brazil. These are great successes – millions free from disability and unnecessary suffering. But for other neglected tropical diseases, progress has stalled. Parasites such as hookworm and trichuriasis have barely decreased and the prevalence of schistosomiasis has actually increased.

For some NTDs, such as hookworm, trichuriasis and schistosomiasis, existing drugs are less effective and will not be sufficient to achieve elimination. New strategies and tools are needed. Vaccines such as those currently in development by the Sabin Vac-

cine Institute could be powerful tools. Yet this research and development is severely underfunded.

Today, we are entering a new era of global health and development. The Sustainable Development Goals look at health in the context of many other factors including climate change and Earth sciences and the social fabric. Likewise, the Catholic Church is advancing this concept through the establishment of the new Dicastery for Promoting Integral Human Development.

We are adjusting our development strategy because the face of poverty is changing. NTDs are found among the poor, even those living in wealthy economies, especially G20 nations. This map shows the concentrated pockets of poverty-related neglected diseases in the world's wealthiest countries. Our old norms of global health focused in developing versus developed nations are no longer accurate. In a new book just published I refer to this changing paradigm as 'blue marble health.' As Pope Francis put it, "On the one hand we are seeing a reduction in absolute poverty, on the other hand we cannot fail to recognize that there is a serious rise in relative poverty, that is, instances of inequality between people and groups who live together in particular regions."

Today the wealthiest economies of Latin America are found in the G20 nations of Argentina, Brazil and Mexico, yet these three nations account for most of the world's Chagas disease cases led by Argentina. Less than 1% of people living with Chagas disease in these wealthy nations have access to essential NTD diagnostic and medicine. Or if we look to Brazil, while it is Latin America's largest economy, the northeastern region that includes the states of Pernambuco, Bahia, Paraiba, Ceará also accounts for the single largest concentration of NTDs in the Americas led by schistosomiasis, leishmaniasis, Chagas disease and dengue, among others. Therefore it's no surprise that Zika virus infection, with devastating effects for mothers and their unborn children, is concentrated in this same region, where poverty especially urban poverty is severe and widespread.

We need prophetic voices in these countries to call attention to the health problems affecting their poorest citizens. Catholic leaders could be a witness to this hidden suffering, urging policymakers to take strong action and invest in treatment and prevention.

It is clear that poverty is one key driver of NTDs; the other is conflict. For example, Ebola virus emerged due to the political destabilization following conflict, and now these same forces are in play in the conflict zones of the Middle East and North Africa, including Syria, Iraq, Yemen, and Libya. This region appears to be likely to become the next big 'hot zone' of emerging NTDs. We are witnessing a catastrophic situation with leishmaniasis for example where there have been hundreds of thousands of disfiguring cases that the locals call "Aleppo evil".

In this new era of development, as we seek an integrated approach to combat the diseases that thrive in poverty and conflict, we urgently need new diagnostics, drugs, and vaccines to end the suffering caused by these diseases.

The Sabin Vaccine Institute is an organization of scientists, researchers and advocates dedicated to reducing needless human suffering from vaccine-preventable diseases and NTDs. Since its founding in 1993 in honor of Dr. Albert B. Sabin, the developer of the oral polio vaccine, Sabin has been at the forefront of global efforts to eliminate, prevent and cure infectious and neglected tropical diseases.

At Sabin, we are leading efforts to develop half a dozen vaccines to combat NTDs affecting the world's poorest people. We relocated our vaccine development team to Texas, where diseases once thought to be limited to low-income countries are now found in areas of extreme poverty in our own backyard. I established the National School of Tropical Medicine at Baylor College of Medicine to advance efforts against these diseases. We are developing a vaccines for Chagas that will hopefully soon enter the clinic. We're also developing vaccines for leishmaniasis, schistosomiasis and human hookworm.

Increased funding is needed in order to help increase momentum for the development and testing of new vaccines, advance products currently in development and create a sustainable path to deliver them to people in need worldwide. Greater investment today will lay the foundation for tomorrow's new and better vaccines to tackle neglected tropical diseases.

We call our NTD vaccines "antipoverty" vaccines because of their potential not only to improve health but also lift the poorest people out of poverty. The global effort to control and eliminate NTDs shares three key principles with the Church's social teaching: the life and dignity of the human person, the preferential option for the poor and vulnerable, and the commitment to the common good.

It is clear that NTDs are an affront to human dignity and obstacle to human flourishing. No one should suffer unnecessarily from these ancient diseases in the twenty-first century. NTDs make a preferential option for the poor and vulnerable, targeting marginalized communities denied basic human rights such as health care, clean water and education. To succeed in the effort to end extreme poverty, the global community must make a preferential option for the poor and vulnerable by scaling up the effort to fight NTDs. One of the most basic things we can do to overcome what Pope Francis has termed the "globalization of indifference" and advance the common good is to take decisive action against NTDs: expanding treatment coverage to reduce prevalence today, advancing research and development of new tools to achieve elimination in the coming years, and in the interim, ensuring the basic rights and dignity of patients, combatting all forms of stigma and discrimination.

The unnecessary suffering of over one billion people is a challenge to the conscience of the Church and the world. As one of the largest social service providers in the world and as an institution with a powerful moral

voice, the Catholic Church is in a unique position to advance the fight against NTDs in three ways.

First, Catholic institutions can directly support NTD treatment and prevention programs, working through the Church's vast network of hospitals, health centers, schools, and parishes to reach every at-risk community with treatment and encourage healthy behaviors to prevent NTDs. Second, Church leaders in communities affected by NTDs can minister to sick individuals and their families and tackle stigma and discrimination. Third, the Church can mobilize much-needed financing by encouraging charitable giving by Catholic institutions and individuals and public investment by world leaders to support NTD treatment and advance research. Indeed, a coordinated push at every level of the Church could be the tipping point in the effort to control and eliminate these diseases for good.

For this reason, it has been an honor to speak at this conference. I am deeply grateful for this opportunity to share with you a vision for how we can one day eliminate the world's NTDs as a powerful expression of solidarity with the poor.

The Role of Associations of Patients, their Families and Socio-Health-Care and Pastoral Workers

H.E. MSGR. NUNZIO GALANTINO
General Secretary of the Italian Bishops' Conference - CEI, Bishop Emeritus of Cassano allo Ionio, Italy

1. 'As you did it to one of the least of these my brethren, you did it to me'

I will read my brief observations on two very well-known verses in the Gospel of Matthew: 'as you did it to one of the least of these my brethren, you did it to me….as you did it not to one of the least of these, you did it not to me' (Mt 25:40,45).

These are words which, located in the context of this international conference, tell us that even one person with a rare disease is precious in the eyes of God, to the point of being identified with him or her! For this reason, to work to include and take care of patients and their family relatives, who in addition to an invasive and tremendously difficult disease also have to endure the indifference of those who are responsible for public government and research, is a duty that we cannot, and we must not, shirk!

At a time when the international crisis is having an impact on finance and the economy seems to be increasingly directed towards 'an economy of exclusion and inequality' (EG, n. 53), which has often been denounced by Pope Francis, the risk of seeing an increase in indifference or at least delays is more than real. This forgets the fact that although rare diseases are rare, those who are affected by them are significant in number given that millions of people throughout the world suffer from them[1] and many of these live in indigence and poverty.

2. The Role of Associations in Relation to Civil Society and Church Society

After saying this, it is not easy, and perhaps it is not even possible, to define in a precise way the role of associations of patients, of their families, and of socio-health-care and pastoral workers. The social contexts of our planet are different and whereas in some of these contexts specialised services to help patients with these complex conditions are absent, in others essential services, even for patients who do not have rare diseases, are absent. I will confine myself in this paper, therefore, to offering some observations of a general character that arise more from the heart of a pastor than from an expert, recognising in the reality of associations, even before their functional character, an expression of an ecclesial communion that bears witness – in the real world of situations – to the commandment of mutual love of Jesus and the invitation of the Apostle to be unanimous in sharing the sufferings of our brothers and sisters.

The primary role of associations of patients and for patients is first of all the sensitisation of civil (and ecclesial) society and the upholding in the world of health and health care of the primacy of the sick person, his or her centrality and the fact that he or she is 'the beginning, the subject and the goal' (GS, n. 25). St. John Paul II never lost an opportunity to observe that 'Christians must courageously and lucidly intervene to safeguard essential values and rights connected with the dignity and the supreme destiny of the human person' (Dolentium hominum, n. 5). But there are also many lay people who, in responding to the at times desperate cry of forgotten and neglected sick people, feel as a matter of conscience that they should come together in associations in order to make their voices heard on behalf of these patients.

With what goals? To combat the therapeutic neglect of sick people who are onerous in economic terms and not very satisfactory when it comes to clinical results; to assure that they have access to due and necessary care and treatment, over time as well; and to support the rights of patients and 'give voice' to the needs of patients and their families. All of this requires engagement at both a cultural and a political level. A cultural effect which is the source and stimulus for every other transformation of the environment and society 'can be accomplished through work done not so much by an individual alone but by an individual as "a social being", that is, as a member of a group, of a community, of an association, or of a movement' (CL, n. 29). As the crisis that we are going through is above all a crisis of an anthropological nature, coming together in associations to promote a culture of life and care can only contribute to attacking the deep causes of the culture of indifference and the discarding of people.

3. Health Care: a Luxury for the Few?

But this is not enough! The associations that exist – and not only them – tell us that it is increasingly necessary to promote and require justice so that patients, their families and research receive the resources that are needed. To go from recommendations and hopes to concrete choices in favour of the poor, as we know, is not always easy. Health-care systems vary from country to country and although in some countries health care for the poor is assured, at least partly, in other nations receiving treatment is a luxury limited to those who can afford insurance-based, or private, medical services. The exclusion of some pathologies from the list of essential care levels further increases the sense of abandonment of patients and their families, with consequences of a psychological character as well that worsen their drama further.

In our country the list of exempted rare diseases (and thus the responsibility of the National Health Service) has only been updated recently with an increase in the number of such diseases (from 378 to 480) placed amongst the 'ECL' (essential care levels). This is a praiseworthy and important sign for patients and their families. But since care for people with rare diseases is principally funded through resources that are ordinarily allocated to the National Health Service and divided annually between the regional governments, they vary from region to region in relation to respective and real budgets. The organs of central government must be careful to insure that what is allocated to them actually reaches patients and research.

4. Associations…why the Rights of the Weak are not Weak Rights

Thus the difficult and at times frustrating action carried out by associations, that is to say monitoring that the legislation of countries is adapted to ensure the rights of the weak are not also weak rights, should be strongly supported given that the disproportion between commitment and results is enough to discourage anybody.

In my view, special attention must be paid to associations of families of patients who have rare and neglected diseases. Every time that the dramatic experience of illness knocks at the door of a home, the whole family is involved. For this reason, together with care for the patient, accompanying and supporting his or her family is the first care that is needed. The difficult pathway to which families of sick people are subjected is truly an uphill pathway. Becoming aware of an unforeseen and unwanted situation is frequently aggravated by feelings of guilt at not having generated healthy children. The very description of a disease as 'rare' or neglected' can only further accentuate a feeling of dismay and increase questions that nobody can answer with certainty: how will the situation develop? Will the right treatment for a cure be found? How many economic resources will be needed to treat the sick child? Will I be helped and supported in providing daily care to my child?

To come together in an association means to face up to the feeling of loneliness inherent in the rarity of the disease; it means with the help of those who have already gone down this difficult road to work through both the initial trauma and the prolonged and consuming hardship that unforgiving time delivers remorselessly and inevitably to its unfortunate victims. For these reasons, it is advisable that these associations should not be made up only of the families of sick people; the presence of other families without members who have a rare pathology can be a positive signal of inclusion as well as a sharing of the energies that are needed to face up to various challenges. The creation of a network of information and communication and the exchange of experiences, we are told by the families of patients themselves, can only be of great help and benefit.

5. Two Observations to End this Paper

Moving towards ending my paper, I would like to make two further observations: the first is about health-care workers and the second is about pastoral care.

We know how much, in the field of rare diseases, research is valuable; for patients and families research means the hope of life. Whereas the administrators of public governance have to allocate the resources that are needed, health-care workers, even more, have to share the results of their research work. We need widespread science for everyone and we well know that without research there can be no medicine. But this science must become a widespread patrimony so that everybody can use it. It is said that scientists have little love for the dissemination of their research! This is without doubt a special area for action by associations of medical doctors and for Christian health-care institutions that are also institutes for research and care of a scientific character (IRCCS): placing their heritage of research in a system.

Lastly, an observation about pastoral care. Although frequently in certain situations in which poverty of health is chronic and long lasting patients feel that they are only a burden, the Christian community can be that setting in which – through works and gestures – patients perceive that their existence is always a 'very good thing' and not a difficult problem that has to be solved and borne with hardship! To achieve this goal which is so arduous, abandonment at the level of therapy should not be conjoined with abandonment at the level of pastoral care. A presence at the side of patients and their family relatives can help this experience to be lived not only as a clinical event but al-

so as an existential event. Pope Francis writes with great clarity in *Evangelii gaudium*: 'I want to say, with regret, that the worst discrimination which the poor suffer is the lack of spiritual care' (EG, n. 200). The Christian community responds in this way to its vocation to be a sacrament of the presence of Christ at the side of man, a presence which like our Lord accompanies and shares.

'To those who suffer', we read in *Lumen fidei*, 'God does not provide arguments which explain everything; rather, his response is that of an accompanying presence, a history of goodness which touches every story of suffering and opens up a ray of light. In Christ, God himself wishes to share this path with us and to offer us his gaze so that we might see the light within it' (n. 57). ■

Note

[1] Rare diseases (RD) are a broad and heterogeneous group of pathologies that are defined as such on the basis of their prevalence in a population. At a European level, as in Italy, on the basis of the recommendations of the 'Community Action Programme for Rare Diseases 1999-2003', a disease is defined as 'rare' when it afflicts not more than 5 patients in every 10,000 inhabitants. Overall, these pathologies are very numerous. Indeed, the World Health Organisation has estimated that between *6,000 and 7,000 different rare diseases exist* and that these afflict about 3% of the population. Overall, it is estimated that between 27 and 36 million people are affected in the European Union alone, *and about 1-2 million of these are in Italy* (data from the Advanced Institute of Health Care, Italy).

FIRST SESSION • Rare Diseases

1. Rare Diseases: a Global Commitment from Science to Public Health Care

DR. DOMENICA TARUSCIO
Director of the National Centre for Rare Diseases, the Advanced Institute of Health Care, Rome, Italy

Rare diseases are a numerous (about 7,000-8,000) and very heterogeneous group of pathologies which are defined as being such on the basis of their low prevalence in the population. On the basis of the definition of the European Union, they afflict five people in every 10,000 inhabitants. According to the World Health Organisation, although they are rare individually together they make up 10% of human pathologies and it is estimated that 6%-8% (about 27 to 36 million citizens) of the European population has one rare disease. These diseases can attack all the organs and apparatuses of the body and they do this at all ages; about 80% are genetic and the remaining 20% have multi-factor origins. Many rare diseases are clinically complex, present difficulties at the level of diagnosis – with a consequent delay in their being diagnosed, and are grave, degenerative and chronic in their impact. About a third of them reduce life expectancy by at least five years, whereas others do not have a significant impact on the length of people's lives if they are diagnosed early on and treated in an appropriate way. They can attack the physical and/or mental abilities of people, as well as their sensory and behavioural capacities. The disabilities connected with them limit school, educational, professional and social opportunities and, indirectly, they can also lead to the practice of discrimination.

Delay at the level of diagnosis depends on a variety of factors, amongst which there is a low clinical knowledge of a disease on the part of medical doctors, something that is often connected with the extreme rarity of the disease involved, the presence of clinical signs that are not very clear, the absence or limited availability of diagnostic tests, and the fragmentation of help at the level of medical care and assistance. The result is that many patients do not manage to obtain a correct diagnostic or prognostic assessment of their pathology during the course of their lives.

Furthermore, the aetio-pathogenesis of many rare diseases still remains unknown and in many cases therapies that cure the disease simply do not exist. However, the scarcity or absence of effective specific aetiological therapies does not imply that it is impossible to treat these patients. Indeed, numerous forms of treatments for symptoms – as well as ones that are substitutive, rehabilitative and educational – exist that can improve the clinical development of the disease and life expectancy, as well as the level of autonomy and quality of life of the lives of patients and their family relatives.

Because of the characteristics described above, rare diseases constitute a priority for public health care and a difficult challenge for the health-care systems of many countries.

The scale of the problem and the possibility of success at the level of action require strategies in scientific research and public health care that are planned at an international level.

International scientific research should be encouraged, with the fostering of the sharing of data and new knowledge and the assuring of the transferability of results to clinical practice with the final objective of having a positive impact on the daily lives of patients.

The final objective is prevention, monitoring, diagnosis and treatment in relation to these pathologies; preventing the disability and the early deaths of patients; and improving the quality of life of patients through intersectorial, multi-disciplinary and interdisciplinary action.

To achieve these goals, international cooperation between institutions, researchers, policy-makers associations of patients, and all the stakeholders should be stimulated.

Over the years, starting in 1984 and the enactment of the Orphan Drug Act in the United States of America, many initiatives have been taken at the international, European and national levels.

The IRDiRC

For many years, researchers, clinicians, research consortiums and institutions of various countries developed studies and research on rare diseases often in a fragmentary way, with limited resources, without an international coordination that would have utilised joint efforts

to achieve a single effective direction. In response to this need, in 2011 the European Commission and the National Institute of Health (USA) established the International Rare Diseases Research Consortium (IRDiRC) whose ambition was to construct a network at a global level of researchers, clinicians, patients, industries, and fund providers to create synergies, optimise resources, and thus accelerate scientific research in the field. The IRDiRC has two principal goals which should be achieved by the year 2020: to identify 200 new therapies and implement new diagnostic instruments for all rare diseases.

Federations of patients, including EURORDIS which contributes to the production of documents and proposals and assuring the presence of patients in the decision-making processes of the IRDiRC, belong to this consortium.

Ever since the creation of this consortium, the Advanced Institute of Health Care has taken part, through its president, in the executive committee, and has also taken part, through the Director of the National Centre for Rare Diseases, in the interdisciplinary scientific committee.

The general policies of the IRDiRC advocate cooperation in research into rare diseases; the involvement of patients and their representatives in all the relevant aspects of research and in the sharing of data and resources (for example biological samples); and the need to have a sufficient number of patients to carry out studies that have a sufficient statistical validity. All the documents can be accessed at the site www.irdirc.org.

In order to accelerate the cultural and political change that is needed to achieve the goals that have been fixed for certain key sectors indicated by the scientific committees and which are seen as being of priority importance by the executive committee, various task forces have been created, amongst which we may list the International Consortium of Human Phenotype Terminologies; Patient Relevant/Reported Outcome Measures; Small Population Clinical Trials; Matchmaker Exchange; Automatable Discovery and Access; Data Mining/Repurposing (further information is available at http://www.irdirc.org/activities/current-activities)

Diseases and Orphan Medicinal Products

Rare diseases have been identified by the European Community (EC) as one of the sectors where the added value obtained from specific action on a European scale can provide its greatest contribution.

Since 1999, rare diseases have been identified by the EC as priority sector for Community action in the field of public health care. The European Parliament and the European Council approved Decision n. 1295/1999/EC of 29 April 1999 which, within the framework of action in the sector of public health care (1999-2003), adopted a community action programme for rare diseases which had the following goals: a) improvement in scientific knowledge about rare diseases, with the encouragement of the creation of a European information network for patients and their families; b) the training and updating of health-care workers in order to improve early diagnosis: c) the strengthening of international cooperation between voluntary and professional organisations involved in care; and d) support for the monitoring of rare diseases in the member States.

In 2000, the Official Gazette of the European Community published the Rule of the European Parliament and Council on orphan medicinal product (EC) n. 141/2000. The aim of this Rule was to establish a community procedure for the assigning of the definition of orphan medicinal products and to offer incentives for research, development and the placing on the market of orphan medicinal products defined as such. Article 4 of this Rule established in the European Medicines Agency (EMA; www.ema.europa.eu) the Committee on Orphan Medicinal Products (COMP; www.ema.europa.eu). In 2003-2008 the First Community Programme was launched and its priority goal was to support national policies in the field of health care of member States and to contribute to an increase in supportive action between member States through the promotion of health and safety and improvements in health-care action. The specific objectives were: 1) to improve the health of citizens; 2) to promote health and reduce health inequalities between groups of the population; and 3) to increase information and knowledge. In this last objective reference was explicitly made to the added value offered by organisations of patients with rare diseases in the creation and sharing of knowledge in the various fields of these diseases.

In 2004 the Rare Diseases Task Force (RDTF) was established at the General Directorate for Health and Consumers of the European Union (EU – DG Health and Consumer) which was established by the Decision of the Commission 2004/192/EC of 25 February 2004 in the programme of 'Community Action in the Field of Public Health' (2003-2008). The RDTF had numerous components, amongst which the heads of research and public health-care projects on rare diseases financed by the EC; experts from various member States; and representatives of the European Medicines Agency and of associations of patients. The principal goal of the RDTF was to help the European Community in the promotion of the best strategies for the prevention, diagnosis and treatment of rare diseases, recognising the great added value that comes from the coordination of action on a European scale. The specific objectives were many in number and included improvement in information about the diagnosis, screening, treatment and cure of rare diseases; the promotion of a network of centres of expertise for the diagnosis and treatment of rare diseases; the promotion

of monitoring and the availability of epidemiological data of high quality that could be compared in Europe; the promotion of the development of systems of international classification and the codification of rare diseases, in cooperation with the World Health Organisation as well; and the promotion of the spread of clinical good practices to improve the quality of life of people with rare diseases.

Rare diseases were also mentioned as a priority in the second Community action programme for rare diseases in the field of public health care (2008-2013). The two principal guidelines for action were: to facilitate the exchange of information through the existing networks for rare diseases and to develop strategies to improve the coordination of activities at a European level as well as trans-national cooperation.

In November 2008 the Communication of the Commission to the European Parliament, to the Council, to the European Economic and Social Committee and to the Committee of Regions was adopted: 'Rare Diseases: a Challenge for Europe'. This Communication outlined a Community strategy to support the member States in the diagnosis, treatment and cure of European citizens with rare diseases in relation to three chief areas: 1) improving the recognition and visibility of rare diseases; 2) supporting national plans or strategies for rare diseases in the member States; and 3) strengthening cooperation and coordination in relation to rare diseases at a European level.

In June 2009, the Recommendation of the Council on action in the sector of rare diseases was published. This document recommended to the member States that they should: 1) draw up and adopt national plans and strategies for rare diseases, preferably by 2013, in order to direct and organise pertinent initiatives in the field of rare diseases within the framework of their healthcare and welfare systems; take note of the drawing up of orientations and recommendations for the planning of national initiatives drawn up by the EUROPLAN project (the European project coordinated by the National Centre for Rare Diseases of the Advanced Institute of Health Care; www.europlanproject.eu); 2) aim to assure that rare diseases were adequately codified and accessible in all healthcare ICT systems, encouraging a suitable recognition of such diseases in national systems of care and refunding based on ICT, in a way that respected national procedures; 3) encourage research into rare diseases and promote the participation of national researchers in research projects on rare diseases financed at all appropriate levels, including the Community level; 4) identify centres of expertise in the member States by the end of 2013 and consider the possibility of promoting their creation, with the promotion of the participation of such centres in European networks as well; 5) support the sharing at a European level of best practices as regards diagnosis and medical care, with the training of workers, and the development of European recommendations as regards diagnostic tests and screening; 6) consult patients about policies in the field of rare diseases, facilitate the access of patients to updated information, promote activities engaged in by organisations of patients, such as sensitisation, training, the exchange of information and better practices, with the construction of networks and the involvement of very isolated patients; and 7) in cooperation with the Commission aim to assure, through suitable mechanisms of funding and cooperation, the long-term sustainability of infrastructures created in the field of information, research and care for rare diseases.

In 2010 the European Union Committee of Experts on Rare Diseases (EUCERD) was created through the Decision of the EC n. 2009/872/EC of 30 November 2009. EUCERD took the place of the Rare Diseases Task Force (RDTF) of the European Community. EUCERD, which was to last for three years, had the goal of helping the EC in the drawing up and implementation of Community action in the field of rare diseases in cooperation and consultation with the member States, the European authorities competent in the field of research and action in health care, and other interested parties that work in this field.

In 2013 the European Commission appointed the Expert Rare Diseases Committee. This group of experts on rare diseases, which was to last three years, provides opinions and consultation to the Commission for the drawing up and implementation of activities of the European Union in the field of rare pathologies and fosters exchanges of relevant experiences, policies and practices amongst the member States and the various interested parties.

The European Reference Networks (ERNs)

The EU directive n. 24 of 9 March 2011 on the rights of patients in relation to trans-frontier care upheld the right of patients to freely choose their provider of health care and clarified rules in the field of medical care in another country of the EU and the conditions to be respected as regards obtaining a refund. This directive introduced rules directed towards assuring that patients have 'safe and high quality health care, defending the rights of patients in every member State they go to, assuring that patients receive all the information that is necessary to exercise their rights, and creating an efficient system of cooperation between the different health-care systems of the member States, facilitating forms of cooperation and mutual assistance between countries as well'.

Directive 2011/24/EU also envisaged the constitution, the general concept and the forms of implementation of the European Reference Networks (ERNs).

ERNs are made up of networks

of clinical centres characterised by clinical and scientific excellence. The primary objective of the ERNs is to share best scientific and clinical knowledge amongst the health-care workers and the relevant centres of the various countries of the EU.

Therefore, the aim of these networks of reference is to apply common criteria in order to combat rare diseases which require specialised treatment; to act as centres of research and qualified settings for the diagnosis and treatment of patients of other countries; and to assure the availability of institutions to provide care where this is necessary.

The countries of the European Union had until 25 October 2013 to incorporate this directive into their national legislation. Subsequently, the European Commission promulgated two measures for its implementation (http://ec.europa.eu/health/ern/docs/ern_delegateddecision_20140310_en.pdf; http://ec.europa.eu/health/ern/docs/ern_implementingdecision_20140310_en.pdf), with the identification of the objectives that the ERNs had to pursue and criteria for the identification of centres that could form a part of them and for the assessment of European networks of reference and their members, as well as ways to achieve the facilitation of exchange of information and expertise in relation to the institution and assessment of such networks. The publication of the implementing measures gave a strong acceleration to the creation of ERNs and at the present time we are at the stage that involved the selection of candidacies for participation in the first ERNs, whose creation is envisaged by 2016. However, the discussion about the criteria that the members of the ERNs should meet was set in motion by the European Community's Expert Group on Rare Diseases (EUCERD) which in 2013 drew up recommendations which concentrated on the special features of rare diseases and the criteria for the definition and the assessment of European networks of reference for rare diseases, as well as for the exchange and dissemination of information (http://ec.europa.eu/health/rare_diseases/docs/eucerd_ern_en.pdf).

In addition, the Recommendation of the Council of the European Union on action in the field of rare diseases (8 June 2009) encouraged the member States of the EU to promote cooperation between the health-care services of the various countries of the EU and participation in centres of expertise in the European networks of reference.

Lastly, in June 2015 the CEGRD (Commission of Expert Group on Rare Diseases) Group approved twenty-three ERNs which constituted the aggregation of twenty-three macro-groups for all rare diseases. Therefore, each ERN would be dedicated to an extremely broad group of pathologies which often require different needs at the level of care and treatment and involve differentiated diagnostic and treatment features.

In Italy, in July 2015, the Ministry for Health published a ministerial decree that established the National Organisation of Coordination and Monitoring for the Development of European Networks of Reference. This national organisation, in harmony with those that already existed at a European Community level, suggests rules, models and indicators of reference directed towards the valuing of excellence in national health-care institutions for participation in the ERNs.

The centres of expertise in Italy that meet the criteria requested by the European Commission have been recognised by the Ministry of Health and have presented their candidacies to take part in the European networks of reference for rare diseases.

The ERNs will provide a framework of reference for the health-care pathways of patients with rare diseases through a high level of integrated expertise. The ERNs will promote access to common instruments such as registers, telemedicine and guidelines for best clinical practices for the diagnosis and treatment of rare diseases.

Rare Diseases in Italy

The ministerial decree (MD) of 18 May 2011 n. 279 established the 'National Network for the Prevention, Monitoring, Diagnosis and Treatment of Rare Diseases' and the National Register of Rare Diseases. This is the regulation that was envisaged by the legislative decree of 29 April 1998 n. 124 (art. 5, section 1, letter b) in relation to health care for patients with rare diseases. It also laid down rules for exemption of participation in costs relating to rare diseases for correlated health-care services included in levels of health care, as well identifying specific organisational forms to assure appropriate health-care services to individuals afflicted by such diseases.

To this end, there was then established the above-mentioned national network made up of centres, preferably hospitals, specifically identified by regional governments through deliberations and formal decisions. This network is dedicated to cooperation and the exchange of information to facilitate the diagnosis, treatment and care for patients afflicted by rare diseases and includes the National Register of Rare Diseases and the regional registers.

The National Register of Rare Diseases was established in order to allow the national planning of action directed towards the defence of individuals afflicted by rare diseases and to implement the monitoring of rare diseases (MD 279/2001, art. 3). This network, therefore, is the source of the flow of health-care information which through the regional and inter-regional registers is centralised by the National Register of Rare Diseases which had its head offices at the Advanced Institute of Health Care (ISS). The ministerial decree 79/2001 also has a list of rare diseases (individual diseases or groups of diseases) where the right is recognised for their sufferers to exemption from taking part in the costs for the correlated provisions of health-care services (art. 4).

The pathway of the patient is described starting with the idea that he or she has a rare disease on to the recognition of the right to exemption (art. 5); the way in which services are to be provided (art. 6); and the way in which services are prescribed (art. 7). Lastly, the updating of the contents of the regulation is envisaged with periods of at least three-years to do this (art. 8). As regards the updating of the contents of the MD 279/2001, it should be observed that recently new 'essential levels of assistance' have been approved relating to rare diseases that will witness the placing of new pathologies inside the system of protection.

The National Network of Rare Diseases has been created and developed as a set of the institutions and services of the regional systems which work together in an integrated way, with each one acting on the basis of its own specific capacities and functions, to develop action involving prevention and to implement action involving monitoring and activity directed towards diagnosis and treatment and the promotion of information and training.

All the regional governments in Italy by now have created systems for the gathering of epidemiological data (regional registers of rare diseases) that are able to monitor the activities of the regional networks. These registers, through the flow of their data to the National Register, contribute to epidemiological activity relating to rare diseases at a national level. These activities are able to provide relevant information for regional, national and international planning in the field of public health care. The development and the improvement of these epidemiological activities stand out as a critical element as regards the efficiency of the entire system of the national network and in the integration of this network at a European Community level (European Reference Networks, ERNs; Directive 2011/24/EU on the rights of patients in relation to trans-frontier health care).

The National Health-Care Plan (PSN) 2013-2016

The Council of the European Union recommended to the member States through the Recommendation on Rare Diseases of 2009 that they should draw up and implement appropriate plans or strategies for rare diseases or explore measures within the context of other strategies for public health care in order to assure to individuals with rare diseases access to high quality care from the diagnostic and treatment point of view. Therefore, Italy as well created its own National Plan for Rare Diseases 2013-2016 (http://www.salute.gov.it/imgs/C_17_pubblicazioni_2153_allegato.pdf).

Taking into account the many activities developed in Italy starting with the establishment of the National Network for Rare Diseases (MD 279/2001), the principal objective of this plan is the development of an integrated, global and medium-term plan for Italy in relation to rare diseases that is centred around the needs at the level of care and treatment of an individual with such a disease and his or her family, drawn up with the involvement of all the stakeholders involved and based upon the experiences in the field already achieved and within the framework of the recommendations of the European Union.

The National Plan for Rare Diseases has thus re-launched the objectives of the MD 279/2001, albeit with a more realistic and operational approach, and taking into account the developments that have taken place in the field at a European level, in particular as regards the development of the ERNs. In the expectations of the National Plan for Rare Diseases, activities should be engaged in with the involvement of all the institutional actors on the national committee, to which the Ministry of Health and other involved Ministries, the regional governments, the AIFA, the ISS, the AGENAS and the associations of patients with rare diseases belong. This committee, which is required to administer the system, has the task of outlining strategic guidelines that should be implemented in the fields of diagnosis and care and treatment, research, protection and social help, training, information and the ICT systems, as well as the task of indicating the priorities that exist as regards the employment of resources dedicated to rare diseases, and engaging in activities at the level of monitoring. In addition, the standing committee fo verifying the actual provision of 'Essential Levels of Assistance' (ELA), based upon the agreement between the central government and the regional governments of 23 March 2005, should introduce amongst the tasks to be verified initiatives relating to the implementation of this National Plan taking into account the periods of time and the processes that are needed to implement the action envisaged by the various situations that exist at a regional level. Action that is of special relevance for the activity of the National Network for Rare Diseases is the implementation and the improvement of the national network and watching over and monitoring this network.

The implementation and the improvement of the national network should proceed in the context of a plan shared by the regional governments – respecting the general national recommendations – in relation to the prevalence of individual diseases and groups of diseases, taking into account assessments inherent in the activities of individual institutions/centres of the SSN and their experience as documented through case histories and data relating to their activities and scientific production. In addition to assuring that the care that is provided to patients with rare diseases is expert and of high quality, this planning should minimise differences in the supply of services and their accessibility in the various regions of Italy.

To this end, it will be necessary to implement various initiatives, for which the information produced by the National Register of Rare Diseases with its activities involving the monitoring

of the network and patients will be of very great use. Examples of such activities are the following:

– Identifying the institutions/centres of the network for rare diseases using objective criteria and, as far as this is possible, ones that are agreed upon and shared, respecting the requirements envisaged by the recommendations of the European Union. These centres should have a broad area of users, large numbers of significant activities and appropriate performances; they should develop clinical research, have official links with the other parts of the national network, and maintain records on the clinical history of patients, during the move from childhood to adulthood as well. They should perform the tasks envisaged for the European centres of expertise, being able thereby to be candidates for the ERNs.

– Strengthening the networks that already exist by facilitating the functional connection between institutions/centres and other institutions and services that are involved so as to take responsibility for patients and assure continuity in the provision of care and treatment.

– Carrying out a periodic assessment of these institutions/centres on the basis of both indicators of activities and results and the satisfaction of patients, with the participation of associations and through procedures involving external audits as well, following the model of what has already been put into practice in various countries of the European Union.

– Assuring that the spread of innovative practices at the level of care and treatment in relation to rare diseases always remains in a framework of safety and proven effectiveness, with the protection of patients.

– Using in an integrated manner ICT systems for regional monitoring (including the regional networks which also have the function of providing support for care) and national monitoring (including the National Register of Rare Diseases), as elements involving knowledge on which to direct policies and the actions of the government and assessments of the system.

– Minimising differences in the supply of services and their accessibility between the various regions of Italy and above all else allowing patients to be directed in a correct way towards competent institutions and centres.

As regards the activities involving surveillance and monitoring, the regional or inter-regional registers and the National Register of Rare Diseases should improve the coverage and the efficiency of the gathering of epidemiological date in line with the performance of their institutional tasks. To this end, it is necessary to adopt all those measures that are needed to improve the quality of information and to produce results that are useful in supporting the initiatives of public health care and to improve clinical practice. In particular, the procedures, contents and expiry dates of the gathering of data by the regional/inter-regional registers for the National Register of Rare Diseases, and the analyses of the data contained in the National Register of Rare Diseases at the ISS, should be made uniform and standardised. While awaiting the updating of the list of rare diseases, the National Register and the regional and inter-regional registers can broaden the gathering of data contained in the minimal data set already agreed upon and might extend the survey to other diseases, amongst which rare tumours, in harmony with what takes place in the rest of the European Union. This could also be done through the creation of a database designed to gather epidemiological data on rare diseases during the inclusion stage and thus data not yet contained in the National Register of Rare Diseases, and in a way that respects the rules and regulations that are in force as regards the protection of personal data.

Lastly, they should also take into consideration the 'Core Recommendations on Rare Disease Patient Registration and Data Collection' that were drawn up and adopted by the EUCERD (www.eucerd.eu). They could also engage in a census of the registers of diseases, assessing their quality and the extent to which they correspond to the rules and regulations in force, their economic sustainability, and whether it is advisable to maintain them.

Rare Diseases and Information for Citizens

The National Plan for Rare Diseases 2013-2016 expressed itself in favour of the strengthening and support of the various institutional sources of information that already exist as well as the promotion of their use.

In this direction, since February 2008 the Green Telephone for Rare Diseases has operated with its head offices at the National Centre for Rare Diseases at the Advanced Institute of Health Care. Planned and created with the need to provide information principally on rare diseases and on institutions and centres for rare diseases that operate in Italy, the Green Telephone for Rare Diseases constitutes a sources of centralised information in the national context, above all in line with what is envisaged by the MD 279/2001 on the 'Regulation for the Institution of a National Network for Rare Diseases and the Exemption from the Costs of Taking Part in the Connected Health-Care Services'.

In addition to providing information on the national network on rare diseases, the Green Telephone for Rare Diseases was expressly created to offer contents and instruments that would promote knowledge and good practices in the field of rare diseases.

Rare Diseases without a Diagnosis

Given the characteristics of rare diseases (few patients with each individual disease, difficulties at the level of diagnosis, etc.), international cooperation is crucial in the sharing of fragmented resources in individual countries in order to carry out better diagno-

ses and provide better treatment. Rare diseases without a diagnosis are those that have not obtained a diagnosis from the medical doctor who is the point of reference of the patient. Some patients wait for years to have a final diagnosis. These rare diseases include groups of pathologies that do not have a name; pathologies with well described phenotype; pathologies with an unknown molecular base or pathologies that are due to unknown non-genetic factors. In 2008 the NIH in the United States of America launched its 'Undiagnosed Disease Programme' with the specific objective of providing a diagnosis to patients who have been waiting for a diagnosis for years and studying the aetiopathogeneis of new pathologies. In 2013 a specific financing of the NIH supported the national 'Undiagnosed Diseases Network'.

However, the problem of undiagnosed patients is global. Recently the National Centre for Rare Diseases of the Advanced Institute of Health Care contributed to the launch of Undiagnosed Diseases Network International (UDNI), and to the development of its activities and its governance, through the publication of principles and good practices and the development and the running of the web site www.udninternational.org.

The UDNI seeks to diagnose patients without a diagnosis in the world and includes, in addition to Italy and the United States of America, other European countries (such as Bulgaria, Spain, Hungary, etc.) as well as Canada, Japan and Australia.

The UDNI involves centres with experience that are recognised at an international level, and its scientific resources and know-how seek to fill in the gaps in knowledge that impede a diagnosis. As a consequence the UDNO fosters the translation of research into medical practice. The active involvement of the patient is of fundamental importance. After the launch of the UDNI in 2015, many countries activated their own national networks (for example Australia, Italy, Japan), operating within the framework of the UDNI in cooperation with the other members of the UDNI. Other information is available on the UDNO web site (http://www.udninternational.org).

The UDN Italy

Within the framework of the UDNI, the Advanced Institute of Health Care and the NIH-USA have activated, thanks to funding from the Ministry for Foreign Affairs and International Cooperation, a UDN Italy project whose objectives are in line with the UDNI, that is to say gathering data from Italian patients without a diagnosis through the National Network for Rare Diseases, using common standards and technologies, in order to characterise them at a phenotype and genotype level; developing a national database that is interoperable at an international level; developing bio-ICT instruments for data sharing at a national and international level; and strengthening and increasing international cooperation.

2. Treatment and Research of Rare Diseases in Catholic Hospital Services in Australia

MRS SUZANNE GREENWOOD
Chief Executive, Office of Catholic Health, Australia

Introduction - Scale of Catholic health services in Australia within the context of the Australian health system

Catholic Health Australia represents Australia's Catholic hospitals and aged care providers. Together, Catholic Health Australia member organisations form the largest non-government grouping of hospitals, aged and community care services in Australia.

The role of Catholic Health Australia (CHA) is advocacy for the Catholic providers – to be the credible, ethical and influential voice of Catholic health, aged care and community care services in Australia, and to support the mission of CHA members – the various Catholic hospitals, aged and community care providers.[1]

The scale of Catholic care provider in Australia is not as large as other countries – we have almost 10,000 hospital beds across more than 80 hospitals. Two-thirds of which are private hospitals and one-third of which are public – government-funded hospitals.

Approximately one in ten Australians who are in hospital are being cared for in a Catholic hospital: Australia's population is approximately 24 million people, with 1 birth every 1 min 46 sec, 1 death every 3 min 23 sec, and a net gain of 1 international migrant every 2 min 37 sec.[2] Overall, Aus-

tralia's total population increases by one person every 1 minute 32 seconds.

Australia has one of the highest life expectancy rates in the world, but has an ageing population, increasing levels of chronic disease, and escalating demand for the best of quallity care, which in turn increases cost.

Rare Diseases – Incidence in Australia

Australia has adopted the widely-cited definition agreed and adopted by the European Union[3] – that a rare disease is a specific, clinically serious disorder or condition that is a life-threatening or chronically debilitating disease which is statistically rare, with an estimated prevalence of 1 in 2,000 people or of similarly low prevalence and high level of complexity that special combined efforts are needed to address the disorder or condition. This is less than 0.05 percent of the population.

On this basis, current conservative estimates indicate that approximately 6-8 percent of Australians in total are affected by a rare disease. There are estimated to be more than 8,000 rare diseases in Australia. Many have no formal title. The difficulties of rare diseases are: diagnosis is often difficult or delayed; many rare diseases have no effective treatment; some require new expensive treatments; information about rare diseases is often scarce or difficult to access for the health professional, patient, family and carers; and the psychological burden and lack of practical support is a major issue in the treatment and management of rare diseases.

Research priorities of Catholic Health Australia members

The response of the Catholic health sector to these difficulties is more research. Catholic Health Australia held an Inaugural Medical Research Symposium in 2016[4] for Catholic clinical research institutes, bringing together researchers from across Australia to encourage networking, learning, and to celebrate achievements and ongoing initiatives in research.

The key note speaker was distinguished Australian research biologist, Sir Gustav Nossal AC CBE. Sir Gustav has enjoyed international recognition for his breakthrough contributions to the fields of antibody formation and immunological tolerance. He has served as the Chairman of the committee overseeing the Global Programme for Vaccines and Immunization of the World Health Organisation. This was a significant event which facilitated ongoing research co-operation between the various Catholic health care facilities.

Research priorities of Mercy Health

Mercy Health's research is grounded in the Mercy mission of compassionate care founded by Catherine McAuley more than 150 years ago and continued to today under the guidance of the Sisters of Mercy. Their researchers realise her vision to 'care first' for those in greatest need with a special focus on the health of woman and babies.

Recognising that many rare diseases are genetic, Mercy Health has a research priority investigating the impact of non-invasive prenatal testing in pregnancy, and developing new diagnostics to predict preterm birth. Areas of research specialty include perinatal, paediatrics, gynaecology and palliative care.

Research priorities of Cabrini

The Cabrini Institute was established 20 years ago by the Cabrini health care group - Cabrini is owned and operated by the Missionary Sisters of the Sacred Heart of Jesus who came to Australia in 1948. The Institute has a focus on clinical epidemiology, medical oncology, nurse education and palliative care.

Cabrini have achieved significant advancements in medical research particularly through university partnerships, such as with the Australian Catholic University, and through their various academic departments such as the Monash Department of Clinical Epidemiology at Cabrini Hospital.

Research priorities of St Vincent's Health Australia

St Vincent's Health Australia is Australia's largest Catholic health and aged care provider. St Vincent's Health Australia is a ministry of the Catholic Church under the stewardship of Mary Aikenhead Ministries, as established by the Sisters of Charity. St Vincent's has many research institutions and programs including the Aikenhead Centre of Medical Discovery – which is Australia's first hospital-based biomedical engineering facility.

The Centre will help achieve three major health outcomes for Australians: improved management of chronic illness, ageing well, and prevention of disease. Biomedical engineering innovations will be the Centre's focus including: tissue engineering – engineering tissues, cells and genes; drug design and delivery – developing intelligent drugs, smart delivery systems; and medical bionics – innovative devices to replace organs and body processes.

Research areas of strength include, among other fields of research: oncology/haematology, gastroenterology, neurosciences, cardiology, endocrinology, orthopaedics, and palliative care.

Research priorities of Mater Health

Mater Health Research was established in 1998 with a primary focus in cancer research. The institute has since grown and now runs additional research programs in immunology, neurosciences and cognitive health, chronic disease biology, and pregnancy-relat-

ed disorders, including high profile research being undertaken in preventing stillbirths. The Mater Research Institute currently supports over 400 researchers and students working to provide better health outcomes for all people in the community.

Research priorities of St John of God Health Care

St John of God Health Care fosters a high quality and ethical research culture that enhances clinical practice. They engage in research with the greatest potential to improve health care, with a focus on translational research – research that moves from 'bench to bedside' – improving outcomes for their patients.

Areas of research strength at St John of God Health Care include oncology, mental health, and neonatal health.

Research priorities of Calvary Health Care

From humble beginnings in a stocking factory, Mary Potter and the Sisters of the Little Company of Mary established the first Calvary Hospital in Rome in 1882. Three years later, six courageous Sisters sailed to Sydney, Australia, and began the first Calvary health care services in Australia. The main research focus areas are medical oncology, radiation oncology, haematology, and palliative care.

Conclusion - Future Challenges for Australia

Australia has very few sisters and clergy working in our Catholic facilities.

Catholic Health Australia has had two responses to this dilemma to support those with rare diseases.

Firstly, pastoral care: quality pastoral care is foundational to Catholic health care. To be a provider of Catholic health care requires pastoral care to be part of all that we do.

In 2015, Catholic Health Australia conducted a pastoral care mapping survey of the Catholic health and aged care sector in Australia. Based on the survey findings, CHA has prepared a Pastoral Care Mapping Survey Report, an executive summary of the key findings and recommendations, and a pastoral care assessment tool. This tool has been developed so that the recommendations coming out of the pastoral care mapping survey can be used by Catholic hospitals as a way of recognising strengths and determining areas for improvement.

Secondly, Catholic Health Australia recognises that formation of our lay leaders in the health care ministry is vital to ensuring our continued Catholic identity. CHA will therefore launch, in July 2017, a ministry leadership formation program for senior leaders within the health ministry to protect our Catholic identity and our healing ministry into the future. ■

Notes

[1] http://cha.org.au/images/2020_CHA_Strategic_Direction_Statement.pdf
[2] http://www.abs.gov.au/Population
[3] https://ec.europa.eu/health/rare_diseases/policy_en
[4] http://cha.org.au/events/recent-events#2016

3. The History of Alkaptonuria in Slovakia and the World

DR. HELENA GLASOVÁ
The Institute of Pharmacology, Clinical and Experimental Pharmacology,
The Slovak Medical University in Bratislava,
The Institute of Clinical and Translational Research, Biomedical Research Centre, The Slovak Academy of Sciences, Bratislava,
The Slovak Republic

Introduction

The thirty-first international conference of the Pontifical Council for Health Care Workers (for Health Pastoral Care) focused upon the great challenges posed to contemporary medicine and health care by rare and neglected diseases. The successful achievement of a 'culture of health that is welcoming and supportive at the service of people with rare and neglected diseases' must take into account numerous and complex medical, epidemiological, social, economic, juridical and ethical aspects of these seemingly not similar conditions. It also requires serious joint multidisciplinary efforts on the part of all relevant stakeholders, including health-care professionals, patients, their families and friends, scientists/researchers, industries, universities, non-profit organisations, volunteers and health-care payers at the na-

tional and international levels. The history of one particular rare disease – alkaptonuria (AKU) – both in Slovakia and in the international context may serve as an example of such successful, and already moderately optimistic, joined efforts.

AKU – the Black Urine, Black Bone Disease

AKU is a rare autosomal recessive multisystem disorder affecting approximately 1 in every 250,000 people globally. A higher prevalence rate of around 1 in 19,000 people is found in some countries, such as Slovakia. The rarity of the disease makes it an ultra-orphan indication.

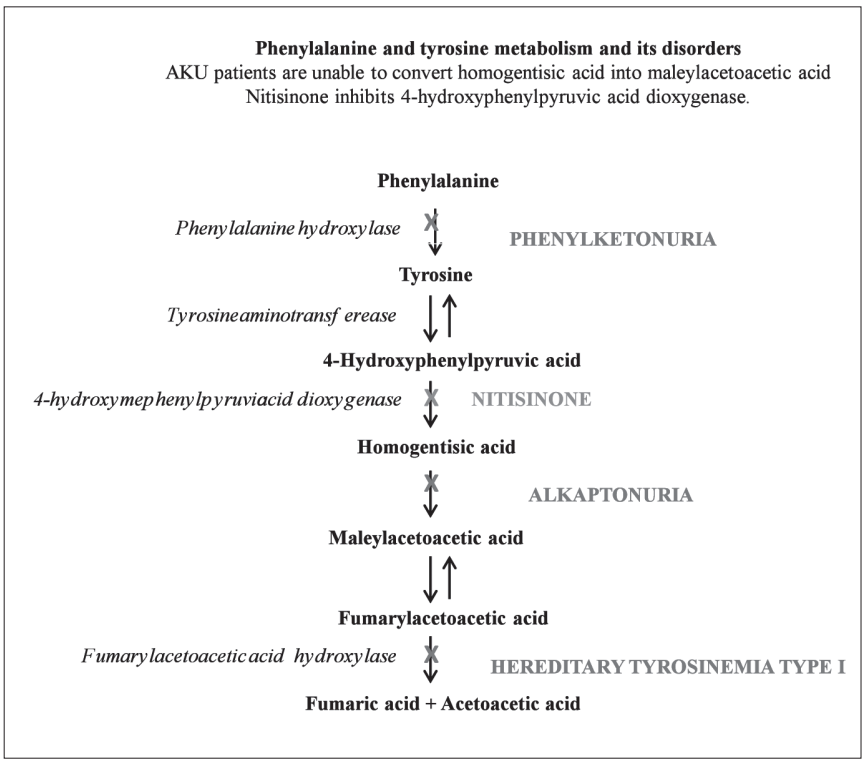
AKU is characterised by a deficit in the activity of an enzyme – homogentisate 1,2-dioxygenase (HGD) – in the liver, caused by mutations in the HGD gene (fig. 1). HGD deficiency leads to increased levels of a pathological intermediary product within the metabolic pathway of phenylalanine and tyrosine – homogentisic acid (HGA). AKU patients are unable to convert homogentisic acid (HGA) into maleylacetoacetic acid.[7,8]

The hallmark of the disease is passage of urine that becomes black when left standing. HGA turns black on oxidation, leading to black urine and occasional black sweat. A small proportion of patients, however, do not develop these symptoms. It was discovered that the darkening was delayed in an acidic solution and accelerated in alkaline conditions. This led Boedeker in 1859 to describe the urine as containing an '*alkapton*', later leading to the name 'alkaptonuria'.[7,8]

Despite efficient and marked excretion of HGA in urine, part of it is oxidised via benzoquinone acetic acid to a melanin-like polymeric pigment and deposited in the extracellular matrix of connective tissues, in particular in cartilages. This leads to ochronosis and subsequent progressive premature severe degenerative spondyloarthropathy and arthritis. Severe arthritic pain is the most severe symptom in AKU. The onset of ochronosis is in the late 20s or early 30s; the most affected joints are the spine, hips and knees.[7,8]

Currently, no pharmacological treatment is available for AKU. Dietary therapy restricting phenylalanine and tyrosine is difficult to maintain and has not been shown to be effective in reducing HGA in adults and it has no demonstrable efficacy in improving symptoms. Experimental treatment with vitamin C to enhance HGA degradation has not proved helpful either. Treatment of the disease's *sequelae* includes analgesia, physiotherapy, surgery and joint replacement.[7,8]

Fig. 1 Molecular basis of alkaptonuria and related inborn diseases of phenylalanine an tyrosine methabolism6.



AKU – a History of Early Medical Genetics

AKU is one of the four disorders originally defined as inborn errors of metabolism and the first condition noted as following Mendelian inheritance by Sir Archibald Garrod in 1902.[2] He identified a familial pattern of inheritance and concluded that an inherited biochemical abnormality had to result in the passage of an abnormal intermediate in the urine. Remarkably, at that time serial biochemical reactions in the metabolic disposal of nutrient substances had not yet been described. Proposed autosomal recessive genetics of AKU was later confirmed by Hogben in 1932.[2,3,4,9]

AKU is an autosomal recessive disorder caused by a single gene defect mapped to chromosome 3 between regions 3q21-q23 which is the site of the homogentisate 1,2-dioxygenase (HGD) gene. Mutations of the HGD gene lead to corresponding changes in the amino acids sequence in the HGD protein. Substitution of the amino acid *valine* for *methionine* at position 368 is the most common HGD mutation found in European populations. Mutations in the HGD gene impair the activity of HGD by changing its structure. AKU patients are homozygous or compound heterozygous be-

cause of 'loss of function mutations' in the HGD gene. Hitherto about 115 such mutations have been identified worldwide.[5]

The History of AKU in Slovakia

Slovakia is the country with the second highest world prevalence of AKU, its principal endemic region being in the north. It also possess an impressive history of epidemiological and medical efforts to deal with the condition, including screening, early diagnosis, implementation of necessary dietary measures, and state-of-the-art management of its chronic complications. The first case of AKU in Slovakia was diagnosed in 1947 and by 1953 102 AKU patients from 15 families had been identified (at that time only approximately 100 cases were known globally). From 1956 to 1960 80 more AKU patients in 13 more affected families were identified by a sole investigator, the physician and clinical biochemist Dr. Anton Neuwirth (1921-2004)[10]

It is worthwhile mentioning that Dr. Anton Neuwirth has been one of the truly outstanding Christian personalities of recent Slovak history. A distinguished physician, scientist, intellectual, diplomat (he served as the first ambassador of the Slovak Republic to the Holy See in 1994-1998), and politician (he was a member of the Slovak National Council and honorary chairman of the Christian Democratic Movement), he was a prisoner of faith under the Communist regime. After his return from years in Communist prisons, he was sent to a remote medical practice in a rural northern territory of Slovakia. There, true to his scientific education and his spirit of being a clinical researcher and physician, he discovered and painstakingly analysed the second largest part of the unique Slovak AKU patient population. Working in quite simple conditions and led by his own professional enthusiasm, he was able to draw up detailed family trees (genealogy analyses) that allowed the detection of possible carriers. He also provided detailed counselling and education to AKU families concerning the risks and necessary measures to be undertaken, but he also provided them with the personal medical care that was needed. Subsequently, as he was not allowed for 'political reasons' to proceed further with his work and care, for the good of his patients and for the sake of the science he generously donated his entire meticulously gathered documentation to his colleagues for further follow-up and study.[6]

Let us briefly quote here from the testimony of Dr. Anna Záborská MEP, nowadays a prominent Slovak physician, the daughter of Dr. Anton Neuwirth: 'Unforgettable were the days, when, after his return from prison, he as a physician discovered the endemic occurrence of a rare hereditary disease – alkaptonuria (AKU) – at Horné Kysuce, a rural region in the north of Slovakia. On his own initiative he performed metabolic screening investigations in the garden of our home – examining the samples of urine of his patients – and then visited the patients in this whole region in order to explain to the affected families measures by which they could survive this serious disease. Definitely, this medical testimony influenced the decision of myself and my siblings to study medicine'.[10]

The History of AKU in the World

Although no proven treatment for AKU yet exists, some novel and promising developments are already underway. In 2003, the AKU Society was founded in the United Kingdom by an AKU patient, Bob Gregory, and a biochemist, Prof. Lakshminarayan R. Ranganath. They were joined later by Nick Sireau whose two sons were born with AKU. Nowadays, the AKU Society has a global network with a strong potential to foster research into AKU and connect and support AKU patients, their relatives and carers. Sister societies have been established in twelve other locations worldwide: in France, Italy, the Netherlands, Poland, the USA, Canada, Slovakia, Jordan, Germany, Sweden, India, and Pacific Asia.[1]

In 2012 the DevelopAKUre Consortium, a comprehensive European network of universities, hospitals, pharmaceutical and biotech companies, research organisations, and national AKU patient groups, was established. It received funding from the European Commission's Seventh Framework Programme to conduct research into the effectiveness and safety of a new and promising medicinal drug – nitisinone – in AKU patients in a series of international multicentre clinical trials. The Slovak National Centre for AKU at the National Institute for Rheumatologic Diseases in Piešťany, following the above-mentioned unique tradition, successfully took part in these truly global research activities.[1]

Interestingly, nitisinone is a competitive inhibitor of 4-hydroxyphenylpyruvate dioxygenase, an enzyme which metabolises 4-hydroxyphenyl-pyruvate to HGA. In this way, this treatment prevents the accumulation of the toxic metabolic intermediates – maleylacetoacetic and fumarylacetoacetic acid – in patients with another rare inborn condition: hereditary tyrosinemia type 1. It has been registered in the EU for its treatment since 2005. Nitisinone also reduces HGA plasma levels and HGA urinary excretion in AKU patients. It has been posited that reduction of HGA levels might prevent the onset, or slow the progression, of ochronosis in AKU patients.[1,8] The above-mentioned European Commission Seventh Framework Programme (FP7) funded studies aimed at proving the supposed efficacy and safety of nitisinone in AKU patients, and, if successful, the eventual regulatory approval of the drug for this therapy.[1]

To end this paper, it may be observed that historical, Slo-

vak and international aspects of the history of AKU, which have been briefly presented in this paper, may be considered unique examples for dealing – in a highly scientific, ethical, efficient, sustainable and indeed Christian way – with this well-defined but still rather debilitating and rare inheritable disease. The history of AKU may also serve as a concrete example to elucidate various interconnected facets of the complex phenomenon of rare genetic diseases, thereby, it is hoped, inviting the interest and necessary efforts not only of researchers and medical professionals but also of all stakeholders, including the broader community and the general public, to foster necessary developments and ultimately to offer hope, and possibly in the longer run, a cure, for patients with these 'difficult-to-diagnose', and even more 'difficult-to-treat', inherited genetic diseases.

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Correspondence to: Assist. Prof. Helena Glasová, MD, PhD, the Institute of Pharmacology, Clinical and Experimental Pharmacology, the Slovak Medical University in Bratislava; the Institute of Clinical and Translational Research, the Biomedical Research Center, the Slovak Academy of Sciences, Bratislava.

Address: Limbová 12-14, 83303, Bratislava, Slovak Republic, e-mail: helena.glasova@szu.sk

FIRST SESSION • Neglected Diseases

1. Epidemiology and Health-Care Policies

DR. ODILE TCHANGMENA BEFEUKA
"Agenzia Italiana del Farmaco" - AIFA, Italy

Neglected tropical diseases (NTD) are 'a group of chronic infectious diseases that promote poverty and are widespread above all in rural areas and poor urban areas in low- and middle-income countries'. These diseases 'promote poverty because of their impact on health, on development in children, on pregnancy, and on productivity in adults of working age because of their stigmatising character' (*PLoS Neglected Tropical Diseases*).

The World Health Organisation (WHO) lists some of the characteristics which these diseases have in common: they constitute an indicator of the poverty of populations; they afflict above all bands of the population that have a low level of visibility and little political power; they tend not to spread in geographical terms; they cause stigma and discrimination, above all to the disadvantage of girls and women; they have an important impact on morbidity and mortality; they are neglected by research; and they can be controlled, prevented and probably eliminated by using effective, practical and low-cost strategies.

In the list of NTD of the WHO seventeen pathologies are recognised that are due to micro- or macro- parasites (the Anderson and May classification). Microparasite diseases: 1. viral aetiology: dengue disease and rabies; 2. bacterial aetiology: trachoma, Buruli ulcer, endemic treponematosis and leprosy; 3. protozoan aetiology: Chagas disease (CD), human African trypanosomiasis and leishmaniasis. Macro-parasite diseases (with a helminthic aetiology): cysticerosis, dracunculiasis, echinococcosis, lymphatic filariasis, parasite trematodes transmitted by foodstuffs, onchocerciasis, schistosomiasis and geohelminthiasis. The World Health Organisation adds certain other 'neglected conditions' (chronic suppurative otitis media, eumycetoma, nodding syndrome, podoconiosis, scabes, snake bite, strongyloidiasis). In the *PLoS Neglected Tropical Diseases,* the list of NTD is even more extensive.

Epidemiology: NTD are endemic in 149 countries of the world, of which at least 100 have two neglected tropical diseases that are endemic and thirty have six or more endemic NTD.

Health-Care Policies

The current plan of the World Health Organisation for the control of NTD envisages the integrated use of five different strategies:

- *The first strategy* is preventive chemotherapy. This strategy envisages the distribution of medicinal products on a large scale for populations at high risk. These are low-cost medicinal products: albendazole, mebendazole, praziquantel, ivermectin, diethylcarbamazine and azithyromycin. The target diseases of this strategy are: filariasis, onchocerciasis, geohelminthiasis, schistosomiasis and tracoma.

- *The second strategy* is the diagnosis and intensive treatment of cases. This is especially useful for those pathologies for which a preventive therapy cannot be used given that the medicinal products that are available have a toxic impact of a certain impact. Amongst the pathologies which are the target of this strategy we may list: Chagas disease, human African trypanosomiasis, leishmaniasis, leprosy and endemic treponematosis

The World Health Organisation

- *The third strategy* is the control of vectors. Indeed, various neglected tropical diseases – amongst which dengue disease, Chagas disease, human African trypanosomiasis, lymphatic filariasis and onchocerciasis, are transmitted by insect vectors – whereas helminthic diseases such as schistosomiasis, dracunculiasis and treponematosis require molluscs or crustaceans that act as intermediary hosts to complete their life cycles. This strategy requires the cooperation of the sectors of agriculture and engineering (the use of pesticides).

- *The fourth strategy* is the improvement of conditions of hygiene and sanitation.

- *The fifth strategy* consists of initiatives relating to veterinary public health. Many neglected tropical diseases – cysticercosis/teniasis, echinococcosis, human African trypanosomiasis, Chagas disease, rabes, leishmaniasis, alimentary trematodoses – have a zoonotic component, that is to say they can be transmitted to man by vertebrate animals (directly or indirectly through a vector), and because they have an impact on the health of livestock they can have an effect on the wellbeing of a community.

G7-2016

The G7 highlighted the vital role of research in the development and introduction of new

means of combatting neglected tropical diseases: the cooperation of key partners with the WHO – Global Observatory on Health Research and Development; supporting research connected with NTD in geographical areas which are most in need of help; strengthening basic research (prevention, control and treatment) and research focused on the rapid and targeted development of readily usable medicinal products; and supporting response mechanisms at a local level and utilising health-care systems in positive way in order to make appropriate therapies and medicinal products available, with the aim of controlling and/or eliminating neglected tropical diseases by the year 2020.

Italy

The Ministry of Health – CCM. Within the framework of the project area three spheres of action have been identified: transmissible diseases; non-transmissible pathologies; and systemic initiatives, for a total of eleven lines of intervention. These lines of intervention constitute a priority for the Italian government and they are in line with the provisions of the National Prevention Plan and with the recently approved national plans, or ones that are about to be approved, by the State-Regions Conference and coordinated by the Ministry for Health – General Directorate for Health-Care Prevention. Surveillance ISS – systematic surveillance of infectious diseases for migrants in centres for immigrants (2015). Regional projects – Caritas – S.I.M.M. – I.N.M.P. ■

2. The Prevention, Treatment and Research of Neglected Tropical Diseases: a Sub-Saharan African Perspective

PROF. SAMUEL KALLUVYA
HIV/AIDS Coordinator,
The Catholic University of Medicine,
The Bugando Medical Centre,
Tanzania

Neglected tropical diseases (NTDs) are a group of diseases that are found in the tropics and sub-tropics and especially in impoverished rural areas and slums in towns and cities. They commonly affect poor communities without safe water, good hygiene and sanitation. Hence the term 'poverty diseases'. The impact of these diseases leads to the aggravation of poverty. According to the WHO, there are 17 NTDs which include most of the common NTDs in sub-Saharan Africa: the socially transmitted (helminthiases); lymphatic filariasis; onchocerciasis; schistosomiasis; protozoan infections such as human African trypanosomiasis and leishmaniasis. Bacterial NTDs include Buruli ulcer, trachoma and leprosy.

Importantly, it is possible to eliminate completely a significant number of NTDs. The prevention of NTDs in sub-Saharan Africa is paramount for several reasons. 1. There is a disproportionately high disease burden in this region compared to other regions of the world. Of the 1.4 billion people afflicted by NTDs, sub-Saharan Africa bears the brunt of the burden of NTDs. Almost all cases of onchocerciasis and schistosomiasis occur in Africa. 2. The high rates of new infections of NTDs. 3. The high number of disability-adjusted life years – a measure of the burden of these diseases. 4. The economic cost of NTDs is quite high, creating a vicious circle of poverty. 5. NTDs cause high morbidity and disability levels in terms of blindness and body disfigurement. 6. Overall, there are huge unmet needs for the prevention of NTDs. For example, the need for preventive chemotherapy is 95% and 90.4% for onchocerciasis and schistosomiasis respectively. For most NTDs, preventative chemotherapy coverage is low. 7. There is low treatment coverage of at-risk populations in the African region compared to other regions in the world. 8. There is a growing body of evidence that shows that there are deleterious interactions between NTDs and HIV/AIDS, TB, and malaria. Helminthic NTDs increase susceptibility to HIV infection. It has also been observed that genital schistosomiasis in young girls and women increases their risk of contracting HIV. It has been suggested that schistosomiasis may also blunt CD4 responses in HIVinfected individuals with schistosomiasis co-infection in antiretroviral treatment. Leishmaniasis can accelerate the advance of HIV in patients. NTDs worsen the prognosis of HIV/AIDS, tuberculosis, and malaria. 9. Weak health-care systems in sub-Saharan Africa are already overburdened by infectious diseases such as HIV/AIDS, malaria and tuberculosis, as well as by a growing epidemic of non-communicable diseases. It is important that the burden of NTDs is removed. 10.

Studies have shown that the prevention of NTDs is quite cost effective. 11. The prevention of NTDs is effective in reducing onward transmission and may result in the elimination of NTDs.

Prevention Strategies for NTDs

Prevention and control measures for NTDs should be implemented in an integrated manner and should be multispectral and involve all key stakeholders. These last include those in health, agriculture, water and irrigation, forests, as well as environmental management and policy makers. Community resources should be harnessed to support community-based initiatives to prevent NTDs.

The prevention of NTDs should also be targeted, with the targeting of at-risk populations and geographical areas where NTDs are endemic. The prevention of NTDs should be school-based and community-based, and include the following:

1. *Mass distribution administration (MDA)*. Due to the high co-endemic levels of NTDs, mass drug administration targeting four or more helminthiases, socially transmitted helminthiasis, lymphatic filariasis, onchocerciasis and schistosomiasis, is recommended. Therefore, combinations of drugs which include albendazole or mebendazole for treatment of STHS, drugs specifically for treating schistosomiasis; praziquantel and invermectin for onchorcerciasis; and melarsopol or eflornithine for human Africa trypanosomiasis. Preventive chemotherapy coupled with vector control is an effective tool in the elimination of NTDs.

2. *Intensified case management (ICM)*. A key component of ICM is disease surveillance and intensified case-finding. This strategy is suitable for both protozoan NTDs such as human African sleeping sickness and leishmaniasis and the bacterial neglected tropical disease, Buruli ulcer.

3. *Vector control*. This requires integrated multispectral collaboration involving the ministries of health, of agriculture and irrigation, of forestry, of the environment, of livestock, of the mass media, as well as community leaders in the affected communities. Vector control aims at stopping the transmission of diseases.

4. *The provision of safe water and sanitation and the promotion of hygiene (WASH)*. The geographical distribution of NTDs overlaps with areas of unsafe water and poor sanitation and hygiene. WASH initiatives are effective in the control of NTDs. Patients are often afflicted by more than one neglected tropical disease. It is important to combine a number of NTD prevention and control initiatives to target a number of causative agents of NTDs at the same time. With concerted efforts, and more funding, the elimination of a number of NTDs is a feasible goal in sub-Saharan Africa contexts.

The Treatment of NTDs

Drugs used for preventive chemotherapy are also used for treatment of NTDs. The most important challenge in the treatment of NTDs is the lack of new, effective, safe and affordable drugs.

The currently used drugs for the treatments of NTDs are very old and some of them such as melasorpol are quite toxic. There is also a possibility that some of these drugs have already provoked resistance.

Early treatment of NTDs is hampered by a lack of cheap and accurate point of care diagnostic tools.

NTD Research

This is an area which has also been neglected. There is inadequate funding to undertake research into NTDs. This explains the many research gaps in relation to NTDs. 1. Research to provide surveillance and mapping data of NTDs in at-risk geographical areas and populations. 2. Research to track trends in efficiency and resistance of drugs for the prevention and treatment of NTDs. 3. Research to develop new diagnostic and vector control tools to enhance the diagnosis and control of NTDs. 4. Research to develop new effective, safe and affordable drugs for preventive chemotherapy and treatment for NTDs. 5. Research to develop effective vaccines for NTDs. 6. Research to provide evidence on how best to integrate the prevention and control of NTDs with the prevention and control of HIV/AIDS, TB and malaria. 7. Research into the interaction of NTDs with HIV/AIDS, TB and malaria, including drug-interaction when drugs for NTDs are co-administered with those used for the treatment of non-communicable diseases, tuberculosis or malaria.

Conclusion

There is a disproportionately high burden of NTDs in sub-Saharan Africa. NTDs have a huge economic and health impact and perpetuate poverty. Preventive chemotherapy, active case-finding, the prompt treatment of NTDs, and vector control make it feasible to plan for the elimination of most NTDs.

Undoubtedly, more funding for the prevention, control and treatment of NTDs is required to help align global targets for the prevention, control and elimination of NTDs.

More research funding is also required for the development of new, effective, safe and affordable drugs for preventive chemotherapy and the treatment of NTDs.

This will also help to promote research to fill identified research gaps in relation to NTDs.

3. The Great Challenges of Sickness Caused by the Ebola Virus in the Democratic Republic of the Congo

DR. MARIE KAPEPELA KAKICHA
Paediatrician at the Unit for Infectious Diseases, the Faculty of Medicine, the University of Kinshasa, the Democratic Republic of the Congo

Introduction

Ebola virus disease (EVD) is, together with Marburg virus haemorrhagic fever, a haemorrhagic fever caused by a *filovirus*. These are hospitalising diseases caused by inter-human contact and in particular by inter-family and inter-hospital transmission.

EVD was identified for the first time in 1976 following epidemics that broke out in the Democratic Republic of the Congo and in the Sudan. It continues to afflict equatorial Africa. Epidemics of this disease followed one another from 1976 to 2016 in the following countries: the Democratic Republic of the Congo, the Sudan, Gabon, Uganda, Congo Brazzaville, Guinea, Liberia, and Sierra Leone. Some cases were exported outside Africa and at the present time 27,378 people are registered as having had this disease, with 12,654 deaths (42%) caused by it.

1. The History of EVD

Marburg virus disease was identified for the first time in Germany and Yugoslavia amongst laboratory personnel who had been in contact with a monkey (*cercopithecusaethiops*) imported from Uganda. In total, 29 people were affected, of whom 23 were in Marburg and 4 in Frankfurt, with 2 in Belgrade (they all worked in laboratories and 7 of them died).

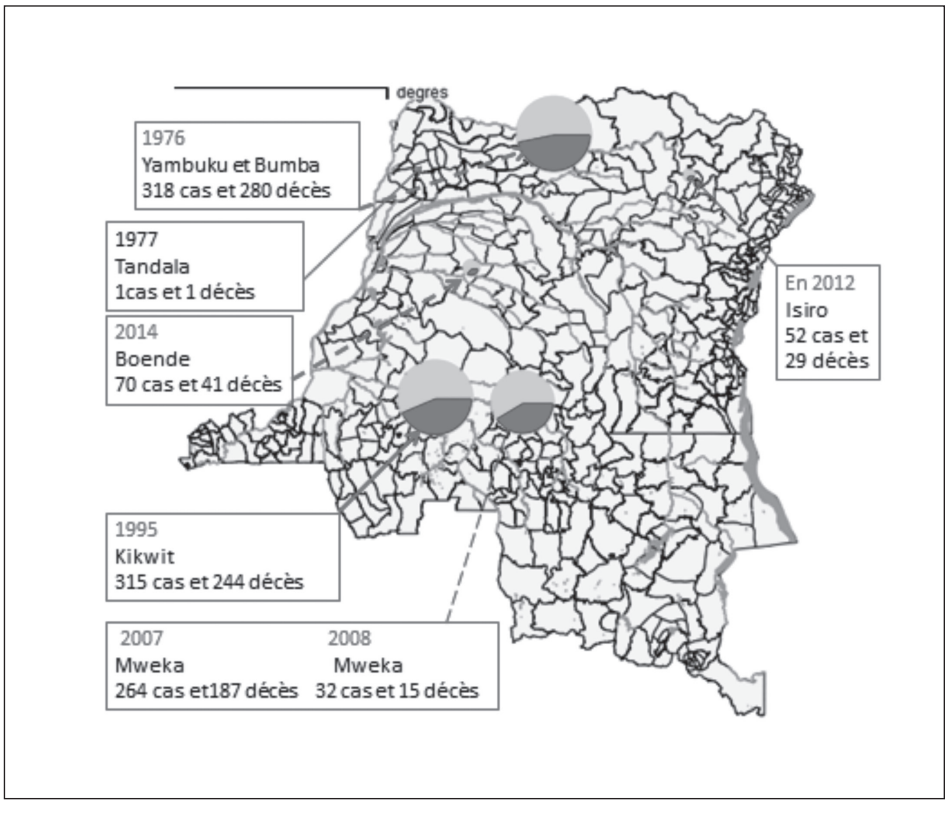
In the Democratic Republic of the Congo the first epidemic of Ebola was recorded in Yambuku and it afflicted the city of Bumba. This was the first epidemic of Ebola to be recorded in the world and subsequently, in the Democratic Republic of the Congo, seven epidemics took place between 1976 and 2014:

– From July to November 1976 a grave epidemic of Ebola virus disease (viral haemorrhagic fever) broke out in the North of the Democratic Republic of the Congo, in Yambuku in the Province of the Equator, producing 318 cases and 240 deaths, that is to say a death rate of 88%. The Zaire Ebola virus was identified as being responsible for this disease.

– A year later, therefore in 1977, a case and a death following illness caused by the Ebola virus was registered in Tandala in the same Province of the Equator.

– In 1995 an epidemic of great magnitude afflicted the city of Kikwit in the Province of Bandundu. It is estimated that the number of victims involved 310 cases and 250 deaths, that is to say a death rate of 80%. The Zaire strain of the Ebola virus was responsible for this important epidemic in the Province of Bandundu in Kikwit.

– In 2007 and 2008 in the health-care area of Mweka, in the Province of Western Kasaï, two



epidemics of Ebola broke out in the year 2007 (264 cases and 187 deaths, that is to say a death rate of 70.8%) and also in 2008-2009 (32 cases and 15 deaths, that is to say a death rate of 46.8%).

– In 2012 an epidemic hit Isiro in the Eastern Province and produced 52 cases and 29 deaths, that is to say a death rate of 56%.

– In 2014 the seventh and last epidemic took place in Boende in August, with 71 cases and 41 deaths, that is to say a death rate of 56%.

At the outset these epidemics were sporadic but they then became more frequent and moved to other countries in Africa and the world.

2. Objectives of this Paper

To inform, to sensitise and to share the experience of the Democratic Republic of the Congo in order to prevent and to reduce the duration of epidemics and their death rates.

3. Methods

This work is based on documentary research; reports on the epidemic in Boende, declarations issued by the health-care authorities of the Democratic Republic of the Congo, and conversations with leading figures in the field (the National Institute of Biomedical Research, the Directorate for Combatting Diseases).

4. The Current Situation

– Current knowledge

The origins of Ebola virus disease

The Democratic Republic of the Congo has various risk factors as regards the outbreak of diseases which in potential terms can produce an epidemic and above all ones that have origins in animals. Amongst these factors, we may refer in particular to a vast country covered in large measure with equatorial forests, with an extensive water network, and more than seven national parks and reserves which have wild animals of various species; frequent contacts between men and wild and domestic animals, above all in a rural context; various practices that involve risks: the handling and/or the consumption of dead wild animals that are potentially infected with disease, hunting activity that is not sufficiently regulated, porous frontiers that facilitate the uncontrolled movement of animal species, and a lack of integration of the monitoring of human and animal health within a 'one health' framework.

The last epidemic in the health-care area of Boende in the Province of the Equator, which benefited from the experience of the past, may act as an example for this paper. At an ecological level, the health-care area of Boende is characterised by a hot and humid tropical climate where the temperature varies between 21°C and 31°C. There are two seasons: the great rainy season (September to April) and the dry season (May to August). This area is located in the central basin of the Democratic Republic of the Congo, most of which is covered by a large forest with the remaining part being a marshy area in which the roads are not in a good state.

The water system is very important. Rivers such as the Tshuapa, the Lomela and the Salonga and small rivers bring water to the health-care area of Boende which is rich in fauna and flora typical of the ecosystem of equatorial forests.

Reservoirs and transmission

The origin of an epidemic is not known because the patient zero has not been identified. The large monkeys (gorillas, chimpanzees) are very sensitive to this disease. They are not reservoirs but perhaps vectors because various epidemics afflicting man have been accompanied by the deaths of domestic and wild animals, as happened in Mweka in 2007, in Isiro in 2012, and in Boende in 2014.

Bats are potential reservoirs and could produce an infection without apparent signs of it. But no virus was isolated between 1976 and 1998 in 30,000 analyses carried out on mammals, birds, reptiles, amphibians and arthropods, starting with the regions of the Ebola epidemic.

The epidemics of these two diseases (Malburg disease and Ebola disease) took place in countries in Africa whose ecological conditions favour the circulation of these viruses amongst animals. Man is an accidental host who becomes infected and then introduces the disease into his community. The factors that favour the development of their zoonosis and all the ways that the virus is transmitted to man are still not clear, whereas the transmission in nature is said to start with primates near to man and other animals which are said to be the vectors of these diseases. Bats are said to be potential reservoirs, in contact with hunters, miners and farmers.

An epidemic is said to come from an amplification of transmission between humans starting from health-care centres and communities where there is bad hygiene, the absence of water and bad practices.

A health-care centre becomes a source of contamination because of an absence or lack of equipment to separate the health-care staff from the patients and of protective personal equipment; from close contact between the health-care staff, nurses and visitors with patients, with their biological fluids (multi-use material, blood, faeces, vomit, clothes and other objects); and from contact with infected material.

Inside a community one is dealing more with: direct contact with infected individuals (biological fluids, sheets, objects), the handling or consumption of contaminated fur, above all of bats or large monkeys, unsafe traditional funeral ceremonies, and sexual relations (the permanence of the virus in sperm can last up to about two months after the recovery of a patient). Some doubts still exist about transmission through the air and through fruit infected by the saliva of bats, domestic animals and plants.

Five types of Ebola virus are

known about: the Ebola virus, the Sudan virus, the Bundibudyio virus, the Thai Forest virus, and the Reston virus (the Philippines). The virulence varies according to the type and thus the average death rate of the Ebola virus of the Democratic Republic of the Congo is 63%, of the Sudan virus is 53%, of the Bundibudyio virus is 27%, of the Thai Forest virus is 0%, and of the Reston virus is 0%.

Dealing with an epidemic

The specific objectives involved in dealing with an epidemic principally revolve round three initiatives: the strengthening of activities involving the swift identification and prevention of cases of Ebola virus disease in the health-care area of Boende and its hinterland and dealing with individual cases.

To achieve these objectives, various strategies were utilised: the creation of a system of coordination, the strengthening of epidemiological monitoring, of laboratory work, of clinical responsibility for cases, of communication and of hygiene, water and cleansing, and psycho-social and logistical support. Central coordination was established in the capital of the country Kinshasa, in the Provincial capital of Mbandaka, and at a local level in the health-care area of Boende. Six support committees accompanied this coordination.

This action was supported by the local authorities, by sector heads, by groups, by villages, and by the population and their secular and religious leaders. In all this coordination, the Ministry of Health assured leadership with the support of its partners (WHO, UNICEF, MSF, CDC, UNHAS, WINNIPEG, MONUSCO, PAM).

As regards the committees:

Epidemiological monitoring

– *Forward* monitoring which involved the swift identification of cases in health-care institutions and in the community through the registration of cases. All the recording of cases carried out by community health-care intermediaries and by the members of the community were systematically examined by the monitoring team. In addition, for all the cases contacts were registered and followed for twenty-one days.

– *Retrospective* monitoring which involved looking for cases and deaths after the presumed period when the epidemic began. These surveys were carried out at the level of the health-care institutions and at a community level.

Other activities were engaged in, such as the training of community health-care intermediaries, nurses, and members of the framework team of twelve health-care areas; the harmonisation of the instruments of monitoring; the creation of a data bank; the spread of instruments for monitoring (a list of contacts, a registration form of contacts, the definition of cases of EVD); and the daily organisation of meetings to analyse the monitoring data.

In order to direct the initiatives designed to combat the disease in a more effective way, some activities were engaged in such as the regular analysis of data, the creation of the chain of transmission in order to understand the connection between cases, and the drawing up of an epidemiological bulletin that was issued regularly.

Clinical responsibility for cases

Let us remember that the period of incubation of EVD ranges from 2 to 21 days (on average 4-10 days), which are followed by the following symptoms and signs:

Between the first and second days: fever, heavy headache, muscular pains, tiredness, and a reddening of the eye mucus.

Between the second and fifth days: irritation of the throat, pains in the chest and abdomen, a reddening of the skin, diarrhoea and vomit.

After the fifth to ninth day: haemorrhages, hiccups, sleepiness, delirium, coma and death.

This disease is very contagious and contagion is highest between the fourth and seventh days. Convalescence is long and very painful and the patient remains asthenic for a number of weeks.

Before the Centre for the Treatment of Ebola (CTE) was operational, the clinical taking of responsibility for cases was organised in health-care centres and the general hospital of reference.

In general, after the observation of every suspected case (fever, headache, diarrhoea, abdominal pain, vomit, tiredness and bleeding at all levels), the patient was sent to the CTE for a clinical examination and the taking of blood samples for laboratory analysis. If the first blood sample was negative, a second one was done during the following seventy-two hours. If the first sample was positive, the patient was admitted to the CTE and followed until discharged in line with the method: dead or alive. The patient left the CTE and was declared to be cured if the virus load had become insignificant or non-existent. Recovery from the disease is at the same time clinical and biological.

After the confirmation of a case, the patient was isolated in a special room for this purpose, in which the equipment for controlling the infection and safety was placed. For a better clinical treatment of cases, a specific protocol was drawn up which was followed for every case admitted to the CTE. Isolation was organised according to the usual standards and hospital hygiene measures were followed for the whole of the epidemic in the two treatment centres. The centres for clinical treatment of the disease were divided into two sections: one for suspected cases and one for confirmed cases.

The laboratory

A mobile clinic for the local area was created for rapid diagnoses by radiologists.

Communication

Information, sensitisation (of the population through the radio, television, brochures), interpersonal communication and mass communication (markets, churches, meetings, villages)

were utilised to improve people's knowledge about the disease and to improve prevention, and to help in and obtain the notification of cases, deaths, and the acceptance of safe burials. The messages and approaches were targeted and adapted to every goal (the washing of people's hands with disinfectants, universal protection rules, not touching animals found dead, cleaning homes with disinfectants, going from village to village).

Psycho-social help

Specific psychotherapy was engaged in with patients, the members of their families and with communities afflicted by the disease, in order to achieve dialogue, the ending of conflicts, and to manage resistance to some of the measures to combat the epidemic (isolation, safe burial). In this framework as well, food, home and school kits were distributed which took into account the poverty of the context. The personnel responsible for care and treatment received special anti-stress support.

Hygiene, water and health-care services

At this level, material for protection, disinfection and cleaning was distributed and drinking water was made available to people; safe burials were performed and biomedical waste was dealt with.

Logistics

Everything connected with human resources, the transportation of the teams and equipment, laboratory material and samples (motorbike, helicopter, etc.), followed by funding, accounting and safety in the zone of operations acted as support for all the committees.

– Control of Ebola virus disease and the great challenges involved

1. Monitoring

Effective epidemiological monitoring that assures the prevention and early identification of epidemics depends in the Democratic Republic of the Congo on:

Ecological conditions

The reservoirs of the virus have still not been identified given the presence of the basins of the Congo and the Nile with their equatorial fauna and vegetation, and forest areas, held to be responsible, that are very extensive and diversified. Overall, only one epidemic has been observed in a specific place with, as a consequence, a risk assessment that was very difficult to make with an uncertain prediction of the disease.

The organisation of monitoring

The system of monitoring has to be made more effective on a community basis (more involved intermediaries and hunters) and the same may be said about operational studies on all the points at risk which are not taken into account in prevention, the swift identification of an epidemic, supervision and assessment. It is also necessary to organise an effective and flexible communications network (notices at various points, the involvement of hunters, appeals that start from high up and verify the work that is taking place in the field) and a system for the exchange of information with all the relevant institutions.

Organisation within health-care education

At this level one observes an absence or a lack of equipment for individual protection (gloves, jackets, boots, masks…), of specialised equipment pre-installed for the maximum protection, of material for taking samples, cold chains, and laboratory equipment (diagnosis through a rapid test).

The need for the training of health-care personnel at all levels in order to engage in effective action still remains an urgent need and above all else the maintenance in the field of trained personnel is required. The use of clinical specialists is recommended given the association of other pathologies with Ebola virus disease.

2. Responses

Treatment

Treatment was essentially that of symptoms with nutritional support; antivirals and vaccines were not at that time available.

Logistics

It was difficult to reach the epicentre of the epidemic because of the distance, the fact that the region was in a central area of the country, and the fact that access to it was difficult by road. In addition, it was difficult to engage in activity in the field (mobility, access, the distance needed to reach involved individuals, contacts, internet…).

Socio-cultural obstacles

Some difficulties were connected to local culture. The population resisted accepting some measures to combat the disease that were proposed by the health-care personnel (isolation, unsafe mortuary lavatories). Numerous legends circulated to do with how the epidemic was perceived (trafficking in blood, genital organs). Many rumours were dealt with through dialogue and psycho-social accompanying.

The total involvement of all the players

The community, community and religious leaders, the political-administrative authorities at all levels, medical personnel of all categories, the mass media (radio, television, press…), traditional healers and experts in animal health should all be involved and their contribution should be coordinated in an effective way. The management of socio-economic damage for destabilised survivors after epidemics has been partly considered (loss of productivity and purchasing power in an already precarious context).

5. Comments

The epidemic was limited thanks to these initiatives but also naturally enough to the presence of two rivers that cordon off the zone afflicted by the epi-

demic and to the lack on the part of the inhabitants of means of transport which meant that people with the infection could not move around.

70 people were struck by the disease with 49 deaths (61%), above all at the beginning of the epidemic. It should be emphasised that diagnosis at the outset was not easy and the sick people were treated for malaria, influenza and dysentery, above all because they displayed the symptoms of fever, abdominal pains and faeces with blood in it.

Compared to previous epidemics that broke out in the country, the response time was reduced to fifteen days and the duration of the epidemic was brought down to forty days. The end of the epidemic occurred three months after its outbreak had been declared, that is to say forty-two days after the notification of the last case. This demonstrates a decrease in the response time, of the duration of the epidemic, of the number of people afflicted, and of the number of deaths.

6. Conclusions and Recommendations

Conclusions

This last epidemic of Ebola virus disease in the Democratic Republic of the Congo provided us with new lessons, questions without answers, and challenges. However, the following facts facilitated work in the field and the achievement of better results:

– The political commitment and important contributions of the partners.

– A multi-sectorial approach (psychologists, the mass media, those who deal with the health of animals).

– Dialogue with the population and the team spirit of the actors.

– The contribution of laboratory diagnoses with rapid tests on the ground.

– Approaches and messages adapted to the objectives (village by village, the cleaning of homes with disinfectants, universal protection rules, not touching animals found dead).

– The reduction of the response time and of the duration of the epidemic even though the death rate was still high.

Recommendations

Efforts have still to be made in the following areas: the implementation of monitoring on a community basis and in line with the 'one health' approach; the prior positioning of materials, equipment and financial resources in order to engage in a rapid organisation of a high-quality response; funds that can be used rapidly for a rational management of epidemics and research into questions that are still unanswered (earning, exploration, response, supervision and assessment); the strengthening of the ability of teams to act rapidly at all levels of the heathcare pyramid (specialists) and the retrieval of the socio-economic level of survivors who have been destabilised by the epidemic.

4. The Zika Epidemic in Brazil

DR. MARIA INEZ LINHARES DE CARVALHO MD
Vice-President, The World Federation of Catholic Medical Associations – FIAMC, Brazil

Introduction

The outbreak of Zika began in early 2015 in Brazil and then spread to other parts of South and North America; it also affects several islands in the Pacific and Southeast Asia.[4] In January 2016, the World Health Organisation (WHO) said the virus was likely to spread throughout most of the Americas by the end of the year.[5] In February 2016, WHO declared the outbreak a 'Public Health Emergency of International Concern' as evidence grew that Zika can cause birth defects as well as neurological problems.[6, 7] As of mid-2016, a widespread epidemic of Zika fever, caused by the Zika virus, is ongoing in the Americas, the Pacific and Southeast Asia.[2,3]

The virus can be transmitted from an infected pregnant woman to her foetus, and can then cause microcephaly and other severe brain anomalies in the infant.[8, 9, 10] Zika infections in adults can result in Guillain–Barré syndrome.[10] Prior to this outbreak, Zika was considered a mild infection, as most Zika virus infections are asymptomatic, making it difficult to determine precise estimates of the number of cases.[11] In approximately one in five cases, Zika virus infections result in Zika fever, a minor illness that causes symptoms such as fever and a rash.[12, 13] The virus is spread mainly by the *Aedes aegypti* mosquito which is commonly found throughout the tropical and sub-tropical Americas. Men infected with Zika can transmit the virus to their sexual partners.[7, 15, 16, 17] A number of countries have issued travel

warnings and the outbreak is expected to reduce tourism significantly.[7, 18] Several countries have taken the unusual step of advising their citizens to delay pregnancy until more is known about the virus and its impact on foetal development.[19]

Epidemiology

The Zika virus was first isolated in 1947, in a rhesus monkey in a forest near Entebbe, Uganda.[20] Although serologic evidence indicated additional human exposure during subsequent decades in parts of Africa and Asia,[24] before the 2007 Yap Islands Zika virus outbreak only 14 cases of human Zika virus disease had been documented. Researchers generally believe that the virus was brought to Brazil by an infected traveller who had been exposed to the virus in French Polynesia, who was then bitten by a mosquito that then infected others.[25, 26, 27] The specific event that brought the virus to Brazil was uncertain until March 2016. Brazilian researchers had suggested that the Zika virus arrived during the 2014 FIFA World Cup tournament.[25] The Zika virus usually has very mild or no symptoms, so it took almost a year for Brazil to confirm the first case of the disease. By then, the outbreak was already widespread. Factors associated with the rapid spread of the Zika virus in Brazil include the non-immune population; high population density; the tropical climate; and the inadequate control of *Aedes* mosquitoes in the country.[28] Confirmed cases have been reported in 40 countries or territories in South America, North America, and the Caribbean,[29] as well as 16 in the western Pacific and one in Africa since the beginning of 2015.

Many countries with no cases of mosquito transmission have reported travel-related Zika cases: people who moved or came home from a Zika-affected region before they showed symptoms.

In Brazil

As early as August 2014, physicians in Natal in north-eastern Brazil began to investigate an outbreak of illness characterised by a flat pinkish rash, bloodshot eyes, fever, joint pain and headaches. While the symptoms resembled dengue fever, testing ruled out this as well as several other potential causes.

By March 2015, the illness had spread to Salvador, Bahia, and had appeared in three different States.[20] Then, in May 2015, researchers from the Federal University of Bahia and the Evandro Chagas Institute determined, using the RT-PCR technique, that the illness was an outbreak of Zika virus.[21, 22]

Latest Data on the Zika Epidemic in Brazil (October 2016): 2015-2016

200,465 cases were laboratory confirmed as well as 3 deaths: 2 cases in Rio de Janeiro and 1 case in Espirito Santo. As regards pregnant women, there were 16,473 probable cases, with 9,507 confirmed by clinical and epidemiological or laboratory criteria, according to Sinan-NET data. Newborn, stillbirth or foetal miscarriage: 9,862. 31% (3,035) of cases remain subject to research. 6,827 investigated, with *2,063 confirmed with microcephaly and/or damage to the nervous system.* 4,764 cases were discarded.

Transmission

Adult *Aedes aegypti*. This is a mosquito and is a vector or carrier of the Zika virus. Zika is a mosquito-borne disease. The *Aedes aegypti* mosquito usually bites in the morning and afternoon hours, and can be identified by the white stripes on its legs.[30] Zika can also be sexually transmitted by a man to his sexual partners.[8] The sexual transmission of Zika was documented in nine countries – Argentina, Canada, Chile, France, Italy, New Zealand, Peru, Portugal, and the United States – during this outbreak.[32]

Aedes albopictus This is a cousin of *aegypti* that prefers areas with vegetation and keeps the virus active in your body after ingestion of contaminated blood. These mosquitoes live in tropical, sub-tropical and temperate climates, but can live in a broader temperature range and at cooler temperatures than *Aedes aegypti*. Because these mosquitoes feed on animals as well as people, they are less likely to spread viruses such as Zika, dengue and chikungunya. This mosquito has a lower ability to transmit Zika and dengue.

Transmission

Zika is transmitted from pregnant women to the foetus ('vertical transmission') and causes microcephaly and other severe brain anomalies in infants born to women infected with the virus.[8, 10]

Symptoms

It is estimated that 80% of cases are asymptomatic.[15] The main clinical symptoms in symptomatic patients are low-grade fever, conjunctivitis, transient joint pain (mainly in the smaller joints of the hands and feet) and maculopapular rash that often starts on the face and then spreads throughout the body.[33] Zika infections in adults can cause Guillain-Barré syndrome.[10]

Guillain-Barré syndrome

Signs and symptoms of Guillain-Barre syndrome may include: prickling, 'pins and needles' sensations in your fingers, toes, ankles or wrists; weakness in your legs that spreads to your upper body; unsteady walking or an inability to walk or climb stairs; difficulty with eye or facial movements, including speaking, chewing or swallowing; severe

pain that may feel achy or cramp-like and may be worse at night; difficulty with bladder control or bowel function; a rapid heart rate; low or high blood pressure; and difficulty in breathing.

Diagnosis

It is difficult to diagnose Zika virus infection based on clinical signs and symptoms alone due to overlaps with other arboviruses that are endemic to similar areas.[34] The methods currently available to test for Zika antibodies cross-react with dengue antibodies. An IgM-positive result in a dengue or Zika ELISA test can only be considered indicative of a recent flavivirus infection. Plaque-reduction neutralisation tests (PRINT) can be performed and may be specific. [35] The Zika virus can be identified by RT-PCR in acutely ill patients.[7]

Prevention

To prevent the transmission of the Zika virus, WHO recommends using insect repellent , long-sleeved clothes to cover the body, and screens and mosquito nets to exclude flying insects from dwellings or sleeping areas. It is also vital to eliminate any standing water near homes to minimise breeding areas for mosquitoes. Authorities can treat larger water containers with recommended larvicides.[30, 14] Furthermore, the Centres for Disease Control and Prevention (CDC) recommend that containers holding water near homes either be sealed or scrubbed once per week, because mosquito eggs can stick to them.[31]

The Great Hope

Brazil and Colombia will intensify fighting Zika and dengue with Wolbachia bacteria

London (Reuters). Health officials in Brazil and Colombia will launch wide-ranging mosquito control campaigns using a naturally occurring bacteria known as Wolbachia to combat the spread of dengue viruses and of Zika in their populations. Tests on small technical scale, which involve infecting mosquitoes with Wolbachia to prevent them from spreading the virus, showed a significant reduction in their ability to transmit Zika and dengue, leading donors to support more comprehensive plans. The Wolbachia bacterium naturally arises in many insect species around the planet, and research has shown that it can significantly reduce the ability of mosquitoes to transmit viruses to humans. When mosquitoes with Wolbachia are released in one area, they mate with local mosquitoes and transmit the bacteria to future generations. Within a few months, most mosquitoes carry Wolbachia and the effect is self-sustained. Wolbachia-harbouring mosquitoes displayed lower viral prevalence and intensity and decreased disseminated infection and, critically, did not carry infectious virus in the saliva, suggesting that viral transmission was blocked.

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SECOND SESSION • Rare Diseases

1. The Principal Rare Diseases

PROF. RAFFAELE MANNA
DR. ELENA VERRECCHIA
The Faculty of Medicine and Surgery, The University of the Sacred Heart, Rome, Italy

Rare diseases (RD) are a broad and heterogeneous group of pathologies defined by their low prevalence in a population. At a European level, as in Italy, a rare disease is defined as a disease that afflicts not more than five patients out of 10,000 inhabitants. Taken together, these pathologies are very many in number. Indeed, the World Health Organisation estimates that there are between 6,000 and 7,000 different rare diseases which together afflict about 3% of the population. The incidence of rare diseases, in addition, can vary from region to region. It is therefore difficult to establish which are the principal rare diseases, not least because they vary according to the sensitivity of the specialist and his or her knowledge of the rare disease involved. In order to facilitate the diagnosis and treatment of rare diseases, a number of reference centres have been created.

At the Gemelli Polyclinic of Rome, a Centre for Research into Periodic Fevers (CFP) has been operational since 1997. This centre engages in activity that involves the diagnosis and treatment of rare periodic illnesses linked to inflammations that can arise at various stages in the life of a patient and require a special expertise and specific genetic tests. These fevers have a diagnostic delay of up to thirty years (on average fourteen years) and involve a high human and economic cost for patients and their families. In Italy, this centre is seen as a point of national reference for autoinflammatory periodic fevers on a par with centres in London (UK) and Bethesda (USA).

Patients with periodic fevers of unknown origins who are sent from all over Italy but also from abroad (Malta, Switzerland, Tunisia, Egypt) come to the CFP. Over the last ten years consultations have been requested for over 1,200 patients for the purposes of diagnosis and treatment. Patients from the regions of Lazio, Abruzzi, Umbria, Campania and Calabria are followed in a continuous way with periodic access to the clinic. 350 patients have family Mediterranean fever. Others have periodic fevers linked to mutations of the receptor gene of the TNF (TRAPS), Hibernian fever, 'cryopin-associated periodic syndromes' (because of mutations linked to the CIAS1 gene) where in some cases the fever is brought on by the cold; a fever linked to mutations of the mevalonate kinese gene (MVD, also called the IperIgD syndrome; PFAPA (periodic fever with pharyngo-adenitis and aphthosis); Still's disease, which has one variety in children and one in adults; and 1 CROM (chronic recurrent osteomyelitis). In addition to recurrent fevers, other syndromes exist which are characterised by a different kind of clinical emergence that makes these illnesses difficult to diagnose, such as recurrent recurrent monoarthritis or recurrent pleuropericarditis. Periodic fevers have also been diagnosed caused by a deficit of the C1Q esterases inhibitor (hereditary angioedema). The worst complication of these pathologies, when they are not recognised, is AA amyloidosis which involves kidney failure, to the point of needing dialysis, or mutilating arthritis. The diagnosis of other pathologies in the case of fevers of unknown origins is notably shortened when the team is specialised in the field and uses algorithms that are constantly updated and self-testing.

The paradigm of these autoinflammatory conditions is family Mediterranean fever. Family Mediterranean fever (FMF) is an autoinflammatory illness with brief recurrent episodes of fever and serositis that lead to pain in the abdomen, the thorax, the joints, and the muscles. It is typical in the South-East Mediterranean. It usually emerges before the age of thirty. The earlier its appearance, the more the phenotype is grave. It is sub-divided into FMF type 1 and FMF type 2. Type 1 has attacks (once a week every 2-3 years) of fever and serositis which last for 1-4 days and end spontaneously. Stress, exposure to cold, meals rich in fats, infections, some medicinal products, and the menstrual cycle are possible trigger mechanisms. The attacks are preceded by light symptoms (myalgia, headache, nausea, dyspnoea, arthralgia, back pain, asthenia and anxiety) and last for about 17 hours. They are accompanied by fever (38-40°, for 12-17 hours, with antibiotics not having an effect); extended or localised abdominal pain (often similar to acute abdominal pain); constipation (diarrhoea in children); joint pain (in the large joints); arthritis (joints of the upper/lower limbs);

and pain in the thorax with pleurisy and/or pericarditis. In 7% to 40% of patients, the skin is also involved. Amyloidosis type AA is a grave complication. Type 2 involves amyloidosis which is the first and only symptom. Differential diagnosis takes place with hyperimmunoglobulinemia D, periodic fever syndrome, periodic fever associated with the TNF receptor (TRAPS), and PFAPA (periodic fever, aphtas, pharyngitis and cervical adenopathies).

For family Mediterranean fever, as for many of the autoinflammatory diseases, treatment with Colchicine is used (orally or by injection). This reduces or eliminates the attacks and prevents amyloidosis type AA. The dose varies from 0.03 mg/kg corporeal weight a day to a maximum of 3mg a day and is taken continuously and over a long period. Colchicine has been shown to be a medicinal product that is able to improve the quality of life of these patients, although some patients with this condition do not respond to this treatment. Today new biological medicinal products are available, such as anti-bodies against the receptor or directly against the cytokines responsible for the inflammatory cascade (Anakinra, Canakunimab, Tocilizumab, Enbrel etc.). These medicinal products have been shown to be extremely effective but in some cases there are still considered off-label for these pathologies. For this reason, the CFP has taken part in an international study on the efficacy of a biological medicinal product, Canakinumab, in order to extend its therapeutic recommendation to other autoinflammatory conditions. The current research is based upon the stratification of patients on the basis of genetic mutations and selection for biological medicinal products.

Recently the centre was also recognised as a centre of regional reference for liposomal illnesses, in particular Fabry disease and Gaucher's disease. These diseases, which are defined in overall terms as liposomal, are a group of about fifty diseases caused by an alteration of one of the functions of the liposomes (the organelles responsible for breaking down and recycling materials produced by cellular metabolism) and in particular by a lack or malfunctioning of the enzymes responsible for their activity. These alterations involve an accumulation inside the liposomes themselves of materials that are not broken down and this in turn leads to damage to the cells and tissues. These are systemic pathologies that can affect more than one organ and their most typical clinical symptoms are: a swelling of the liver and the spleen; injury to the central nervous system with a progressive loss of neurological functions; and alterations of the eyes, the heart and the muscular system. The age when these diseases emerge varies but they usually appear in childhood.

Fabry disease is caused by a reduced or absent activity of the liposomal enzyme a-galactosidase which causes a gradual accumulation of a sphingolipid, globotriaosylceramide, preferentially at the level of the endothelial cells of the smooth muscle of the blood vessels. With the passing of the years, these deposits localise in all the organs and principally in the myocardium, the kidney, the eyes, the skin, and the central nervous system, and alters their functions. Overall, this is a grave disease, which progressively gets worst. It has a difficult diagnosis and brings about an unsatisfactory quality of life.

The clinical symptoms are generally light when the disease first makes it appearance but they get worse with the passing of time. One of the characteristic signs of this disease, which is present in 85% of patients who have it, is acroparesthesia, that is to say stinging pains in the extremities, associated with major attacks of fever, in particular during the summer and when the seasons change. With the advance of age, heart disease emerges early on with an alteration in the heartbeat. Subsequently, cardiomyopathy is experienced, with a concentric hypertrophy of the left ventricle, ischemic cardiopathy, and a deficiency of the heart valves. As a first symptom of the accumulation of sphingolipids at the level of the kidney, a worsening proteinuria is witnessed with a progressive reduction of the working of the kidneys that can reach the stage of end-stage renal deficiency (ESRD). Treatment in these cases remains peritoneal dialysis or haemodialysis, followed by a subsequent kidney transplant. The vascular system of the central nervous system is also affected by the accumulation of sphingolipids in the endothelial cells, and this causes a high risk of transitory and/or permanent ischemic attacks, even when the patients are young. At the level of the eyes, the sphingolipid accumulates in the cornea and the retina, altering sight. At the level of the ears, vascular alterations can bring about tinnitus, giddiness and sudden hypoacusis.

Since the year 2001, a specific treatment has been available based upon the injection of the absent enzyme produced from genetically modified stem cells – this is defined as enzyme replacement therapy (ERT). This medicinal product, produced by two different companies, is recognised by the EMA and the Italian Ministry of Health. Clinical studies are demonstrating the efficacy of ERT in slowing down the grave development of this disease and in some cases in preventing the deterioration of more than one organ which is characteristic of Fabry disease, especially when this therapy is begun early on. Recently a new medicinal product has been introduced which is taken orally, Migalastat, for the treatment of Fabry disease. The CFP, with the approval of the EMA as an orphan medicinal product, and at the level of recognition by the AIFA, took part in the experimental trials for Galafold.

Because of their rarity both family Mediterranean fever and Fabry disease are not much known about by medical doctors

unless they are ultra-specialised, and their diagnosis often requires a very long period of time – on average 14-18 years. Their principal characteristic is rarity and this in part is the result of the difficulties that patients encounter in obtaining an appropriate and rapid diagnosis, and as a consequence suitable treatment. The low level of scientific knowledge about them that springs from their rarity often causes a long period of time between the appearance of these diseases and their diagnosis. This has a negative impact on the prognosis of the patient involved. In particular, the diagnostic-therapeutic pathways are often complicated by the small number of institutions and health-care workers (and often the fact that they are not distributed in a homogenous way in the geography of a nation) who are able to provide satisfying responses to the health needs of patients afflicted by a rare disease who, indeed, often feel abandoned. In the majority of cases they do not have an illness that has to be fought but a condition that has to be accepted and treated. At times, the task of health-care workers is not to heal but to take care of these patients and this can be achieved in the best way by uniting scientific knowledge with deep solidarity. In some cases, a rare condition involves the risk of illness more than illness in the strict sense of the term. In some cases, it is important to adopt all preventive measures in order to minimise or at time remove the possibility of health damage associated with a congenital or acquired risk factor. In these cases, as well, notable specific training is needed in order to lead the carriers of these conditions to find a balance which combines the greatest possible safety with the lowest level of medical intervention.

Today, however, an increased awareness of rare diseases has contributed to a reduction in delays at the level of diagnosis, not least because of meetings involving the dissemination of scientific knowledge, even though often only a possible diagnosis is posited as the result of the capacities and the wish to be informed of a few medical doctors. The confirmation of such a diagnosis, and above all the therapeutic approach and the follow-up, are entrusted to specialised centres. The strength of these centres is multi-specialist assistance with a trained and sensitised personnel who have knowledge that goes beyond training at a theoretical level, and specialised as well as basic clinical experience. With these goals, the CFP of the Gemelli Polyclinic works with other centres that deal with rare diseases in order to allow patients with rare diseases not to feel abandoned but helped in a complete way.

2. Rare Pathologies: the Current Situation in Taiwan

PROF. DR. VINCENT HAN-SUN CHIANG
President,
Professor, the College of Medicine,
The Fu Jen Catholic University, Taiwan

Rare diseases affect only a very small portion of the total population and therefore patients tend to receive insufficient attention from the government and society. The result of this is that their access to medical treatment, educational and job opportunities, and holistic care is constantly neglected, if not completely denied. Over the last two decades, progress has been made through the joint efforts of the government and non-profit organisations in Taiwan. With the establishment of a network which integrates social welfare, medical care, legislation, and academic research related to rare diseases, we hope to safeguard human life and dignity for those who are afflicted by rare diseases. This paper provides an overview of legislation, social and financial resources, research grants, clinical diagnosis, genetic screening, prevention, and the future prospects for care of patients with rare diseases.

Prevalence in Taiwan

In the report of the Taiwan Foundation for Rare Disorders released on 4 October 2016, there are 246 kinds of rare disorders in the country. For the list of the top ten laboratory-diagnosed rare diseases in Taiwan (2015), please refer to table 1. There is as yet no consensus on the definition of a rare disease. In some countries and regions only the prevalence rate is considered, while in others the criteria of genetics and diagnostic difficulties are included. The Rare Disease and Orphan Drug Review Committee in Taiwan de-

fined a rare disorder as 'a disease or condition that affects fewer than 10,000 people among the total population in Taiwan'. Currently, the total number of cases of rare diseases reported to the Health Promotion Administration of the Ministry of Health and Welfare of Taiwan is 10,620.

Legislation and the Support Network

In 2000, the Legislative Yuan and Facilities of Taiwan implemented the following legislation that aims at improving care for patients and families with rare disorders: the Rare Disease Prevention and Orphan Drug Act; the Rare Disease Prevention and Orphan Drug Enforcement Rules; the Rare Disease Medical Aid Subsidy; the Orphan Drug Projects Application; and the Orphan Drug Designation and Research Application.

After the enforcement of these laws, the public and private sectors are now better equipped to provide better and more comprehensive treatment programmes targeting the individual needs of patients with rare disorders. For the time being, 94 items of orphan drugs are admitted with over 1,000 patients obtaining access to medication; moreover, 40 types and well over 100 health nutrients can readily be dispensed. Besides medication and nutrition, the Ministry of Health and Welfare of Taiwan established a Rare Disease Special Nutrition and Emergency Drug Logistics Centre to coordinate resources so that patients and caregivers can have efficient single-window service. In addition, 22 Genetics Counselling Centres have been established in northern, central, southern, and eastern Taiwan to guarantee local services.

Social Resources and Financial Assistance

In addition to the coverage of National Health Insurance (NHI), the government also provides subsidies for cases and items not refunded by NHI, which largely encompass nutrition counselling, infant formula milk powder for babies with rare diseases, and auxiliary medical equipment. The Foundation for Rare Disorders offers different types of financial aid to help ease the burden of caring for patients and their families.

Patient Medical Financial Assistance

Patient Medical Financial Assistance was set up by the Taiwan Foundation for Rare Disorders in 1999 with the aim of subsidising expenses for genetic tests, diagnosis, operations and drugs. As of December 2015, financial assistance had been allocated to 1,830 people, for a total of NT$48,551,613 (approximately US$ 1,566,181).

Patient Family Living Financial Assistance

To support households with patients with rare disorders, Patient Family Living Assistance was created in 2000 to meet the needs of patients who require long-term or intensive care. From 2001 to 2014, a total of 1,507 people were subsidised for a cost of of NT$30,072,870 (approximately US$970,092).

Long-term Care and Treatment Financial Assistance

Long-term Care and Treatment Financial Assistance was set up in 2004 to provide supplementary financial support to patients whose medical expenses are not fully covered by the government or other social welfare systems. The programme is tailor-made for financially challenged families. By the end of 2014, financial assistance had been allocated to 713 people, for a total of NT$47,018,753 (approximately US$1,516,733).

Research Grants

To strengthen academic research in the field of rare pathologies in Taiwan, the Taiwan Foundation for Rare Disorders provides research grants and scholarships to encourage advanced research among medical professionals and scholars as well as graduate students in studies related to rare diseases. Committed to facilitating gov-

Table 1: Top Ten Rare Disease Laboratory Diagnosed in Taiwan (2015)

Rank	Name of the Rare Disease	Test
1.	DiGeorge Syndrome	22q11.2 MLPA Analysis
2.	Porphyria	Urine PBG/ALA Analysis, Urine Porphyrin HPLC Analysis, Hemoglobin Porphobilinogen (PBGD) Deaminase Activity Analysis, Blood Plasma Scanning Analysis
3.	Prader Willi Syndrome	SNRPN Gene Mutation Test
4.	Wilson's disease	ATP7B Gene Mutation Test
5.	Rett syndrome	MECP3 Gene Mutation Test
6.	Tuberous Sclerosis	TSC1/2 Gene Mutation Test
7.	Citrullinemia type II	SLC25A13 Gene Mutation Test
8.	Achondroplasia	FGFR3 Gene Mutation Test
9.	Myotonic Dystrophy	DMPK1 Gene Southern blot Analysis
10.	Williams-Beuren Syndrome, WBS	7q11.23 MLPA Analysis

(Source: Taiwan Foundation for Rare Disorders)

ernment legislation, the Foundation welcomes research projects relating to diagnoses, clinical treatment, medication, long-term care, psychological needs, case studies on support groups, and big-data analysis relating to rare diseases. It is hoped that the scientific data and results collected through their research work can contribute not just to improving the quality of lives of patients and their caregivers but also to bringing them a sign of hope. As of 2014, 37 research projects had been awarded for a total of NT$15,310,000 (approximately US$493,870); 85 dissertations had also been awarded for a total of NT$3,150,000 (approximately US$101,612).

Clinical Diagnosis and Genetic Screening

Cooperation with medical Centres

In 2009 the Taiwan Foundation for Rare Disorders signed cooperative agreements with medical centres and laboratory examination centres for the diagnostic testing of rare disorders. A financial subsidy was also provided. In the year 2005, a sum of NT$3,007,405 (US$97,013) was provided for diagnostic testing. Out of the 510 cases of suspected rare disorders, 184 were accurately identified, with an accuracy rate of 36.1%. From 2009 to 2015, a sum of NT$13,434,741 (US$433,378) was provided for the diagnostic testing of 2,060 suspected cases, with 647 cases confirmed.

Cooperation with international genetic screening laboratories

Despite the advanced technology of genetic screening in Taiwan, there are limitations and these prevent individual cases from being discovered. International cooperation is therefore needed to achieve more precision in identifying rare conditions that are beyond our diagnostic capacities. The Health Promotion Administration of the Ministry of Health and Welfare of Taiwan authorised the Taiwan Foundation for Rare Disorders to offer cross-border services in sending specimens to international organisations for advanced genetic screening. In 2015, five patients with rare diseases travelled to the United States of America and Europe for genetic tests and medical treatment. Through international cooperation, victims with the rarest pathologies are given a chance to seek appropriate medical care abroad to relieve their physical suffering and emotional anxiety. These concrete actions testify that our ultimate value of human life and dignity is not to be compromised by the principle of economic returns. With the financial support of the Taiwan Foundation for Rare Disorders, a full subsidy was allocated to families with financial difficulties. From 2001 to 2015, the Taiwan Foundation for Rare Disorders offered 445 patients the opportunity to take the screening test overseas, and spent a total of NT$5,138,792 (approximately US$165,767) on genetic screening expenses.

Prevention

Second generation newborn screening

To develop screening tests for the newborn in more than 20 kinds of rare diseases (such as IVA, MSUD, and GA-1 and others), the tandem mass spectrometer is utilised to analyse the distribution of compounds in the blood of infants. In light of the progress of the technology of genetic screening, new genetic screening items have been added, e.g. pompe disease and severe combined immunodeficiency (SCID). To further create a supportive environment for families with infants who are born with genetically inherited rare diseases, the Taiwan Foundation for Rare Disorders has given grants to 141,125 patients, for a total of NT$24,923,570 (US$803,986). The philanthropic partnership comprising investment from enterprises and three screening test centres allowed 15,590 newborn babies from low-income households and aboriginal families to receive subsidies amounting to NT$3,244,350 (US$104,656). Following the principle of subsidiarity, the majority of the grant was distributed to the underprivileged and marginalised groups to maximise its effect.

Database of Specimens of Rare Diseases in Taiwan

On top of international linkages, we also pay attention to rare diseases that are indigenous in the country and among the people. The Ministry of Health and Welfare and the Taiwan Foundation of Rare Disorders took the initiative in 2013 of collaborating with Academia Sinica, the leading research institute in Taiwan, in the establishment of the Database of Specimen of Rare Disease and Taiwan Biobank. This seamless cooperation between the governmental, academic and private sectors ensured that genuine scientific study on these rare diseases could be achieved through the sharing of knowledge.

Prospects for Future Development

Treatment of patients with rare pathologies is more than a medical issue: it requires an interdisciplinary team with medical staff, social workers, psychological counsellors and pastoral specialists to ensure holistic care for patients and their caretakers, especially immediate families. For patients from financially challenged families, a well-rounded subsidy mechanism guarantees that the long-term and intensive treatment plan can be readily accessed. I strongly believe that the availability and quality of care for patients with a rare pathology and their families serves as a benchmark of a civilised society. In some ways, these patients with rare conditions are the least of our brothers. ‘I say to you, whatever you did for one of these least brothers of mine, you did for me’ (Mt. 25:40). It is in giving and caring for these patients that we live out our identity

as Catholics and disciples of Jesus. In *Ex Corde Ecclesia*, Saint John Paul II instructed us as to the dual role of a Catholic university: educating and evangelising. Likewise, a Catholic hospital can best embody its identity if the medical staff and supporting team can heal in a way that allows the patients to believe in God's love. In the prayer for the Jubilee Year of Mercy, His Holiness Pope Francis prays to Lord Jesus Christ saying: 'You are the visible face of the invisible Father, of the God who manifests his power above all by forgiveness and mercy: let the Church be your visible face in the world, its Lord risen and glorified'. As we are days away from the closing of the Jubilee Year of Mercy, let us constantly reflect on how we can cure and care for patients with a rare pathology so that they witness the mercy of God.

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3. The Spanish Federation for Rare Diseases: a Voice for more than Three Million Inhabitants of Spain

DR. SANTIAGO DE LA RIVA
Vice-President of the FEDER Foundation, Spain.

The Concept of Rare Diseases

Rare diseases, according to the EU definition, are diseases that affect less than 5 in every 10,000 inhabitants. However, in the USA rare diseases are those affecting less than 200,000 inhabitants of the United States. Therefore, the term 'rare' means of 'low prevalence' in the population. There are many different rare diseases; some are clearly physically visible and others are hardly visible since they affect the inner organs.

The Common Characteristics of Rare Diseases

80% of them have a genetic origin and are transmitted geneticallly from generation to generation. They are chronic diseases and seriously affect the lives of patients; in half of them, their lives are at risk. 30% of the patients die before they are 5 years old. There is no total cure for rare diseases (RD).

Although there are many different rare diseases, around 7,000, it is not so rare to have a rare disease. In Spain there are around 3 million people affected by one or more rare diseases. This means that around 30 million people are affected in Europe and between 6-8% of the world population, i.e. 400,000,000 inhabitants.

The Natural History of a Rare Disease

Before the diagnosis

Pathologic symptoms normally appear in early childhood, but general practitioners or primary care clinicians often ignore the diagnosis. Patients and their families suffer a pilgrimage from doctor to doctor looking for a diagnosis. The mean time to obtain a diagnosis is between 5-10 years. In the best cases, diagnosis arrives after 1-2 years. The main problem is that the health of the patient progressively deteriorates and the condition aggravates due to the delay in finding a diagnosis. Finally, the diagnosis is obtained, but since it is a rare disease, and there is no cure, and few experts, this is the beginning of the second phase of its natural history

After the diagnosis

The Spanish Federation of Rare Diseases, FEDER, through its 'information and orientation' service helps families to find specialised clinicians and associations for each diagnosed disease. The RD patient associations are the main force in looking for solutions. This is the social phenomenon known as patient 'empowering'. It is not so easy to find a specialised service for each rare disease in the health system. Families have to invest practically all their budgets to meet specialists, to buy medicines to palliate the disease, and in many cases they have to deal with the physical dependence of the patients. Social inclusion in schools and work are added problems. There is great deal of uncertainty about the future of the patients. In many cases, this future involves death.

The Feelings of Patients and Families with Rare Diseases

We can mention some examples of what patients say: "Doctors don't know anything about my disease; it is me who has to tell them about my symptoms. You feel afraid and alone thinking

that nobody can help you from a clinical point of view. Even worse, you have heard so many times the terrible sentence: 'there is no cure for your disease'".

To summarise, doctors do not know about rare diseases; there is no cure in the great majority of cases; and there is not enough documented information about them.

In some cases, affected people have described their experiences in books. For example, the case of Hayley Okine with progeria (premature ageing) who wrote 'Old before my Time'; José Antonio Fortuny suffering from spinal muscular atrophy who produced 'Talking with Axel'; and Nick Vujicic, with tetraphocomelia, who wrote 'An Unlimited Life'.

The Need to Become Stronger through Associations: FEDER

However, the best feeling of patients and families is the strength they have to come together in associations and become empowered in this way. On top of that, there are national federations of rare disease associations who defend the rights of rare disease patients and try to find solutions. This is the case of the Spanish Federation for Rare Diseases – FEDER.

FEDER represents all rare diseases, even those suffered by people who have not yet been undiagnosed. FEDER was born in 1999 from six rare disease associations. Currently there are more than 350 associations under the common umbrella of FEDER. In 2010, FEDER was deemed a non-profit organisation, of public interest, in Spain. FEDER is the national Spanish platform for rare diseases and covers more than 800 different rare diseases. FEDER represents more than 3 million people affected by rare diseases in Spain.

FEDER requests from the government a series of policies for the welfare and benefit of the rare disease community: fairness in obtaining a diagnosis; fairness in having medication and health care; support from the Ministry of Health of Spain for the endorsement of reference units in hospitals specialised in rare diseases; the drawing up of 'Patient's Pathways'; support for a national registry of rare diseases; fairness in disability evaluations; support in education in schools for children with special needs; advocacy for work inclusion and adapted working places; and the encouraging of research into rare diseases. Among all these requests, some special needs deserve a particular focus.

The Diagnosis of Rare Diseases

There is an urgent need to build a specific programme to attend to all those patients who have not yet been diagnosed. The lack of a diagnosis leads to a long pilgrimage through national and local health system centres that in many cases worsens the patient's condition.

There is an urgent need to explore the causes of 'the status of undiagnosed patient' case by case, and to promote a specific programme to reach a quicker diagnosis through genome and exome sequencing, so that clinicians may be assisted by the new technology of 'next generation sequencing' (NGS).

Research into Rare Diseases

Investigation is the only way to find a diagnosis and a possible cure for rare diseases. Only 10% of all rare diseases receive some kind of active research. But the research budget is insufficient and has been reduced since 2009 by more than 50%. This makes FEDER constantly call for an increase in the budget dedicated to research into rare diseases.

We expect from research an earlier diagnosis with a shortening of the long waiting times marked by uncertainty; an active search for therapies; and the development of orphan drugs to treat rare diseases. Only 0.4% of the total number of rare diseases has some specific treatment.

We can imagine different types of therapies by gene or cell therapy, by the discovery of new drugs and antibodies, and using repurposing or the second use of 'old known drugs'.

We could say that the search for therapies may be run with two gears. One gear for a speed race, against the clock, to find drugs which may be used immediately by the patient. Of course, these drugs are already known in other contexts and for other diseases and therefore can be used safely if they demonstrate that they are efficient in the treatment of a rare disease. At least we expect that this second use of 'old drugs' may help to stop the advance of the disease and may improve the quality of life of patients.

The other gear is a long distance race. Research is constantly looking for new compounds, engineering new genetic therapies to correct a mutated gene, or the use of multipotent health cells for replacement therapies. However, these sophisticated therapies require years of research in the laboratory and tests on animals before they can be administered to humans. The mean time for such drugs to reach the patient where they are successful is calculated as on average 10-15 years.

Patient Pathways in Spain: Reference Units of Health Care

Since Spain is divided into seventeen autonomous territories as regards its health system, we cannot speak of a single national health system. There are, instead, different autonomous systems.

This system is a problem when we consider patients with rare diseases, since it is very difficult to find specialists in all the different autonomous regions for diseases with a low prevalence.

FEDER requests that any patient suffering from a rare disease in any autonomous community in Spain should have the right to be attended to at an expert reference centre, independently of the autonomous region where the centre is allocated. However, the current situation is complicated because the decision to transfer the patient to a different autonomous health system for care is a bureaucratic matter. The lack of sufficient economic resources in expert hospi-

tals for rare diseases leads to the refusal of patients from different autonomous communities

Hitherto in Spain different centres, services and expert units have been designated by the central national health system for certain groups of rare diseases. However, there are still several groups of rare diseases for which no central government endorsement has been considered. This does not mean there are no expert centres for those groups of rare diseases. However, for political reasons, the central government has not supported them hitherto.

What Conditions should a Rare Disease Reference Unit or Centre Meet ?

First of all experience, measured in terms of the number of treated patients and years of work in relation to a rare disease. These health care providers should have specialised physicians who are patient-centred by vocation. Patients from rare disease associations should recognise the centre as reliable for the treatment of a particular rare disease. The management of the disease should be done with a multidisciplinary approach, where all the professionals and specialists of the health centre work in a coordinated way.

A Final Consideration

I would like to finish with a positive thought. Since rare diseases are a very serious problem of health and involve an important part of our society, we should try to find solutions and build bridges of understanding to deal with the political, administrative and bureaucratic problems. We should build networks of hope..

SECOND SESSION • Neglected Diseases

1. Ten Neglected Tropical Diseases in Africa: the Realities of the Local Areas and the Efforts Made to Deal with them

SR. MONICA LUPARELLO
Professor at the Catholic University of Mozambique - UCM, Mozambique

Introduction
Neglected tropical diseases

According to the publication *PLoS Neglected Tropical Diseases*, neglected tropical diseases (NTD) are 'a group of chronic infectious diseases that promote poverty and are widespread above all in rural areas and in poor urban areas in low- and medium-income countries'. In the view of the same publication, these diseases 'promote poverty because of their impact on health and development in childhood, on pregnancy, on the productivity of adults of working age, and because of their stigmatising character'.

According to the World Health Organisation (WHO), 'NTD, although they are different from a nosological point of view, make up a single group inasmuch as all of them are strongly associated with poverty, they proliferate in environments with scarce resources, especially in tropical areas, they tend to co-exist and the majority of them are ancient diseases that have afflicted humanity for centuries'.

The World Health Organisation has listed the characteristics that these diseases have in common: they constitute an indicator of the poverty of populations; they afflict above all else parts of the population with a low level of visibility and little political power; they tend not to spread geographically; they cause stigma and discrimination, above all to the detriment of girls and women; they have an important impact on illness rates and death rates; they are neglected by research; and they can be controlled, prevented and probably eliminated by using effective and practicable low-cost strategies.

A List of Neglected Tropical Diseases

The WHO at the present time includes in the list of neglected tropical diseases seventeen that are due to mico- or macro-parasites according to the classification of Anderson and May.

Diseases caused by micro-parasites. With a viral aetiology: Dengue and rabies; with a bacterial aetiology: trachoma, Buruli ulcer; endemic treponematosis and leprosy; last May micetoma was added. With a protozoan aetiology: Chagas disease (CD), human African trypanosomiasis and leishmaniasis. Diseases caused by macro-parasites (with a helminthic aetiology): cysticercosis, dracunculiasis, echinococcosis, lymphatic filariasis, trematode parasitoses transmitted by foodstuffs, onchocerciasis, schistosomiasi e helminthiasis.

Neglected tropical diseases are endemic in 149 countries, in at least a hundred of which two such diseases are endemic and in thirty of which six or more are endemic.

Neglected Tropical Diseases in Africa

Sub-Saharan Africa is the region with the greatest prevalence of neglected tropical diseases. In Africa, Nigeria is without doubt the nation with the greatest number of such diseases in absolute terms, followed by the Democratic Republic of the Congo and the nearby nations of Central Africa and the countries of the Sahel. Guinea worm disease, Buruli ulcer, and human African trypanosomiasis are present only or above all in the continent of Africa. In all the 47 countries of the region at least one neglected tropical disease is endemic and in 36 of these countries (78%) at least five are co-endemic. They have a negative impact on the physical and mental capacities of the people who are afflicted by them and they perpetuate the cycle of poverty.

Viral Aetiology

Dengue fever

Every year there are 50-100 million infections with dengue fever. Dengue fever is caused by a flavivirus and develops because of the bite of the mosquito *Aedes aegypti*. There is no treatment for dengue fever or for grave dengue fever other than palliative care.

Rabies

There are two forms of rabies: furious rabies and paralytic rabies. Every year 60,000 people die in the world because of rabies. The greatest prevalence of this disease is in rural areas and it af-

flicts children in a disproportionate way. Rabies is usually fatal after the appearance of symptoms. It is caused by a *lyssavirus* that is transmitted through wounds or insect bites by infected animals. It can be prevented through the vaccination of humans and dogs and the washing and disinfection of bite wounds (post-exposure prophylaxis). Rabies provokes hyper-activity, hydrophobia and aerophobia. Death by cardio-respiratory arrest takes place within the space of a few days. Paralytic rabies provokes a slow advance of paralysis until the arrival of coma and death.

Bacterial Aetiology

Trachoma

21.4 million people in the world have trachoma, of whom 2.2 million are partly blind and 1.2 million totally blind. This disease afflicts above all women and children. The risk of mortality with this disease is very low, even though re-infections can lead to blindness. Trachoma is caused by a micro-organism that spreads directly in the eyes or through flies. It can be treated with antibiotics. The only known method of prevention is personal hygiene.

Buruli Ulcer

It is not known how common Buruli ulcer really is. The risk of dying because of this disease is low, even though the secondary infections can be lethal. Illness from this disease takes the forms of deformity, disability and skin lesions, which can be prevented by early treatment. This disease is caused by bacteria and can be treated with antibiotics and surgery.

Yaws

The data on the incidence of yaws are limited, even though it is known that this disease afflicts above all children. The risk of dying because of this disease is very low, but if not treated it can provoke deformations and disabilities. This disease involves a chronic bacterial infection caused by treponemas. It is treated with antibiotics. It can be prevented through improved hygiene and an increase in hygiene and healthcare services.

Leprosy

In March 2013 there were 189,018 known cases of leprosy in the world and 232,857 new cases were diagnosed in the year 2012. At the present time there are 1-2 million people who have been disabled or disfigured because of past or present leprosy. Leprosy provokes physical and aesthetic disabilities if it is not treated but it is curable if it is treated early on. It is caused by bacteria and transmitted through small drops from the mouths and the noses of infected individuals.

Micetoma (Maduromicosis, Madura foot)

This is a chronic, progressive local infection caused by fungi or bacteria, which affects the feet, the upper extremities or the back, and is characterised by tumefaction or the formation of multiple fistulae. The infection advances slowly over months or even years, with a gradual extension and destruction of contiguous muscles, tendons, fasciae and bones. Lastly, the damage to the muscles, deformity, and the destruction of tissues precludes use of the limbs that have been attacked. The development of the disease can last a long time, at times for more than ten years. In cases neglected because of added bacterial infection and sepsis, death can take place.

Protozoan Aetiology

Human African trypanosomiasis

Human African trypanosomiasis is also known as African sleeping sickness. At the present time there are 10,000 cases of this disease. It is always fatal if not treated. Human African trypanosomiasis is transmitted by vectors and is spread through the bite of the tsetse fly. The current forms of treatment are highly toxic and ineffective. In addition, resistance to the medical products of such treatment is spreading. The most common symptoms are fever, headache, lymphadenopathy, nocturnal sleep, personality changes, cognitive deterioration, and coma.

Macro-Parasite Aetiology

Cysticercosis and taeniasis

Taeniasis is an infection caused by the adult taenia whereas cysticercosis is an infection by taenia larva. Both these diseases belong to the helminthiasis group. Cysticercosis is the commonest avoidable cause of epilepsy in the developing word. This disease is not fatal, even though it can cause epilepsy, whereas forms of neurocysticercosis can be fatal. Cysticercosis is usually contracted after eating undercooked contaminated pork. Taeniasis takes place after the ingestion of contaminated foodstuffs or following contact with contaminated water or soil.

Dracunculiasis

Dracunculiasis is also known as Guinea worm disease. This disease is not fatal but it can cause months of inactivity. It is caused by drinking water contaminated with small *copepoda* crustaceans infected with the larva of *dracunculus medinensis*. Dracunculiasis can be prevented through the filtration of water, the immediate identification of cases to prevent the spread of this disease, education in health, and the treatment of ponds with larvicides.

Starting in the year 2012, the four endemic countries as regards this disease have been Chad, Ethiopia, Mali and South Sudan.

Echinococcosis

Levels of echinococcosis are highest in rural areas and more than a million people are infected by this disease every year in the world. This pathology is caused by the ingestion of parasites through animal faeces. It can be prevented by worm treatment for dogs, an increase in hygiene and sanitary services, the correct disposal of animal faeces, health education, and the vaccination of livestock.

Helminthiasis transmitted from the soil

The three species of nematode worms responsible for the transmission of helminthiasis from the soil are *Ascaris lumbricoides*, *Trichuris trichiura* and *Strongyloides*. At the present time,

1.5 billion people in the world are infected by this disease. The risk of dying from this disease is very low. The seriousness of the symptoms depends on the number of worms in the body and includes intestinal problems, a lack of energy, and a compromising of physical and cognitive development of the victim. The parasitic worms are generally transmitted through exposure to human faeces found in the environment or infected soil: for example, because of the practice that is widespread in poorer countries of defecating in common open spaces. This pathology can be prevented through a hygienic preparation of food, the use of clean water, suitable sanitary services, vermifuges, and health education.

Lymphatic filariasis

Lymphatic filariasis is a disease that is also known as elephantiasis. About 120 million people in the world have this pathology and 40 million have malformations caused by it. It is rarely fatal but it has implications for the whole of a person's life, for example lymphedema of the limbs, genital pathologies, and painful recurrent attacks. Most of people with this condition do not display symptoms but are damaged at a lymphatic level. Up to 40% of individuals affected by this disease have damage to their kidneys. Lymphatic filariasis is caused by nematode worms that are transmitted by mosquitoes. It can be treated with anti-helminthic drugs which are relatively inexpensive and washing of the skin can slow down or even reverse the damage. About two-thirds of cases in the world are to be found in South-East Asia and a third are in Africa.

Onchocerciasis

Onchocerciasis is also known as 'river blindness'. 37 million people in the world are affected by this disease, with prevalence being highest in rural areas. This disease provokes blindness, eruptions on the skin, intense itchiness, and a loss of skin pigmentation. This is a disease that is transmitted by vectors and caused by worms that infect flies. Over 99% of cases of this disease are in sub-Saharan Africa.

Schistosomiasis

Over 200 million cases of schistosomiasis exist in the world. This disease provoked fibrosis of the bladder, fibrosis of the liver, portal hypertension, and cervical lesions (which increase susceptibility to HIV in women). This is a disease that is transmitted by vectors of the species *Schistosoma* which have a complex life cycle that alternates between man and fresh water snails. The infection takes place after a person's contact with contaminated water. This pathology is unique inasmuch as the damage to people who have been infected by it is not caused by the worms themselves but by the large volume of eggs that the worms produce. These cause haematuria, the obstruction of the channel of the bladder, kidney insufficiency, cancer of the bladder, and periportal fibrosis. Mass treatment with praziquantel, better access to drinking water, improved hygiene and sanitary services, and health education can be used to prevent schistosomiasis. About 85% of cases of this disease are to be found in sub-Saharan Africa.

What is Being Done to Counter Neglected Tropical Diseases?

On 25 May 2013 Pope Francis received the members of the *Centesimus Annus* Pro Pontifice on the occasion of its international conference on the subject 'Rethinking Solidarity for Employment: the Challenges of the Twenty-First Century'. One part of his message contained the following invitation: 'the need "to rethink solidarity" no longer as simply assistance for the poorest, but as a global rethinking of the whole system, as a quest for ways to reform it and correct it in a way consistent with the fundamental human rights of all human beings…We have forgotten and are still forgetting that over and above business, logic and the parameters of the market is the human being; and that something is men and women in as much as they are human beings by virtue of their profound dignity: to offer them the possibility of living a dignified life and of actively participating in the common good'.

The struggle against neglected tropical diseases involves a broad range of partners who for some time have worked together by offering donations, funds, resources, expertise, time and energy to develop, implement, and broaden strategies that involve suitable action and initiatives. Amongst these partners there are government agencies, private foundations and multinational pharmaceutical companies.

The World Health Organisation gave itself a general goal for the years 2014-2020 as regards Africa: *to accelerate the reduction of the 'burden' of neglected tropical diseases* through the control, elimination and eradication of specific neglected tropical diseases; and *to contribute to the reduction of poverty*, to the productivity and to the quality of life of people afflicted by them.

The practical goals of the World Health Organisation in Africa to be achieved by the year 2020 are the following: to eradicate Guinea worm disease and yaws in all countries in the continent of Africa; to support the elimination of leprosy and further reduce grave disabilities caused by leprosy; to eliminate lymphatic filariasis, onchocerciasis, schistosomiasis and trachoma; to control illness levels caused by Buruli ulcer, human African trypanosomiasis, leishmaniasis, helminthiasis transmitted by the soil and rabies; and to prevent disabilities caused by Buruli ulcer, leishmaniasis, leprosy, lymphatic filariasis and trachoma that lead to blindness.

This plan of the World Health Organisation for the control of neglected tropical diseases envisages the integrated employment of various strategies which strengthen each other in reciprocal fashion: 1. the development of the capacities of national health-care systems; 2. the improvement of planning, the mobilisation of resources, and the financial sustainability of national programmes to combat neglected tropical diseases; 3. the improvement of moni-

toring, assessment, surveillance and research (this principally concerns initiatives to interrupt the transmission of Guinea worm disease in Chad, Ethiopia, Mali and the South Sudan); and 4. Support for the social and physical rehabilitation of people afflicted by neglected tropical diseases (improving cooperation with other sectors such as, for example, social welfare services, education, agriculture and the economy) and contributing to their participation in the socio-economic development of their communities).

1. *Action in Relation to National Health-Care Systems Takes Place Through Various Initiatives:* The first such action is preventive *chemotherapy*. This strategy envisages the distribution of medical products on a large scale for the benefit of high-risk parts of national populations. These medical products have an extremely powerful anti-microbe activity and a very good tolerability profile, and because of this they can be administered without a clinical diagnosis having been carried out. The cost of these medical products is low because of the very substantial donations made by some pharmaceutical companies. The aim of this strategy is twofold: on the one hand, to prevent the long-term damage that these diseases can cause if they are not treated, and, on the other, to reduce their levels of transmission. The key medical products for chemotherapy are albendazole, mebendazole, praziquantel, ivermectin, dietilcarbamazine and azitromicyn. The target diseases of this strategy are filariasis, onchocerciasis, hellminthiasis, schistosomiasis and trachoma.

In Africa the groups at risk that require preventive chemotherapy range from 123 million in the case of onchocerciasis to 470 million in the case of lymphatic filariasis. Advances are being made in strengthening the capacity of national programmes to control of neglected tropical diseases in the continent of Africa. For example, the administration of medical products for lympatic filariasis, onchocerciasis, helminthiasis and trachoma reached about 203 million people at risk in the year 2011. The coverage of direct community treatment with ivermectin (CDTI) for the control of onchocerciasis has reached 80% of the population in many communities. As a result, the transmission of onchocerciasis has been halted in a number of endemic areas.

The second action is the diagnosis and intensive treatment of cases. This strategy seeks to achieve the early diagnosis of sick individuals with the goal of preventing or treating possible complications This action is especially useful for those pathologies for which a preventive therapy cannot be used given that that the medical products that are available have a significant level of toxicity. Amongst the pathologies that have been targeted by this strategy we may refer to human African trypanosomiasis, leishmaniasis, leprosy and endemic forms of treponematosis.

In Africa the management of cases relates prevalently to Buruli ulcer, with 3,443 cases; to African human trypanosomiasis, with 7,197 cases; and to leprosy with 25,231 cases. Indeed, cases of leprosy, human African trypanosomiasis and Buruli ulcer are decreasing.

The third action is *control of the vectors of these diseases*. Indeed, various neglected tropical diseases, amongst which dengue fever, Chagas disease, human African trypanosomiasis, lymphatic filariasis and onchocerciasis, are transmitted by insect vectors, whereas forms of helminthiasis such as schistosomniasis, drucunculiasis and alimentary trepenematosis need molluscs or crustaceans which operate as intermediary hosts to complete their lifecycles. This strategy, which also includes a hidden use of pesticides, must be supplemented by expertise that goes beyond the strictly health-care field and requires the cooperation of the agricultural and engineering sectors.

The fourth action consists of *improvement in hygiene and health-care conditions*. This kind of action is perhaps the most important and has a synergy with the other actions that have just been listed. In the absence of a correct water supply and appropriate sewage disposal, preventive chemotherapy, which is extremely effective in relation to helminthiasis, runs the risk of becoming useless because individuals tend to become infected again since they are exposed to the same contaminated environment.

The fourth action is made up of initiatives involving veterinary public health. Many neglected tropical diseases, amongst which cysticercosis/taeniasis, echinococcosis, human African trypanosomiasis, rabies, leishmaniasis, and alimentary trematodiasis, have an animal component, that is to say they can be transmitted to man by vertebrate animals (directly or indirectly through a vector). In addition, such pathologies, by having an influence on the health of livestock, can condition the wellbeing of a community whose economy strongly depends on such activity.

2. The sustainability and the efficacy of action in relation to neglected tropical diseases increase when that action is implemented inside national health-care systems, coordinated with other existent health-care programmes, and contributes to improvement in a given health-care system. The empowerment of people and communities is also important: the involvement of parts of populations that are afflicted by, or at risk of, neglected tropical diseases, is important for the success of actions that are taken. Communities should thus be authorised and involved in activities that promote the prevention and control of neglected tropical diseases.

In general, access to health-care services is more difficult for women, in particular in rural areas where neglected tropical diseases are highly endemic.

All actions should intentionally address or prevent problems of this type and other inequalities.

It is also necessary to strengthen the capacity of national programmes in terms of infrastructures, adequate human resources, and the supervision of qualified personnel at national, district and local community levels. Natu-

rally, it is of fundamental importance to include medical products against neglected tropical diseases in national lists of medical products.

3. Reference should also be made to the importance of scientific research, which is notoriously lacking if not completely absent in this context, as an essential instrument by which to obtain epidemiological data. Such data is of fundamental importance in planning and monitoring specific initiatives as well as in developing new diagnostic, preventive (for example vaccines) and therapeutic instruments.

It is clear, therefore, that the management of neglected tropical diseases requires a multidisciplinary approach. As regards control strategies at a local community level, as well as medicine there should be an involvement of entomology, veterinary science, agriculture and engineering, whereas with respect to their clinical management various branches of specialisation in medicine and surgery are needed, as well as ones that are more specifically a part of the humanities, such as anthropology and sociology.

The Church at the Service of People with Neglected Diseases

When speaking to the World Health Assembly in Geneva last May, Msgr. Mupendawatu emphasised the commitment of Catholic health-care institutions to 'the fight against AIDS, tuberculosis, malaria and neglected tropical diseases as well as against other transmissible diseases'. In February 2015, in his speech on behalf of the Holy See to the Social Forum of the Council of Human Rights on access to medicines, Msgr. Tomasi, the permanent observer of the Holy See, called the attention of the participants to two obstacles in the way of access to medicines: 'the weak incentive for the so-termed 'non-market' or 'low investment return' forms of treatment, such as those for neglected tropical diseases rare diseases, or even those diseases that have the greatest incidence amongst low-income populations' and the difficulty that derives from the fact that 'many essential medicines have not been developed with appropriate formulations or specific dosages for paediatric use'.

These two speeches, in my opinion, offer the key by which to read the *activity of the Church at the service of people with neglected tropical diseases*:

– On the one hand, a 'glorious' history of commitment and sacrifice on the part of a large number of men and women missionaries who, often in difficult conditions, have taken care of sick people, offering at times more the help of compassion and essential measures of hygiene than the help of medical products which, in fact, did not exist or were still not available; a history of commitment to the creation of wells, the health-care education of mothers…which still continues today, above all in those areas that are most distant from large urban centres.

– On the other hand, sensitisation and/or denunciation in great assemblies, as well as in the communities from which men and women missionaries come, of these diseases…or, to put it better, of the lives of so many of our brothers and sisters who are severely tested and deprived of the most elementary rights.

– From my experience, I can say that at the present time the health-care institutions and entities that belong to the Catholic Church or that work with mixed ownership with national or regional governments are called to place their activities within the framework of the health-care programmes of such governments, thereby offering spaces, structures and personnel to the implementation of the initiatives described above. This cooperation, which today we call 'working in a network', is as necessary as it has ever been in order to avoid thee waste of energy and resources and the scandal of division as regards serving the human person. However, this is not without its difficulties because often powerful international organisations impose on governments, and governments impose on those who work with them, measures which are not always in conformity with Catholic morality, measures that create embarrassment, perplexity and at times also preclude the achievement of effective cooperation.

Mozambique

Schistosomiasis and helminthiasis are present throughout the country. In the year 2010 47% of children between the ages of five and fifteen suffered from urinary schistosomiasis and 53% of them suffered from helminthiasis.

Lymphatic filariasis is endemic in the North and the Centre of the country, with high points of 82% in some districts of the region of Nampula. 16 million people are at risk of contracting this disease out of a population that was estimated in 2013 at 25.83 million.

Trachoma: in the year 2011 a prevalence of this disease of 32% was registered in the North of the country. Onchorcerciasis is also present in Mozambique.

In 2008 the country had a leprosy prevalence rate in the country of 1 in every 10,000 inhabitants, which corresponds to the elimination of this disease at a national level, even though such is not the case in all regions of the country.

In the year 2008, Mozambique adopted the Programme for the Control of Neglected Tropical Diseases, beginning with mass activity in this field in 2009. The programme until the year 2017 envisages the treatment of about 16 million people with onchocersiasis and filiariasis and 7 milllion children with schistosomiasis and helminthiasis.

In 2010 the government approved a strategy for controlling rabies for the period 2010-2014, involving the estimated sum of €50,000 in order to reduce the incidence of rabies in Mozambique. The initiatives envisaged for this strategy were: sensitisation of the population to the importance of vaccination against rabies, the rounding up of wild dogs, and the implementation of campaigns for the vaccination of dogs.

In Mozambique, according to calculations of UNICEF (2014), 53% of the population has access to

sources of drinking water whereas 39% of the population still practises defecation in the open.

The results achieved as regards making the environment healthy have been rather low compared to the advances achieved in the field of access to drinking water. Less than one in every four inhabitants of Mozambique practice methods that separate human waste from human contact in a hygienic way and this constitutes a grave threat to the health of children and is the cause of the majority of deaths because of diarrhoea in overall terms.

Notwithstanding the enormous improvements in this field since 2008, when the coverage was even weaker, Mozambique is far from achieving – in particular as regards its goals of improvement in this area – that of halving by the year 2015 the percentage of people without sustainable access to drinking water and to minimum measures of hygiene.

Last May there took place the '*Campanha nacional de tratamento massivo da filaríase linfática, bilharziose e parasitoses intestinais*' whose principal targets were about 4,000 people in Zambézia, a million and a half in Cabo Delgado and more than 800,000 in the Province of Niassa.

Campaigns for the treatment of intestinal parasites were engaged in at regular intervals throughout the country, even in the most inaccessible, in order to facilitate access to medical products on the part of children of all ages and mothers who encounter difficulties in going to dispensaries or hospitals.

Conclusion

To employ the words of Pope Francis we could say that these, too, are 'outermost fringes of society…How many uncertain and painful situations there are in the world today...wounds borne by the flesh of those who have no voice because their cry is muffled and drowned out by the indifference of the rich! During this Jubilee, the Church will be called even more to heal these wounds, to assuage them with the oil of consolation, to bind them with mercy and cure them with solidarity and vigilant care. Let us not fall into humiliating indifference or a monotonous routine that prevents us from discovering what is new! Let us ward off destructive cynicism! Let us open our eyes and see the misery of the world, the wounds of our brothers and sisters who are denied their dignity, and let us recognize that we are compelled to heed their cry for help!' (The Bull *Misericordiæ Vultus*). ■

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REGIONAL STRATEGY ON NEGLECTED TROPICAL DISEASES IN THE WHO AFRICAN REGION 2014–2020, © WHO Regional Office for Africa, 2014

2. Buruli Ulcer

FATHER FLORENT G.B. PRIULI
Medical doctor,
The Saint Jean de Dieu Hotel of Tanguiéta,
Benin

Introduction

Buruli ulcer is a highly disabling skin disease that is caused by a micro-bacterium called *Mycobacterium ulcerans*. It is a tropical disease that in the main afflicts children under the age of fifteen. It is an emerging threat to public health in a large number of damp inter-tropical rural regions, in particular in central Africa and western Africa (where it is endemic). Over recent years it has become the third micro-bacterial disease to afflict man after leprosy and tuberculosis. In some regions of Benin, Ghana and the Ivory Coast its prevalence is greater than these two diseases.

Buruli ulcer is an affliction that remained neglected for a number of decades because it causes only a few deaths. Nonetheless, Buruli ulcer is often the cause of important functional disabilities. In Africa it is the source of handicaps affecting movement and of important forms of disability. For a long time, because of its marginal character, it only provoked the interest of Catholic and Protestant missionaries which explains why the first research group of the World Health Organisation in 1988 was made up for the most part of missionaries working with local and international medical doctors. This also explains the great experience of religious confessional hospitals in Benin (Tanguiéta) and Togo (Afagnan) in treating this disease. I will offer here the testimony of that experience.

The History and Geographical Distribution of Buruli Ulcer

History

Mycobacterium ulcerans was described for the first time in 1897 in Buruli Country in Uganda. The first observations were published in Australia in 1937 and then in the Belgian Congo in 1942. Since the 1980s there has been an extraordinary increase in cases of this disease in the world. In 1988 the World Health Organisation launched an international initiative against Buruli ulcer (the Yamoussoukro conference) to coordinate specific activities to fight against, and conduct research into, this disease.

Geographical distribution

At the present time the presence of Buruli ulcer has been registered in thirty-six countries, above all in tropical regions with a warm and humid climate, in Africa, South America, Asia and the western Pacific.

– In Africa: Angola, Benin, Burkina-Faso, Cameroon, the Ivory Coast, the Congo, Gabon, Ghana, Guinea, Equatorial Guinea. Liberia, Malawi, Mali, Nigeria, Uganda, the Democratic Republic of the Congo, the Central African Republic, Senegal, Sierra Leone, the Sudan and Togo.

– In Latin America: French Guyana (the most important endemic point in the Americas), Bolivia, Mexico, Peru (the Amazonian forest), Suriname.

– In Asia: India, Indonesia, Malaysia, Japan, Sri Lanka, China.

– In the Pacific: Papua New Guinea, Kiribati (Micronesia), Australia.

Outbreaks of this disease have been limited geographically and have nearly always been around an aquatic ecosystem, near to slow moving watercourses (ponds, marshes, artificial or natural lakes, swampy areas, irrigation systems, rice paddies…). In the year 2014, about 2,200 new cases were registered in twelve of the above thirty-six countries but many others were not diagnosed because people afflicted by this disease largely come from poor and rural areas. The majority of cases are located in western Africa and central Africa, including Benin, Cameroon, the Ivory Coast, Ghana and the Democratic Republic of the Congo.

In Benin, Buruli ulceri is endemic in some regions of the centre and the south of the country (Ouinhi, Zogbodomey, Lalo...).

Forms of Transmission

Buruli ulcer tends to afflict children from the age of two onwards (over 50% of cases of this disease afflict children under the age of fifteen), without distinction of sex. In adulthood it afflicts women more than men (the role of water basins). Often groups of cases of this disease take place around water basins where the water is not drinking water. The transmission of this disease in humans is probably directly through the skin starting with the hydrotelluric water area. Various scenarios have been mentioned: traumatic lesions (cuts, open sores) could become infected when there is more or less prolonged direct contact with water that is contaminated with *Mycobacterium ulcerans*; *Mycobacterium ulcerans* present on the surface of the skin could be introduced into the tissue below the skin by various traumas (insect bites, bites, wounds caused by mines or firearms); and insects from water infested by *Mycobacterium ulcerans* could transmit the disease through insect bites. The role of insects as hosts of *Mycobacterium ulcerans* has by now been clearly established and their role as vectors has been demonstrated at an experimental level. This is

Figure 1: the Distribution of Buruli Ulcer in the World

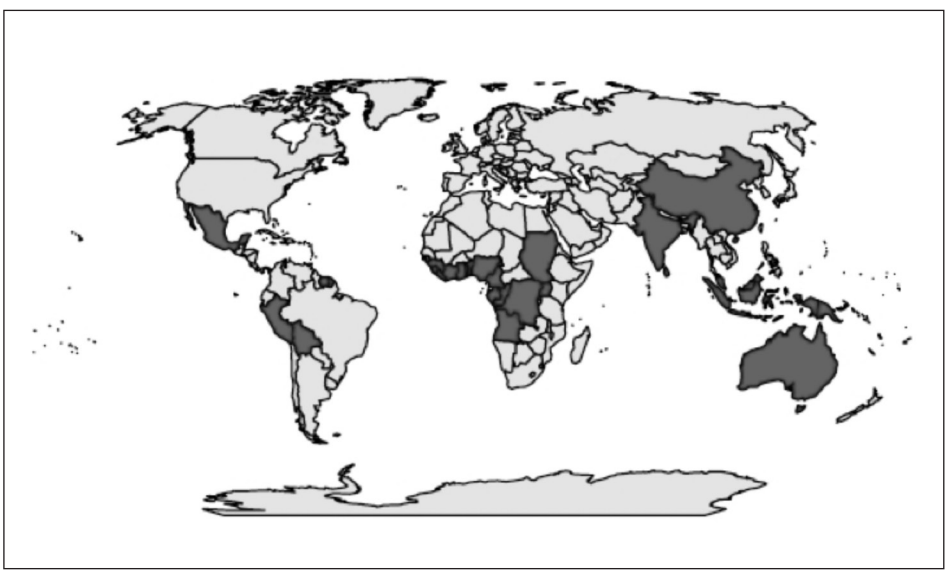


Figure 2: the Distribution of Buruli Ulcer in Benin

confirmed by the fact that living bacilli have been identified in the saliva of these insects. However, the importance of insects in the aetiology of *Mycobacterium ulcerans* remains unknown and this role is difficult to explore because of a lack of knowledge about the biology of these insects. A recent study carried out in Cameroon has enabled us to eliminate the possible role of mosquitos or other domestic insects in the transmission of this disease through the use of mosquito nets as a form of protection.

Symptoms

The manifestations of this disease are due to a necrotising infection of the skin and the soft tissues by a pathogenic agent. This microorganism produces a special toxin, known as mycolactone, which provokes lesions of the skin tissue and inhibits an immunity response. This disease can attack any part of the body but most of the lesions are on the limbs: the lower limbs (60%) and the upper limbs (30%).

Early diagnosis is very important in assuring a better prognosis for the patient. After an incubation period that can vary from a few weeks to a few months, Buruli ulcer develops in three stages:

The Pre-Ulcer Stage

This is the stage when the disease emerges and it can take four clinical forms: nodules, papules, plaques and oedemas. The first symptom is a nodule which develops into plaques and oedemas, before the ulcer itself appears.

– The nodule is the most frequent form. It begins in an area below the skin and it is hard and clear in outline, being one to two centimetres in diameter. Most of the time there is only one such nodule, it is painless, cold, mobile and accompanied by a loss of pigmentation of the adjacent skin surface.

– The papule commences with a notable lesion of the skin which is painless and less than one centimetre in diameter, accompanied by a reddening of the adjacent skin surface. This form is to be observed above all else in Australia.

– The plaque has a hardened look, it is hyper-pigmented, it is more than two centimetres in diameter, it has irregular fringes and it is painless.

– The oedema form involves the sudden or gradual appearance of an oedema which tends to expand to an entire limb, with an extensive coverage of the area where the ulceration began. It can be accompanied by local signs of inflammation and by a high temperature.

We should lay emphasis on the nodular form. In an area where the disease is endemic, a cold and recent nodule, visible in outline, and mobile at deep levels, is a nodule that should be suspected as being an example of Buruli ulcer. Its removal is recommended and it will heal over in four weeks; a relapse will not then follow.

The Ulcer Stage

Buruli ulcer develops in a hidden way and when the ulceration appears it evolves very slowly and remains painless, without systemic symptoms. It appears in any part of the initial lesion and expands more or less rapidly. It involves a more extensive loss of the cutaneous substance, with 'undermined' fringes; it is painless or not very painful, with irregular outer rings. Its development is often long and marked by complications, above all of an infectious kind.

The Cicastrisation Stage and Thereafter

The spontaneous cicatrisation of the lesions appears after various months of the development of this disease. It is the consequence of the cleansing of the ulcer, of the joining of the edges from where the skin ailment begins. The scar tissue is fibrous, sclerotic and there are frequent definitive disabilities such as retraction, ankylosis, amputation or the loss of a limb, and lymphedema caused by scar necking.

Special Forms

Osteomyelitis

Osteomyelitis is a special form of Buruli ulcer. Its frequency is estimated at 14% of cases. It is believed that this is a return of the disease during the course of its development, with damage to the bone. 41% of cases of osteomyelitis relate to the disease, these are contact examples of osteomyelitis, as against 59% which have metastatic origins.

Damage at different points

Various identical or different lesions can co-exist in the same patient. However, this takes place with a relative conservation of his or her general state in a context where there is no high temperature.

Treatment

Medical treatment

Medical treatment involves anti-biotherapy lasting eight weeks that leads to a reduction in the size of the lesions and thus reduces the scale of the surgical operation if this is necessary. In the case of less extensive lesions, this is often sufficient in one case out of every two without having to resort to surgery. In practice, a combination of rifampicin and streptomycin is prescribed. More recently (2011), a French team has tested a promising treatment in Benin, supported by the World Health Organisation, which associates rifampicin with clarithromycin. Buruli ulcer is also treated through the application of montmorillonite clay. At the *Saint Jean de Dieu* Hospital of Tanguiéta we have the advantage and the good luck to have an alternative treatment available – ozone therapy. Because of its cicatrizing, anti-biotic and hyper-oxygenation properties, the ozone used locally for lesions allows an improvement in the treatment of ulcerous lesions.

Surgical Treatment (examples from the hospital of Tanguiéta)

This is based in essential terms on the surgical removal of necrotic tissues and on reparatory

skin grafting. This was the chosen treatment for a number of decades until the spread in 2004 by the World Health Organisation of a recommendation directed towards using anti-biotic therapy in the treatment of Buruli ulcer.

Treatment of the Consequences of the Disease

The treatment of the consequences of Buruli ulcer is often of a surgical character and belongs to the category of plastic surgery. It may be necessary to correct the scar retractions of the limbs. In some situation, it is necessary to have an artificial limb where a limb has been amputated or to have a number of sessions of kinesiotherapy to rehabilitate a limb that lost its ability to function during the illness.

Prevention

Early diagnosis and treatment are the only means that exist to reduce the incidence of this disease to the minimum and to avoid disabilities in the long term. For this reason, Buruli ulcer needs mass campaigns for its early identification: in the Ivory Coast, the ascertainment of nodular forms advanced from 54% of cases in 1998 to 72% of cases in 2001. The best results have been seen in Australia and French Guyana where patients have a medical examination when the disease is at a very early stage and they receive early treatment for their condition.

Health-care education must seek to inform rural populations exposed to the risk of contamination by the hydro-telluric environment when they frequent stagnant basins of water.

Prevention is based upon the frequent washing of clothes, treating lesions with anti-septic solutions, and the need to wear clothes during agricultural work.

It has been demonstrated that the incidence of this disease diminishes in children vaccinated with BCG. The efficacy of vaccination with BCG has also been demonstrated in the prevention of complications affecting bones.

The Role of Protection of the Use of Mosquito Nets

In order to study the risk factors of this disease, the characteristics and the lifestyle of patients afflicted by Buruli ulcer and of people without the disease (in total 168 ‘couples’ of individuals) were compared in a region where the disease is endemic in Cameroon, in the districts of Akonolinga and Ayos, near to the swamp of Nyong.

The risk factors that were identified are in particular: contact with stagnant water; the fact of wearing short clothes during agricultural activity, and the erroneous treatment of lesions. The factors working for protection that were described are: the use of a mosquito net, the frequent washing of clothes, fishing in the waters of the Nyong, and the correct treatment of lesions with anti-septic solutions. The authors conclude that ‘the possible role of mosquitos or other insects present in the domestic environment in the transmission of the disease should be studied’.

FRIDAY 11 NOVEMBER

ROUND TABLE
Socio-Political, Economic and Juridical-Ethical Aspects from the Point of View of Respect for the Lives, the Dignity and the Rights of Patients and the Commitment to be Welcoming and Supportive

1. The Human, Social, Political and Economic Problems of People with Rare Pathologies

MR. KRZYSZTOF ŁANDA
Ministry of Health of the Republic of Poland

Patients suffering from rare and ultra-rare medical conditions have to face a number of difficulties. Access to medical staff who are specialised in a given condition is often limited. In addition, the diagnosis of rare disorders can be a challenging task. This is mostly due to a lack of awareness and limited access to diagnostic services. Often patients have to pass through several health-care providers who multiply unnecessary medical tests in reaching the final diagnosis. This obviously takes time, costs money, and last, but not least, exposes patients to additional distress.

But one of the most important issues when discussing problems of patients with rare diseases is the funding of their treatment. Limited access to innovative medical therapies for patients suffering from rare and ultra-rare diseases often has economic reasons.

The term 'orphan' refers to a medical action. The terms 'rare' or 'ultra-rare' refer to a medical condition or a disease. An orphan action may be considered the only action of proven efficacy in a rare or ultra-rare condition (the clinical definition of an orphan action). However, orphan medicinal products are subject to legal regulations. Consequently, system definitions are used and the term 'orphan medicinal product' represents a complex entity.

The return on investments depends on the number of patients and the product's price. A market price ensuring fair profits to the manufacturer should correspond to the number of treated patients (profits should also reflect the therapeutic innovativeness of the product). It should be stressed here that the number under consideration includes not only patients with a specific condition but the total number of patients with all indications with whom the product is used. Therefore, if with time the product proves effective not only in one but in many conditions, and the total number of patients treated in a specific country subsequently grows (e.g. to 100,000), the regulatory authorities should no longer accept the very high price of the product that was initially indicated with a small number of patients (e.g. 1,000). The manufacturer, in turn, should demonstrate adequate flexibility in relation to the internal pricing strategy if additional therapeutic indications are registered for the product or refunding is obtained in additional groups of patients. Obviously, the manufacturer is reluctant to lower the price once it has been agreed upon. Therefore, mechanisms allowing for an effective and rational pricing policy should be present in an efficient health-care system. This is especially important in the case of highly expensive health technologies used in rare and ultra-rare diseases.

The greatest problem concerning the refunding of orphan products is their high price. However, the prices of orphan drugs may vary significantly. If the manufac-

turer can expect high profits following the refunding of a product, much more restrictive procedures should be applied in its assessment. If an orphan drug is a real therapeutic innovation, its high price should in many cases be accepted. However, if the product's innovativeness is limited or uncertain, the acceptance of a high price for the product is not justified.

In case of high-cost and very high-cost drugs, the acceptable risk of estimations should be much lower than with low-cost drugs. Manufacturer's explanations that conducting appropriate high-quality randomised trials or introducing registers complying with good registry practice (GRP) were not possible are usually unreliable. Difficulties in enrolling a sufficient number of patients are in most cases obviously exaggerated. Economic difficulties in conducting high quality randomised trials may be true but only in the case of drugs with a low price compared to the sales levels and when pre-registration state assistance is not available. However, there are numerous examples of orphan drugs with exorbitant prices that make huge profits for their manufacturers who are nevertheless still reluctant to perform appropriate high-quality clinical trials: probably they are afraid of the results. Economic aspects are not raised very often by manufacturers who receive substantial financial support for research from public institutions.

High-cost orphan drugs may be regulated with different levels of rigour. Nevertheless, the higher the price of a drug, the stricter the regulations that should be enforced in relation both to its assessment and to its use.

Certain orphan drugs may be covered on a refunding list, usually after the indications and rules concerning prescription monitoring have been precisely defined. Some may be placed in other areas of the BBP, e.g. therapeutic programmes with strict inclusion and exclusion criteria for entitled patients and restrictive reporting systems, separate for each orphan drug therapeutic programme. Specific high-cost orphan drugs and very high-cost orphan drugs may be covered on a 'fee for service' basis, from a separate budget, and listed in a separate part of the basic benefit package, e.g. the 'orphan drugs refund list' or together with other very high-cost 'highly specialised procedures'. Although systemic arrangements vary between countries, some common solutions do apply.

Pricing and refunding decisions may be made by different committees and/or different public authorities. Nevertheless, the criteria, procedures and responsibilities should be transparent, precisely described and based on legal acts of appropriate importance. The higher the cost, the more restrictive are the processes of assessment and appraisal that usually take place. Requirements concerning evidence for very high-cost orphan drugs should be higher than for low cost-drugs. As with other 'non-orphan' high-cost drugs, the following analyses should be required: an efficacy and safety analysis based on a systematic review; a treatment cost analysis; and a budget impact analysis.

All analyses should be in comparison to optional treatment, wherever this is possible and clinically applicable. It is understandable that for orphan drugs available evidence may be scarce and of lower quality than is required.

Nevertheless, available evidence should be identified by means of a systematic review and its quality and precision of estimations should be assessed, thus making it possible to manage the 'project risk' (i.e. to determine the risk of making a wrong decision due to actual effectiveness being lower than the efficacy presented in the analyses and costs being higher than expected).

Economic analyses, including cost-effectiveness or cost-utility analyses, are usually not required in the case of orphan drugs (and in most cases such analyses would contribute nothing to the process of decision-making). However, instead of economic analyses rational justification of the price should be required, taking into account all possible indications (including off-label and soft label use if refunding in registered indications is granted); at times the costs of R&D and production; the planned costs of marketing following the obtaining of refunding; the business activity of the manufacturer in a specific country; the proposed price agreements, etc.

It should be stressed that the cost of developing required analyses and price justifications is usually a very small proportion of the envisaged annual (even taking only one year into account) income of a pharmaceutical company producing a drug, if it is covered. Moreover, the product's dossier usually contains a complete set of analyses developed in other countries that may be adapted to the circumstances of a specific country and therefore the financial risk associated with supplying analyses should be considered very small and the requirements reasonable. On the other hand, decision-making without a proper set of analyses is associated with a very high risk and usually leads to wrong coverage decisions that are badly received by the public and sometimes entail serious consequences.

Official decisions cannot be justified without high-quality analyses. Reporting systems for ultra-rare diseases, both for high-cost and very high-cost orphan drugs should collect data on: patients' characteristics (confirming the fulfilment of the inclusion criteria); efficacy and safety (clinically important primary endpoints according to the principles of EBM); and data on major cost-generating events. Such reporting systems should be similar to clinical and economic registers designed according to the principles of good registry practice. Registers for ultra-rare diseases should not only function as a tool of control (the inclusion of appropriate patients and reporting of drug utilisation). They should also collect data on efficacy, safety and general costs associated with illness management. Such 'real life' data make it possible to verify the initial assessment of costs and effectiveness and therefore the initial (sometimes provisional) positive refunding decision, if data

are properly collected according to GRP principles.

If a high-cost orphan drug is placed on a refunding list, special rules concerning its use in individual patients should be considered. A physician's decision concerning the use of a specific orphan drug in a given patient may, for example, require verification and/or authorisation by a supervising authority.

There may be different levels of such supervision: the head of a ward, a hospital therapeutic committee, a hospital director, the competent regional health authority, the national consultant in a specific specialty, the health insurance institution, or the Minister of Health. An initiation of treatment may sometimes require the consent of at least 2, 3 or even 4 of these supervising authorities, provided in writing and using a special form. The physician's application for consent to use a specific high-cost orphan drug in a patient with specific characteristics may be submitted via e-mail or by phone. Such a system works, e.g., in Austria, where an answer from an insurer is usually obtained within 2-3 minutes. Another solution is a regulation that only highly specialised physicians in appointed hospitals are allowed to use or prescribe high-cost orphan drugs. This, however, may entail negative consequences, including an increased risk of corruption, especially where there is not appropriate control or a restricted utilisation monitoring system. Waiting lists are sometimes introduced, although they are widely criticised on the grounds of equal access to health care, controlling the development of an illness in a patient while awaiting treatment, etc.

The availability of high-cost orphan drugs, as can be the case with other expensive drugs, may be increased by means of efficient risk sharing schemes and price agreements between the manufacturer and the regulatory authority, developed in parallel and confirmed prior to the decision about refunding.

To sum up, a different approach to decision-making about refunding for orphan products is needed. The utilitarian approach used for technologies aimed at 'common illnesses' is not suitable for orphan medicinal products. A shift in the direction of an egalitarian approach to the decision-making process about refunding is vital. Price justification rather than a full economic evaluation seems to be a solution for the assessment of orphan products. In addition, separate refunding budgets earmarked for the treatment of rare and ultra-rare diseases should improve access to innovative therapies for patients suffering from such diseases.

2. Subsidarity, the Common Good and the Promotion of Life

H.E. MSGR. VINCENZO PAGLIA
President of the Pontifical Academy for Life, the Holy See

1. The title of this round table conference includes a large number of topics that are of important relevance at the juridical, political, economic, sociological and ethical levels. They are inherent in the lives of very many men and women that are marked by the painful experience of illness. For my part, I would like to emphasise just one aspect – that of the responsibility that the whole of society must feel for the promotion of life, and above all the lives of the weakest individuals, as a 'common good'.

2. One point of departure on this horizon is the principle of subsidiarity. This means that higher communities must respect the relatively autonomous activity of lower or intermediate groups and that they have the moral obligation to help lower communities when these last are not able to achieve on their own their pre-established goals. In the social doctrine of the Church this principle is a fixed point. John Paul II, in *Centesimus annus* (1991), observed when criticising the excess of a 'Social Assistance State', that ' a community of a higher order should not interfere in the internal life of a community of a lower order, depriving the latter of its functions, but rather should support it in case of need and help to coordinate its activity with the activities of the rest of society, always with a view to the common good. By intervening directly and depriving society of its responsibility, the Social Assistance State leads to a loss of human energies and an inordinate increase of public agencies' (n. 48).

This principle, in order to be implemented and to produce results, must recognise that the foundation of its intrinsic constitution is the inescapable principles of freedom and responsibility. Freedom, indeed, is the foundation of subsidiarity and of the ways in which

it can take practical form in action. If the State recognises that the so-termed lower groups or lower communities can achieve specific objectives in an autonomous way, this means that it sees in freedom its principle of reference, and for associations, movements, foundations, macro-aggregations etc. to act, they, also, must see freedom in the same way as their founding principle.

3. But is it enough to appeal to the principle of freedom alone as the first and absolute principle? In reality this principle must be conjoined, if it wants to be truly vital, that is to say at the service of man, with the principle of responsibility. In the teaching of the Catholic Church, indeed, the principle of subsidiarity is only one side of the coin. On the other side, there is the principle of sociality from which the former principle can never be disjoined. This means that the agent, whether an individual or a community, achieves his or its own 'good' not only when his or its private self-interests are looked after, but also when he or it is concerned and work to ensure that others around him or it achieve their own good. It is precisely through this sociality that an individual or a community grows: by being enriched by the other. The entire structure of solidarity between individuals, and between communities and peoples, can be understood only by looking, at the same time, to the principles-duties of sociality and subsidiarity.

If this does not take place, an individualistic and in the end nihilistic negative dynamic is inevitable. Absolute freedom – removed from every tie (in Latin *ab-solutus*) – is in contraction with the radical relational reality that the human person is. The myth of 'absolute' freedom is leading our Western society towards a new dictatorship, the dictatorship of the 'self'. Some philosophers, such as Gilles Lipovetsky, have spoken about a 'second individualistic revolution'. This means that in contemporary society the cult of hedonism and psychology, the choice of the privatisation of life and the acquisition of autonomy by individuals in relation to collective institutions, have become a common norm and a shared value. In this horizon, an individualism without limits grows stronger and as a consequence the sense of community grows weaker. And, as Todorov observes, a new tyranny appears: the tyranny of individuals. Indeed, whereas in the regime of ideologies there was an exaggerated collectivism, today the opposite is happening. The pendulum, it appears, has swung to the other side and no longer seems capable of a balanced position.

The individual is pushed towards a total self-determination. It is as though the 'soil' (the image comes from the psychoanalyst Catherine Ternynck) in which man grows is drained of relationships. But without thus lymph the soil remains sandy, crumbly, insubstantial. And it is difficult, if not impossible, to build solid human social relationships on such a terrain.

Some scholars speak about an 'egocracy' (on the civil front) and 'egodolatry' (on the 'religious' front). On such a horizon, the elimination of an embryo for the most varied of reasons becomes licit; one can interrupt the development of the life of a malformed foetus because it bears a quality of life not suited to common standards, which are defined in utilitarian terms; resort to euthanasia is hoped for because a patient who is incurable, although he or she can be treated for example with palliative care and in relationships of care, does not have the right to citizenship in a society where the quotient of happiness must always, and whatever the case, prevail; and so forth.

The absolute freedom of the 'self' breaks down and pulverises society and thus individuals as well. One could say that we are all more free but certainly we are all more alone, more slaves.

In reality, freedom is, in opposite fashion, a relationship with the other; it is co-existence with the diverse; it is a drive to create a supportive world. Freedom is such only if it places us in a virtuous relationship in order to build up a society on the human scale. It is always *freedom for* the Other, for beyond, for a supportive, free and dignified world for everyone, starting with the weakest. We ourselves, for example, are free *hic et nunc* because our parents re-cognised the true meaning of life and thus gave us the possibility, in the name of a *freedom for*, to be able to express our constitutional freedom through the founding value of life. Only through the recognition of the intangible value of life can freedom be disclosed.

In *freedom for* there takes place the transformation of foreigners into moral friends; the principle of subsidiarity takes on a profoundly ethical meaning; and a family and social fabric is constituted in which the other is equal by essence and therefore by value. There no longer exists the malformed, the diverse or the foreigner: there exists only the person who, like us, calls for our help, for our intervention, for sharing and communion-union and not only for aseptic and anonymous co-existence.

Freedom without responsibility is empty of social value. Indeed, responsibility – from the Latin '*rispondere*' – requires us to see the other as an essential part of our being, as we are reminded by the ancient account to be found in the Book of Genesis: 'God created man in his image; male and female he created them' (Gen 1:27). And to their alliance God entrusts responsibility for stewarding the creation and the generations. Into this dual task freedom is written, as well as responsibility for looking after the creation and the generation of life.

4. And this dual mandate leads us to see life as a *common good*. Expressed in other terms, the intangible value is recognised of the creation and of human beings, of the life of the human foetus or the neonate, and of the weak, the sick, the 'diverse', the elderly – of every human person. Each of these has an intrinsic value and is linked indissolubly to the community as a whole. The defence of life and its promotion cannot constitute the need of individuals or of social micro-aggregations: it has to constitute the common denomina-

tor of a society that is based upon the fundamental rights of the human person.

Political justice itself and the promotion of life can be founded, or can be given practical form, only on the basis of the classic interpretation of the *common good* as distinct from that based on a theological-utilitarian approach of the *public good*. A. Rosmini observed about the common good: 'it is the good of all the individuals that make up the social body and are part of the law', whereas the public good, in his view, was 'the good of the social body taken as a whole'. The consequence of the confusion, which is not only terminological but also and above all conceptual, is that, again to use the words of A. Rosmini, '*the* principle of public good takes the place of the principle of common good; justice is replaced by utility; politics, taking Law into its own overbearing hands, makes of it that government which it finds most pleasing' (*The Philosophy of Law*).

Thus the common good can be defined as the set of the those ethical-social-economic-political conditions that foster the integral development of the person. By integral development is meant the development of the body and the spirit, in a recognition of the single totality of the human person. John XXIII wrote in *Pacem in terris*: 'In this connection, We would draw the attention of Our own sons to the fact that the common good is something which affects the needs of the whole man, body and soul. That, then, is the sort of good which rulers of States must take suitable measure to ensure. They must respect the hierarchy of values, and aim at achieving the spiritual as well as the material prosperity of their subjects' (n. 57).

This approach was upheld as early as the Universal Declaration of Human Rights (10 December 1948): 'All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood' (art. 1); 'everyone has the right to life, liberty and security of person' (art. 3). The defence of life as a common good is a fundamental right; it is an original and not derived right; it is equivalent to a natural right and its positive aspect is exercised fully; and it must not be violated by anyone and it cannot remain a mere affirmation of principle but must be translated into concrete realities that are accessible to everyone. As a right of everyone, the defence and promotion of life is therefore a common good.

As such, it is first of all the responsibility of institutions, but always also the outcome of the active and responsible participation of the whole civil community, in all its forms of expression. The common good is a single thing, even though it has different practical declinations; it is always the good of everyone and of each person; it is always the good of the person and as such it finds in nature and in the dignity of nature its first reference point and its litmus paper.

We should remember the lesson left to us by Jacques Maritain who wrote as follows in his book *The Person and the Common Good*: 'Thus the end of society is not the individual good or the collection of the individual goods of each of the persons that make it up. Such a formula would dissolve society as such to the benefit of its parts: it would go back either to an openly anarchic approach or the old anarchic approach masked by individualistic materialism, according to which the entire duty of the city is to watch over respect for the freedom of each person, through which the strong freely oppress the weak. The end of society is the good of the community, the good of the social body…The common good of the city is neither a simple collection of private goods nor the good of a whole that (like a species, for example, sees its individuals, or like a bee-hive in relation to bees) benefits itself alone or sacrifices its parts for itself… the common good of the city involves and requires the recognition of the fundamental rights of persons (and those of the rights of family society where people are engaged in a more primitive way in political society) and itself involves as a principal value the highest access possible (that is to say compatible with the good of everyone) of persons to their lives and their freedom to develop, and to their communications of goodness which in their turn proceed from this'.

This what Pope Francis asked us in a provocative way some days ago when speaking to the Popular Movements: 'What is going on in the world today that, when a bank fails, scandalous sums of money suddenly appear to save it, but before this bankruptcy of humanity not even a thousandth part is allotted to save those brothers and sisters who suffer so greatly?'

The story of every man, however weak or apparently useless he may be, is a valuable treasure of the whole of humanity, and the social bodies of a community, rediscovering new vigour and the capacity to make positive proposals, are called to place themselves at its service, within a reestablished framework of a fertile dynamic between me and us, between the individual and society.

In this way, we can put into practice the ancient adage of the Talmud: 'Whoever saves a life, saves the whole world'.

3. The Mission of EURORDIS: the European Organisation for Rare Diseases

MS. SIMONA BELLAGAMBI
Member of the Governing Board of EURORDIS, Italy

EURORDIS is a non-governmental federation of associations centred around patients and led by patients that represents thirty million patients with rare diseases in Europe. Its mission is to create a strong pan-European community of associations of patients and people with a rare disease; to make their voices heard at a European level; and indirectly or indirectly to diminish the impact of rare diseases on their lives. Affiliations have grown constantly since 1997, the year of its foundation, and its organisation reflects the approach of sharing by which activities involving co-operation with its own members and national federations and European federations that are concerned with a specific pathology are planned and developed.

What is a rare disease? In Europe a disease or a disturbance is described as 'rare' when it afflicts less that 1 in every 2,000 citizens. At the present time, between 6,000 and 8,000 rare diseases have been identified and these afflict about 6.8% of the population during the course of their lives. About 80% of these diseases have genetic origins and 50% of them appear during childhood. Rare diseases are grave or very grave, chronic and often degenerative diseases that are a danger to people's lives. There are about thirty million people with rare diseases in Europe and over 300 million in the world. Rare diseases have specific features that make them not much known about and also difficult to treat. Indeed, people with rare diseases can be very few in number in a country and, as a consequence, so are the experts on such diseases that belong to different categories in various nations. Reliable information is scarce, research is fragmented, and resources are limited. Sustainability is a problem and patients are often the real experts on their diseases; their loved ones are those who take care of them every day.

Rare diseases present us with many challenges that have to be addressed. A high percentage of people with rare disease are afflicted by movement or intellectual disabilities that have a burdensome impact on the health and daily lives of such people. According to a survey that was carried out by EURORDIS, worrying data exist about delays in diagnosis of these rare diseases – up to thirty years – and about the numerous difficulties that are encountered in gaining access to suitable care and treatment. The other great problem is a lack of treatment (only 5% of rare diseases have an approved treatment. In some cases the symptoms can be treated to improve quality of life and life expectancy). A lack of knowledge about rare diseases in society and a lack of social recognition lead to the isolation not only of the person with a rare disease but also of his or her family unit. Marginalisation within society and health-care systems – which are planned for common diseases and illnesses – is a condition that is often experienced by patients with rare diseases, as it is by their families who also bear a heavy psychological burden: a lack of hope at the level of therapy and the absence of practical support in daily life.

In the same way, the high number and the great diversity of the physical, mental, and behavioural manifestations of rare diseases, as well as the variety of their consequences at a sensorial level, constitute a further obstacle to their identification and treatment. In addition, a combination of these diseases can lead to a number of handicaps at the same time. The levels of severity of these pathologies vary and they can lead to a lower life expectancy, with different consequences for daily life. Their appearance in life also varies and conditions which are relatively common (autism, convulsions) can conceal the rare diseases that give rise to them. In October 2016 the preliminary results of a study now underway carried out by EURORDIS conducted in forty-eight European countries through Rare Barometer Voices, revealed through the replies to 1,840 questionnaires valid throughout Europe (35 countries were represented) about rare diseases that 63% of patients, 36% of parents and 7% of other family members think that daily actions/areas are where the greatest difficulties are encountered.

Starting with these shared facts documented by inquiries carried out by EURORDIS, one can see the only way in which rare diseases can be addressed: by uniting the forces that exist to combat fragmentation and overcome isolation, creating a critical mass to speak with one voice, learning from each other and working together to find common solutions.

EURORDIS develops and promotes activity involving advocacy, information and the creation of a network, and empowers patients and their representatives in various fields. This is an organisation that contributes to the European debate about rare diseases; to the development of strategic documents in the social/health-care field; and to research into, and the development of, medical products and therapies for rare disease.

It has this structure so as to be able to bring together the experiences, the needs and the opinions of all its members in order to plan,

propose and develop various activities and initiatives in a shared way, supported by the work of its staff and a large number of volunteers: the Council of National Federations, with which it has signed a document of mutual commitment and shared goals and the organisation of national conferences for the development of national plans or strategies for rare diseases, and the Council of European Federations for a specific pathology involved in the development of European networks of reference, centres of expertise, clinical experimentations, registers and access to therapies. During its national assemblies, its action plans are voted on and at its two-yearly European conferences workshops are organised on specific subjects of contemporary relevance.

'Rare Connect', which is a platform, is a further instrument that is allowing the development of a communities online made up of patients, their family members or associations who live separately in a geographical sense but who interact to discuss questions and exchange information. This project was launched in 2010 and now has 77 online communities in partnership with 661 patient groups. It is supported by three full-time community managers and 265 voluntary chairmen or chairwomen.

As regards the empowerment of patents, this is necessary for people to become aware of their own capacities and to have confidence in these capacities to act and to take decisions and to then transform them into actions, as well as to take control of their own lives, their own rights and their own social and economic conditions. To this end, in 2008 EURORDIS launched its summer school to inform and train people in relation to the development and regulation of medical products, as well as other things. In recent years, 300 representatives of patients and 20 researchers have been trained and their involvement began in the year 2015. The success of this project is attested to by the involvement of some of these people in the regulatory processes of the European Agency for the Evaluation of Medical Products and their cooperation with pharmaceutical companies.

However, every action requires awareness on the part of society and for this reason in 2008 EURORDIS, together with the Council of Alliances, planned a World Day of Rare Diseases which is now celebrated every last day of the month of February every year. Born as a European event, this has constantly grown over recent years and now involves countries all over the world. In 2017 the subject, which is different every year, will be research because without research there is no hope; without research, the answers that people who are afflicted by rare diseases and their families want, and have a right to, cannot be produced. The following is site where one can see the list of numerous events that are organised in each country: www.rarediseaseday.org.

The expression of the expectations of patients, all of these activities and exchanges of information contributed to the drawing up of the European Regulation on Medical Products, with its designation of over 1,500 orphan drugs and 100 products approved for the benefit of about three million European citizens, and the Directive on the Rights of European Citizens to Trans-Frontier Care which contains article 13, an article specifically on rare diseases that constitutes the legal framework for the implementation of European networks of reference and the mobility of patients within the European Union.

The fundamental values of solidarity and fairness that guide the activities and thus the documents and the contributions of EURORDIS can often be summed up in the following lines which appeared in a document to support an increase in research activity: 'The sense of social justice and solidarity expressed by every reactive society requires action in favour of the most vulnerable groups, such as patients with a rare disease, who need specific measures that must be implemented by their governments and their health-care systems so that they can have the same level of care and treatment as other kinds of patients. In order to contribute to improving the achievement of parity, more favourable treatment is needed of people who are in disadvantaged conditions. In other words, patients with rare diseases need 'positive actions''.

We are very happy that these values are reaffirmed in such relevant European documents as the 'Communication of the European Commission on Rare Diseases – 2008'; the 'Recommendation of the European Council on Action in the Field of Rare Diseases – 2009'; and Regulation 141/2000 on orphan medical products where incentives are envisaged for the development of orphan medical products in order to encourage innovation in this disadvantaged area and thus favour fairness. However we are now witnessing an increasing number of orphan medical products for which refunding is envisaged or there is even an inversion as regards decisions previously taken. EURORDIS has developed a 'Call for Payers' in which a different approach is requested to decisions that have to be taken through early dialogue and a shared evaluation of the value of medical products. In the same way, there is a drive towards supra-national solidarity in order to respond to the shared needs of people with rare disease and to the fragmentation of expertise and limited resources that can find a response only through common strategies, programmes, services and actions. One thus hopes for the birth of European institutions which through a network can foster the exchange of the multidisciplinary skills that are present in various counties, and also that research will even go beyond European frontiers in order to minimise duplications and avoid the carrying out of research in isolated laboratories and optimise scarce resources at the level of information such as databases, registers, systems of international epidemiological surveillance and vigilance in relation to medical products. Once again both the 'Communication' of the Commission and the 'Recommendation' of the Council go in this direction and they may be seen as successes, at least on paper.

Indeed, notwithstanding the steps forward, critical points or challenges remain that have to be addressed, as emerges from the surveys carried out by EURORDIS such as the Access Campaign of 2016 on access to care and treatment. From this it emerges that the greatest difficulty encountered by patients is to find an expert on their pathology despite the existence of centres of expertise in many countries and the InnovCare Project-2016 on social aspects that highlight how the separation of the social sector and the health-care sector is a common phenomenon; there continues to be a lack of connection/coordination between the various services; the pathways of care are still fragmentary; and often patients and associations of patients have to coordinate care and help themselves.

The European networks of reference could constitute an improvement when it comes to these critical points because they are networks of centres of expertise, of workers and of laboratories that are organised at a trans-frontier level. They are incorporated into the national health-care systems and it is expertise that travels and is shared beyond frontiers, with health care being provided at a local level at a higher level of quality. All rare diseases should be included in over the next few years so that 'every patient has a home'.

In the development of these networks the role of EURORDIS has been, and is, to develop the Recommendations/Addendum of the group of technical experts on the EUCERD MR in order to assure that the networks are centred around patients, with the representation of patients structured into the formal governance and operational supply of the networks.

What is needed is the creation of European advocacy groups of patients arranged around groups based on subjects present in the networks outlined in the EUCERD Addendum, together with representatives of rare diseases/associations of patients, as well as the existence of partnerships for the assessment of clinical excellence in the networks (PACE-ERN), a consortium with HOPE and Accreditation Canada International. All this in order to develop technical suggestions for the development of manuals and technical assessment toolboxes for the requests of the networks on behalf of the European Commission.

It is clear that we believe that care must be in line with a holistic, multidisciplinary, ongoing and approach centred around individuals in order to allow the full implementation of their fundamental human rights as recommended by the EUCERD Group of European technical experts on rare diseases to member States. It is to move these rights from the 'Recommendation' to their implementation that EURORDIS is promoting the InnovCare Project by which an assessment will be made of the social needs that have not been met of people with rare diseases and their families, as well as an analysis of the models of social care that exist in various countries. The exchange of skills and good practices will be promoted, as well as the creation of a European network of resources centre for rare diseases. We will try to learn from each other and to influence policy and we will develop a policy for a model of care and treatment by utilising case managers.

The concept of solidarity as Europeans is constantly growing and is becoming international and it is specifically to achieve this that Rare Diseases International came into being. This is an initiative that seeks to create an informal network of organisations of patients with rare diseases in order to form a global alliance that represents patients and their families of all nationalities for all rare diseases. Rare Diseases International is a EURORDIS initiative with national federations all over the world with whom we have signed partnership agreements (MOU) in order to improve the capacities of the members of Rare Diseases International through information, the exchange of knowledge, mutual support, and joint actions. The objective of the committee of non-governmental organisations on rare diseases is to bring visibility and understanding of rare diseases to the United Nations (UN), a platform where rare diseases have received little attention hitherto. It brings together knowledge and experts in order to move towards a greater recognition of rare diseases as a global priority in the field of healthcare policy, research, and social and medical care. The committee of non-governmental organisations for rare diseases was set in motion by Ågrenska Foundation and EURORDIS. It is a significant committee established under the umbrella of the Conference of Non-Governmental Organisations which has a consultative relationship with the United Nations (CONGO).

Its official presentation at the United Nations in New York is envisaged for today, 11 November 2016: www.ngocommitteerarediseases.org

ROUND TABLE
The Question of Medical Products and Access to Treatment

1. Delivering New Medicines for the Treatment of Malaria

MS SYLVIE FONTEILLES-DRABEK
Executive Vice President, Medicines for Malaria Venture - M.M.V., Switzerland

Your Eminences, Your Excellences, I am honoured to be invited to speak before you today on behalf of Medicines for Malaria Venture (MMV). This gives me the opportunity to share with you the work we do to meet the urgent need for new medicines and, equally importantly, for the delivery of these medicines to people suffering from malaria.

Malaria is a preventable and treatable disease, an ancient disease that continues to be a deadly foe. At the turn of this century, the world mobilised its expertise and resources to fight malaria and has succeeded in reducing deaths by 60% and malaria cases by 37% in 15 years. These are impressive gains. Yet in 2015 the disease still infected over 200 million people – almost 100 times the population of Rome. And it killed over 400,000.

Who are these vulnerable people? Most of those who died, almost 70%, were children under 5 years of age. In parts of Africa, young children can often suffer from malaria more than 6 times a year. The disease wears them down, damaging their neurological and biological development.

Pregnant women are also disproportionately affected by malaria, since the parasite sequesters in the placenta, it causes severe anaemia, and the mother is also naturally immunosuppressed during pregnancy. In Africa alone, approximately 10,000 women and 200,000 babies die annually as a consequence of the infection, and there are substantial numbers of infants born prematurely and with low birth weight. These infants clearly do not thrive as well as normal infants.

These people are also the world's poorest. We must not forget that malaria is a cause and a consequence of poverty in developing countries. The disease drains $12 billion from Africa each year and strikes lowest-income households the hardest.

20 years ago, malaria had become one of the world's most neglected diseases. The handful of malaria medicines no longer worked. The pipeline for new antimalarials was virtually empty as the returns on investment in antimalarial drug development were considered too low by industry. As a result, cases were on the rise, with deaths exceeding a million every year.

In 1999, the MMV was created to address this untenable situation, and totally changed the research landscape. As a product-development partnership committed to the discovery, development and delivery of new, efficacious and affordable antimalarial medicines, the MMV succeeded in bringing pharmaceutical and academic researchers together to defeat this disease.

Our partnership model is unique and has been emulated by many. We raise public, private and philanthropic funds and are able to select and support projects, both financially and scientifically, and build a research portfolio of promising antimalarial medicines.

We have an extensive network across 50 countries of over 400 partners from academia and industry, including pharmaceutical companies, biotechnology laboratories, universities and research institutions. I am delighted to say that with the power of these partnerships we have achieved significant progress.

We have developed the largest ever pipeline of more than 65 potential antimalarial drugs and are working with our partners to advance these drugs rapidly so that new medicines can fill the malaria medicine box.

And we have already brought forward six new, quality medicines, which include paediatric formulations, treatments for severe malaria and protection against seasonal malaria. It is estimated that over the last 7 years, around 350 million of these treatments have saved more than one million lives in over 50 countries. One of the key elements of this success is our partners' commitment to developing and bringing to market drugs that are

affordable (between 1 and 2 dollars for treatment of uncomplicated malaria).

Our small team of 84 people from 26 countries remains dedicated to the mission to defeat this deadly disease once and for all. But the path is peppered with challenges.

We do not want the medicines we develop to languish on dusty shelves in medicine stores just because health facilities do not stock them, or because healthcare workers do not know how to administer them.

Our access strategy facilitates policy-change and ensures that new innovative antimalarials emerging from our pipeline are affordable, accessible, available, and reach patients in time to save their lives. We are committed to making this happen.

Before I end, I would like to tell you the story of Saudat - a little 3 year old who almost lost her life to malaria but was given treatment in time.

Saudat was admitted to Murtala Mohammed Specialist Hospital in Kano State, (Nigeria), unconscious, with convulsions and a high temperature. She had severe malaria. Her life was at risk.

Nigeria is a high burden country, where almost every third young child has malaria that causes life-threatening symptoms like anaemi.[1] The MMV had been working in Nigeria with our partner CHAI to encourage the uptake of injectable artesunate, a drug for severe malaria we had helped our partner Guilin Pharmaceutical bring through the WHO prequalification programme. Fortunately, the Murtala Hospital had injectable artesunate in stock and it was administered immediately, and then regularly for a period of 48 hours. Two days later, Saudat regained consciousness and was put on a regimen of oral artemisinin combination therapy to cure her of malaria. Injectable artesunate helped reduce the severity of the infection and saved her life.

And that was not all. Based on Saudat's positive response to treatment, and on similar cases, the paediatrics department at the busiest referral hospital in Kano, Nigeria, as well as other state hospitals, switched from intravenous quinine (difficult to administer and painful) to injectable artesunate to treat all cases of severe malaria. This was an excellent response, especially for all those young ones being admitted on a daily basis.

Saudat is a reminder of why we do what we do. One of the hundreds of thousands of children who have benefited from MMV's work.

Our work so far has been supported by a small group of government, private and philanthropic donors who are as committed as we are to the ultimate defeat of malaria. We are infinitely grateful for their support and we recognise that achieving our ambitious goals will require sustained long-term investment and political commitment. Together with our partners, we will continue to work to free the world of malaria.

Note

[1] http://article.sapub.org/10.5923.j.health.20150503.01.html

2. Progress Toward the IRDiRC Goals: 200 New Treatments for Rare Diseases by 2020

PROF. PAUL LASKO
Department of Biology, McGill University, Montreal, Canada

Good afternoon, everyone. It is a great honour and a privilege to be with you today and to share my thoughts about latest developments in rare disease research and therapeutic development. I will be speaking to you as someone who makes decisions about what research programs to fund, as a scientific director of one of the institutes that makes up the Canadian Institutes of Health Research, a government body that funds health research. I also have been deeply involved in the International Rare Disease Research Consortium (IRDiRC), a body that works to foster better international collaboration and coordination in rare disease research.

There has been a big change over the past 5-10 years in the priorities of many public-sector funders of health research in that they are now recognizing the need to better engage patients in driving the research agenda.

In the United States, in 2010 an independent, non-profit organization called the Patient-Centered Outcomes Research Institute (PCORI) was established by Congress. Its mandate is to improve the quality and relevance of evidence available to help stakeholders make informed health decisions, with the goal of determining which health care

options work best for patients and those who care for them in particular circumstances.

In the United Kingdom, the National Institute for Health Research, which is part of the National Health Service, established INVOLVE back in 1996. Its role is to support active public involvement in the National Health Service, and in public health and social care research.

In Canada, the Canadian Institutes of Health Research, in partnership with provincial Ministries of Health, launched in 2014 its Strategy for Patient-Oriented Research. Among its principles is a statement that patients need to be involved in all aspects of the research to ensure questions and results are relevant. These three examples illustrate a broader trend toward deeper partnerships among patients, researchers, and funders, which in my view is a good development.

Turning more specifically toward rare and orphan diseases, patient support groups that generally focus on a single disease, or a small group of diseases, in a single nation, are organizing into large umbrella groups that have substantial influence on the research agenda. EURORDIS is probably the largest such organization, it is active in 63 countries and covers over 4000 different rare diseases. The US counterpart is the National Organization for Rare Disorders. Genetic Alliance, also based in the United States but active worldwide, is a particularly effective advocacy organization that has pioneered innovative new approaches to empower patients and their families who are living with genetic disease.

One such initiative involves building an open-access public database on mutations in two genes called BRCA1 and BRCA2. There are thousands of different variants in these genes – some confer a high probability of developing breast cancer, others are benign, and for many others the clinical significance is unknown. A major database containing information about these variants is proprietary, controlled by the company that sells the most commonly used genetic test, and not generally open for external research use. This initiative called "Free the Data" enables patients to enter their own genetic and health information on a public database so that it can be shared with other patients and with researchers.

There also are examples of individual patients and their families setting up their own systems to fundraise for research on their disease of interest, and as well actively collaborating with the scientists who do the research.

All that is intended to provide an overall context for the work of IRDiRC, the International Rare Diseases Research Consortium.

IRDiRC was publicly announced in 2011 subsequent to discussions between Francis Collins of the US National Institutes of Health and Ruxandra Draghia-Akli of the European Commission. Its founding goals are to help facilitate the development of a diagnostic tool for every known rare disease, and the development of 200 new therapies, by 2020. To do this IRDiRC has led public- and private-sector research funders in this area to provide more resources to rare disease research, and has pursuing several initiatives to improve collaboration and pool information from patients in different countries. IRDiRC now includes over 40 members from all over the world who collectively have committed over $2 billion US to rare disease research.

First I will show the progress that has been made toward achievement of these goals. On the therapeutic side it is exciting to report that the goal of 200 is nearly achieved – 195 new therapies with orphan designation have been approved by the Food and Drug Administration in the US and/or the European Medicines Agency since 2010. About 1400 new diagnostic tests for rare diseases have been developed and made available since 2010, which is a big success. However there is still a substantial set of diseases for which there is no test. This is often because the patient population for each of these diseases is extremely small – diagnostic tests are usually based on genetic variants, and a particular genetic variant cannot be definitely linked to a disease unless it is found in more than one unrelated patient. In a moment I will talk about an exciting new effort, called Matchmaker Exchange, to find matches between patients with a common genetic variant and similar symptoms, which promises to speed discovery and the development of new diagnostic tests.

I am grateful to Dr Kym Boycott for the material I will now present about Matchmaker Exchange are borrowed from a colleague, Kym leads a Canadian national consortium on pediatric rare disease research and who has been instrumental in this effort. IRDiRC, along with the Global Alliance for Genomics and Health, has supported this work.

This boy named Noah is one of Kym's patients. He has a rare disease that seriously affects his balance and movement, and two years ago Kym's group found a variant in his genes that is a strong candidate for causing his disease. However, up to now no one else has been found with the same variant so a definitive link could not be made. While this is one example, more than half of patients who undergo genome sequencing fail to have a causative variant identified. How can these unsolved patients be matched so that more can be learned about their diseases?

The previous approach to this was informal and haphazard. Kym with two European colleagues during a very nice dinner here in Rome, where they discussed their patients, shared data, and discovered that Kym's collection of patients contained a match with each of the collections of the European researchers. So two diseases gained diagnostic tools as a result of this dinner.

Matchmaker Exchange provides a more systematic approach to the problem. Representatives from 12 different research groups

with large databases, that were entirely disconnected with one another, met at a conference in Boston in 2013 to discuss how to share data. As of today six of these groups are linked, so that a researcher can search all of them for a match with a patient of interest. Importantly, this ability will soon be extended to patients, who will be able to search with their own data.

One of the first successes of this approach was that the tool found a match between a patient being cared for in Ottawa and another in Kansas City, leading to a diagnosis for these individuals. Prior to the software finding the match, these researchers did not know each other so the dinner approach could not have worked. And as for Noah, the boy I mentioned before, Matchmaker Exchange found a match for him just a couple of weeks ago, with a patient in Seattle.

I will close my talk here and simply thank the audience for its attention. ■

Thoughts for Dialogue and Discussion

Care that Respects the Patient and the Environment: a Short Return to the Encyclical *Laudato Si'*

DR. ANTONIO MARIA PASCIUTO
Medical Doctor Specialised in Environmental Medicine, Italy

I would like first of all to thank the Pontifical Council for Health Care Workers (for Health Pastoral Care), and in a special way Monsignor Jean-Marie Mupendawatu, for inviting me as a speaker and chairman to this important international conference, which this year is on people with rare and neglected diseases.

The subject that has been assigned to me is 'Care that Respects the Patient and the Environment: a Short Return to the Encyclical *Laudato Si*'.

My task also involves proposing themes and subjects as an introduction to our dialogue and to the discussion that will follow.

The time available to me for this short introduction (ten minutes) is certainly not enough to examine in a detailed way all the aspects present in the encyclical *Laudato Si'* connected with health and its close connection with the environment.

I will confine myself, therefore, to emphasising the subjects that in my view are the most interesting and stimulating and these I will bring to your attention, bearing in mind the discussion that will follow.

There is a clear continuity between the thirtieth international conference organised by the Pontifical Council for Health Care Workers last year (which took place five months after the promulgation of the encyclical *Laudato Si'*) and this thirty-first international conference. Both centre around the themes of *Salus* (understood as physical, moral and spiritual health), of welcome, and of a new culture that should be embraced by all citizens and all health-care workers: that of a clear awareness that the health of a person is indissolubly linked to the health of the environment, that is to say of the creation, that is to say our common home.

To emphasise this continuity, I will refer to the words pronounced by the Holy Father during the audience that was granted to those taking part in the international conference of last year. 'I hope that in these days of reflection and debate, in which you also consider the environmental factor in its aspects most strongly related to the physical, psychological, spiritual and social health of the person, you may contribute to a new development of the culture of *salus*, understood also in an integral sense. I encourage you, in this perspective, to always bear in mind in your work the reality of those populations, which suffer most the damages that stem from environmental degradation, serious, often permanent injuries to health. And, speaking of these damages that stem from environmental degradation, it is a surprise for me to find – when I go to the Wednesday Audience or to parishes – so many sick people, especially children.... The parents say to me: "He has a rare illness! They don't know what it is". These rare illnesses are the consequence of the sickness that we inflict on the environment. And this is serious!'

The sub-title of the international conference of this year reads: 'Informing to know; knowing to act; acting to treat; treating in a way that respects the life and dignity of the patient and the environment, a welcoming and supportive culture of health, with an outlook of hope on the future'.

Here are some important points for our discussion: 1. The need to engage in correct information so as to acquire adequate knowledge; 2. the need to act, to move therefore to action, once the right knowledge has been acquired; 3. the need to act in a way that respects life, the sick person and the environment (which are all closely connected); to base oneself in action on the principles of welcome and solidarity; 4. the need to have hope in the future, if these are the starting points.

In the short time that remains to me, I want to show you a few slides that highlight the concepts that have just been expressed, with an approach – at the level of understanding – of the dynamics that are at the base of very many chronic rare and neglected pathologies, as an indispensable starting point for being able to treat them.

On the basis of what is clearly expressed in the encyclical *Laudato Si*', I would like to emphasise the importance of living in a healthy environment, in a common home, in which man can lead an existence that is worthy of his divine origins, in order to be able to prevent and treat many pathologies.

I will engage in a very brief return to some aspects expressed in *Laudato Si'* and I will stress the need for care and respect for

the environment (the Common Home), in order to prevent and treat many pathologies, amongst which rare and neglected diseases.

The World Health Organisation (WHO) tells us that about 24% of illnesses in the world are due to environmental factors. A large part of these risks, however, could be avoided through targeted initiatives.

According to the calculations of the WHO, more than 33% of illnesses in children under the age of five are due to environmental factors. Preventing exposure to these risk factors would save about four million lives every year amongst children alone, above all in developing countries (we are dealing here with more than ten thousand deaths every day)!!!

The World Health Organisation tells us that there are 12.6 million deaths every year because of environmental pollution and this is an underestimate. One is dealing here with 35,000 people every day!!!

Contamination of the air, water, the soil, exposure to chemicals, climate change and ultraviolet radiation contribute to affliction by over 100 illnesses.

One person in every four in the world dies because of pollution of the environment: the countries that are most afflicted by this are low- and middle-income countries in South East Asia and the regions of the Western Pacific. In Europe, in the year 2012, exposure to environmental risk factors linked to the place in which people lived or worked caused the lives of 1.4 million people. Amongst rare and neglected diseases we can certainly list those that today are defined as emerging pathologies: pathologies that are certainly connected to so-called 'environmental overload'. These are increasing rapidly. Examples of these are: 1. multiple chemical sensitivity (MCS); 2. chronic fatigue syndrome (CFS); 3. fibromyalgia (FM); 4. sick building syndrome (SBS); electro sensitivity (ES); and yet others.

One is dealing here with millions of patients who do not manage to receive dignity, welcome and support in their infirmity, above all because, *in primis*, research into the causes of their pathologies at a diagnostic level is not sufficiently developed.

At number 67 of *Laudato S*' we read: 'The biblical texts… tell us to "till and keep" the garden of the world..."keeping" means caring, protecting, overseeing and preserving. This implies a relationship of mutual responsibility between human beings and nature. Each community can take from the bounty of the earth whatever it needs for subsistence, but it also has the duty to protect the earth and to ensure its fruitfulness for coming generations'.

At number 69 of *Laudato Si*' we find the following sentences: '"the Lord rejoices in all his works". By virtue of our unique dignity and our gift of intelligence, we are called to respect creation and its inherent laws, for "the Lord by wisdom founded the earth".

At number 70 of *Laudato Si*' we find these words: 'genuine care for our own lives and our relationships with nature is inseparable from fraternity, justice and faithfulness to others'.

At number 79 of *Laudato Si*' we find the following sentences: 'In this universe, shaped by open and intercommunicating systems, we can discern countless forms of relationship and participation', living beings are therefore 'open systems', that is to say in constant ceaseless interaction with the environment in which they live. The environment and health make up an indissoluble tandem. A living organism cannot be healthy is it is 'immersed' in an unhealthy environment (or at least its state of health cannot last long'.

At number 20 of *Laudato Si'* we are told that: 'People take sick, for example, from breathing high levels of smoke from fuels used in cooking or heating. There is also pollution that affects everyone, caused by transport, industrial fumes, substances which contribute to the acidification of soil and water, fertilizers, insecticides, fungicides, herbicides and agrotoxins in general. Technology, which, linked to business interests, is presented as the only way of solving these problems, in fact proves incapable of seeing the mysterious network of relations between things and so sometimes solves one problem only to create others'.

At number 29 of *Laudato Si*' the Pope tells us: 'Underground water sources in many places are threatened by the pollution produced in certain mining, farming and industrial activities, especially in countries lacking adequate regulation or controls. It is not only a question of industrial waste. Detergents and chemical products, commonly used in many places of the world, continue to pour into our rivers, lakes and seas'.

The role of these components in causing chronic pathologies, including rare and neglected diseases, is of very great relevance.

The greatest philosophers, scientists and medical doctors have always asked themselves about the meaning of health, providing the most varied definitions, in an attempt to establish when a person is 'well' or not. At times, however, in order to explain very profound and involved concepts, the best thing to do is to try to simplify. In this case, mathematics can come to our aid. In my view the concept of health could also be expressed in a simple mathematical formula through a fraction, in which as a numerator we have the capacity for compensation that every organism possesses, and the denominator is the disturbance factors (environmental factors, stressing elements of various origins, with which the organism in itself constantly comes into contact).

$$\text{Health} = \frac{\text{Capacity for Compensation}}{\text{Disturbance Factors}}$$

If we wanted to observe better this mathematical formula, and see it from a broader perspective as well, I would say almost a philosophical/theological perspective, we would realise how in the numerator (the higher part of the fraction) we find all the elements that helps us to foster and maintain health. We are specifically dealing with what we have received from God and which allows us to be in good health every day: the immunity system, the

enzyme defence, the purification system, and the excretory organs, which enable us to eliminate from the organism everything that is injurious. In the denominator (the lower part of the fraction), we find what causes the illness. If we see things clearly, these are components 'created' by man and placed in increasing quantities in the environment, in nature, when awareness, respect and love for nature herself declines. Amongst these, we may list, for example, environmental pollutants such as insecticides, pesticides, defoliants, solvents, plastics, heavy metals, phthalates, bisphenols, moulds, nanoparticles, genetically modified organisms, electrosmog, and many others. Here, too, the interpretation could be the following: God has given us everything that allows us to remain in good health. Man has free will to preserve these gifts, to treat them with care and love so as to live in health for as long as possible; or he can damage himself (a disordered lifestyle) and the environment in which he lives (this has been happening increasingly over the last few decades), moving inexorably towards illness. Chronic pathologies, and rare and neglected diseases, should be placed in this category.

Following the multi-factor model that is at the base of chronic pathologies (including rare and neglected diseases), we realise how all of these pathologies are due to a 'genetic component' and an 'environmental component' which interact with each other. As regards the genetic part, there are few ways of acting: many are still at the experimental stage and are certainly are not without grave risks. Suitable attention and loving care given to the creation, to the common home, allow an enormous reduction of the risk of falling ill and notably increase the possibility of an effective cure.

We should then take into account that modern science, thanks above all to epigenetics, has enabled us to understand that our genetic inheritance as well (or at least its way of expressing itself at a phenotype level) is dependent on external influences linked to the environment. By now it has been demonstrated that so-called 'environmental overload', as expressed in number 20 of the encyclical *Laudato Si'*, also damages the genome of those who exposed to it, with negative consequences that are handed down to subsequent generations.

In the light of the awareness that comes to us from the encyclical *Laudato Si'*, medical doctors and health-care workers should work (their mission), in the sense of prevention and cure, through action designed to: 1) 'strengthen' the natural systems of defence and purification that we received as a gift at birth, and 2) reduce to the utmost the so-termed 'risk factors' that are all closely connected with the deterioration of the environment.

The fundamental element from which to start is awareness of what has been said hitherto. A medical doctor must know that very many pathologies, and in particular chronic illnesses (including rare and neglected diseases) and functional disturbances, have as a principal cause (or a joint cause) factors that have environmental origins.

These should be investigated and demonstrated (today we have available internationally recognised laboratory analyses that allow us to engage in a monitoring of the environment and bio-monitoring in that sense).

Clinical environmental medicine is a new branch of medicine. This is a modern discipline (the central role of the environment as a determining cause of very many pathologies) and one that is transversal (every medical specialisation deals with pathologies whose cause or joint cause can be factors of an environmental kind).

Precisely for this reason, ASSIMAS (the Italian Association of Medicine, Environment and Health) has planned for the year 2017 two training schools which will be held in Milan and Rome and will centre around the subjects that have just been referred to.

The last words of the sub-title of this international conference are 'With an Outlook of Hope on the Future'.

We should not imagine or see hope as something that is far away from us. Hope dwells in us and becomes reality, a concrete life if – strong in our awareness and our faith – to this we add works. It was no accident that St. James said: 'faith without works is dead. What is the use, my brethren, is someone says that they have faith but they do not have works?' (James 2:14-26).

Amongst the gifts that God has given to us, there are our qualities, our vocations, our talents as human beings. Each person has available their own talents which we must use basing ourselves on principal ethics and concentrating on what is of priority importance. At the present time the encyclical *Laudato Si'* says this in a clear way: the subject of the environment (understood in a broad sense and not only a physical sense) constitutes one of the greatest priorities. To restore health and dignity to the environment also constitutes the principal pathway by which to address and cure people with rare and neglected diseases.

Each person must do this in their own sphere. A citizen (that is to say a human being) in general should do this, but by translating it into their activity, their mission carried out every day: parents, teachers, priests, scientists, medical doctors, politicians, legislators, administrators, lawyers, judges, businessmen, and journalists.

Following the teachings and the exhortations present in *Laudato Si'*, which are so admirably, clearly and poetically expressed, nothing will be precluded to us.

ROUND TABLE
Good Practises

1. A Concept of Pastoral Care: CELAM – the Latin American and Caribbean Conference of Bishops

FATHER LEOCIR PESSINI, M.I.
Superior General of the Order of Camillians, Brazil

I have been a member of the Pastoral Care in Health Commission of the Justice and Solidarity Department of CELAM (the Latin American and Caribbean Conference of Bishops) since its beginnings in 1994. During these twenty-two years of history, an important legacy has been given to the Latin American and Caribbean Church: guidelines for its action in the health-care world. This document was updated over time and its present version reflects the Conference of Aparecida (2007). Now a new revision and updating has been begun, inserting the thought and the encyclicals of Pope Francis. This vision and concept of pastoral care can be inspiring for the work of the Catholic Church in other parts of the developing world, in many countries that have similar challenges to Latin American countries, for example in Africa and in Asia.

The pastoral care in health is the evangelising action of all the People of God, who are committed to promoting, caring for, defending and celebrating life by carrying out the liberating and salvific mission of Jesus in the world of health.

The document of Aparecida states: 'Pastoral care in health is a response to the great questions of life such as suffering and death, in the light of the Lord's death and resurrection'.

General Objective

To evangelise with a renewed missionary spirit in the world of health, with a preferential option for the poor and sick, participating in the construction of a just and caring society at the service of life.

To carry out its mission, pastoral care in health emphasises three dimensions: solidarity, community and the political-institutional dimension.

The Dimension of Solidarity

Objective

To be the presence of Jesus, the Good Samaritan, with the sick and those that suffer in families, communities, and health-care institutions.

Areas of action

To illuminate, through Christian faith and the person of Jesus, the realities of pain, of suffering, of sickness and of death.

To train agents of pastoral care in health in the human, ethical, bioethical, pastoral and spiritual aspects of their activity in order to announce the Good News of salvation seen from the realities of health and sickness, life and death.

To celebrate with special care significant dates related to the world of health: Christmas, Easter, the feast days of the saints of charity, the world health day, the world day of the sick, the world doctor day, the world nurse day, etc.

To offer human and Christian accompanying to the sick and their relatives in institutions and their homes, respecting freedom of conscience and different religious beliefs.

To help the sick, their relatives and all those that assist them to discover the true meaning of the celebratory and sacramental dimension of faith, especially through the sacraments of Reconciliation, the Eucharist and Anointing of the Sick.

To raise awareness in society and the Church about the reality of suffering, denouncing the marginalisation of the terminally ill and elderly, of individuals with special needs, and those affected by AIDS, drug addiction, alcoholism, mental illness, and cancer.

To encourage the creation of support groups and/or associations for the chronically and terminally ill and their families.

The Community Dimension

Objective

To encourage health education and the promotion of health, with an emphasis on public health and basic sanitation, acting preferentially in the areas of the prevention of sickness and the promotion of healthy lifestyles.

Areas of action

To promote educational action, implementing a culture of healthy lifestyles, with action for prevention and promotion imbued with the values of justice, fairness and solidarity.

To redeem and value popular

wisdom and religiosity in relation to the use of the gifts of Mother Nature and care for the environment.

To verify that the use of different alternative health practices is implemented with the necessary basis, with scientific approval and responsibility, and with respect for indigenous values and cultural beliefs.

To ensure the ongoing formation and training of pastoral agents in the areas of health promotion and the prevention of sickness, with emphasis on social illnesses (tobacco use, alcoholism, addictions…) and the handling of emergency situations, calamities and catastrophes.

To educate people in the new concept of health as quality of life and healthy lifestyle, taking into account people and their biophysical, mental, social and spiritual dimensions.

The Political-Institutional Dimension

Objective

To ensure that the public and private institutions and organisations that offer health-care services and train professionals in this area keep in mind their social, political, ethical, bioethical and community mission.

Areas of action

To contribute to the humanisation and evangelisation of workers in the world of health, in health- care institutions, and in schools that train health-care professionals.

To promote and defend health as a fundamental human right, linked to solidarity, fairness, wholeness and universality.

To participate actively and critically in the official institutions that decide on national, state, regional and municipal health policies through social oversight and participative management.

To promote inter-institutional relationships to help and educate one another with the end goal of sharing material, financial and human resources and generating joint projects and initiatives.

To encourage the ongoing formation of health-care professionals in the areas of humanisation, ethics and bioethics.

To encourage the creation of Catholic associations of health-care professionals.

To raise awareness about the social commitment of health-care professionals who offer educational, prevention and health-care services to the poorest communities, marginalised neighbourhoods, and rural areas.

To reflect, in light of the Christian faith and the person of Jesus, on the reality of health and sickness, as well as the implications of science, technology and bioethics.

To raise awareness in communities about the right to health and the duty to fight for more humane situations: the right to land, to work, to a fair wage, to housing, to food, to education, to recreation, to basic public services, and to the conservation of nature.

Areas for the Action and Promotion of Pastoral Care in Health

1. The Christian community is the historical extension of Christ. Sick people should find in it the privileged place that they found in Jesus; the same preference, closeness and welcome, the same respectful and tender treatment, his healing strength.

2. The suffering person is a responsible and active participant in the work of evangelisation and salvation and this involves the Christian community in a health ministry that is built around the sick person as protagonist and evangeliser.

3. The family occupies the primary place in the humanisation of the person and of society. It is called to be a community of health, to educate people in living a healthy lifestyle, to promote health among its members and in its environment. It is important to retrieve the family as an essential co-worker in care for, and accompanying, the sick members of the community.

4. The parish community engages in human promotion, care for and preservation of health, and pastoral accompanying of the sick and the elderly in faithfulness to its mission to build the Kingdom of God. A cooperative pastoral ministry will take into account the parish and diocesan plans for ministry.

5. Following the example of the first Christian communities, the basic ecclesial communities will show special care for the weakest and those most in need, fulfilling the evangelising and prophetic mission of announcing a more just, community-based, and fraternal life and of speaking out against injustices and situations of social sin.

6. All religious men and women, but in a special way those that profess the charism of Jesus the Good Samaritan, are called to be witnesses to faith and hope in a world that is increasingly dehumanised, techno-centric and materialistic; to enrich the ecclesial community with their presence in a spirit of openness and cooperation with parish activities; and to encourage and accompany health-ministry groups.

7. Health-ministry groups express the vitality and gospel spirit of the People of God; they render present in the Christian community the love and special care of Jesus for the weakest and sickest among us.

8. International, national and local organisations are places where health-care policy decisions are decided. It is necessary to participate actively and critically in them in order to illuminate the actions of the world of health care with the Gospel, and to work in favour of the poorest and least protected among us.

9. The institutions of the world of health care – hospitals, clinics, dispensaries, universities, etc. – are called to educate people about, and promote, health; to care for and defend life from conception until natural death; and to offer comprehensive and human care to sick people and their families, recognising and respecting their rights.

10. Catholic hospitals and clinics should bear in mind that: such institutions are a privileged setting for evangelisation; the health-care personnel should dis-

tinguish themselves by their solid human and social formation; in hospital management the human and spiritual aspects must take priority over the financial and administrative aspects; and when there are partnerships with public health institutions, they should 'ensure that conscientious objection is recognised in legislation, and monitor to ensure that it is respected by governments'.

11. Health-care workers are natural agents of the health ministry. It is important to act together with them, accompanying them in their process of formation, of humanisation, and the strengthening of their human, ethical and bioethical values.

12. Humanisation leads us to affirm that 'being' with a sick person can be more important than 'doing'. Meeting with the other means listening to him, welcoming him with his preoccupations, hopes and difficulties, with his personal history, his fears, his anguish. It means establishing a relationship of peers with him, centred on the person, reaffirming his dignity and greatness. It means not glossing over situations that the sick person and his family are experiencing; offering a comprehensive assistance that satisfies their needs at a physical, emotional, intellectual, social and spiritual level, and not just solving the specific pathology.

Humanisation is a matter of a personal attitude, a lifestyle that goes beyond norms, ideology or a philosophy; it is moving from a functional relationship to an empathic one, centred on the person.

'No institution can by itself replace the human heart, human compassion, human love or human initiative, when it is a question of dealing with the sufferings of another' (*Salvifici Doloris*, n. 29).

'While professional competence is a primary, fundamental requirement, it is not of itself sufficient. We are dealing with human beings, and human beings always need something more than technically proper care. They need humanity. They need heartfelt concern… Consequently, in addition to their necessary professional training, these charity workers need a 'formation of the heart'' (*Deus caritas est*, n. 31a).

13. Pastoral and spiritual care will be carried out by a team guided by the priest, deacon, religious brother or sister or a layperson trained in this specific area. The team will be in a relationship with the other groups in the institution, with the parish agents of pastoral care in health and with those of other religious beliefs.

This will be a significant presence that gathers together all the Christian strengths present in the institution and will make possible the missionary and healing action of the Christian community on behalf of the sick and the relatives who assist them, respecting their beliefs and faith.

'Love is free; it is not practiced as a way of achieving other ends… Those who practice charity in the Church's name will never seek to impose the Church's faith upon others. They realize that a pure and generous love is the best witness to the God in whom we believe and by whom we are driven to love. A Christian knows when it is time to speak of God and when it is better to say nothing and to let love alone speak. He knows that God is love (cf. 1 Jn 4:8) and that God's presence is felt at the very time when the only thing we do is to love' (*Deus caritas est*, n. 31c).

14. The educational institutions actively participate in the growth and integral formation of the individuals. Hence the importance of the fact that in their plans and programmes they include what relates to promotion, prevention, education and humanisation in health care.

15. Volunteer service is a concrete expression of the love of God; it is the duty of every person, and especially of the Christian. With their attitude of love and free and unconditional service, volunteers promote the culture of life, based on the values of solidarity and fraternity.

16. Many groups and associations of sick people organise to support one another. It is important to value, recognise and accompany their efforts; they communicate and convey great human and Christian values to the community.

17. The popular (mass movement) organisations are examples of the resistance of a people that organises in order to survive when faced with growing impoverishment; it is necessary to recognise and support the efforts that are being made in service to the community, training them in the promotion of health and the prevention of illness.

18. 'The new movements and communities are a gift of the Holy Spirit to the Church. In them, the faithful find the opportunity to be formed as Christians, growing, and committing themselves apostolically as true missionary disciples… By their very nature they express the charismatic dimension of the Church; in the modern world, we must respond to the new situations and needs of Christian life' (*Aparecida*, nn. 311-12).

19. In the seminaries and houses of formation of religious, it is important to bear in mind the formation plans of future pastors and offer training and formation in pastoral care in health that illuminates and moulds the heart for the exercise of charity.

20. The media play an increasingly important role as institutions of information and communication. Hence, it is advisable to take advantage of, and implement, education programmes and campaigns that defend life and promote health. ■

Document: Discípulos missioneiros em el mundo de la salude: *Guia para la Pastoral de la Salut em América Latina y El Caribe.* Departamento de Justicia y Solidaridad CELAM - Pastoral de la Salud. Bobotá, 2010), nn. 90-94, pp. 65-71.

2. The Nippon Foundation and the Fight to Eliminate Leprosy

MR. TATSUYA TANAMI
Executive Director, the Nippon Foundation, Japan

What is Leprosy?

As you are aware, leprosy is a disease with both medical and social consequences. It has caused human suffering over many centuries. There are references to leprosy in the Old and New Testaments, ancient Chinese texts and Indian works dating back to the sixth century.

Medically speaking, it is a chronic infectious disease caused by the bacillus *M. leprae*, and is thought to be spread by close and frequent contact with someone who is infectious. Leprosy mainly affects the skin and peripheral nerves. If left untreated, it can lead to devastating disfigurement and disability, which is a major cause of the stigma the disease has attracted. Poorly understood and without a cure for much of its long history, leprosy has struck fear in people's hearts.

It was not until the middle of the twentieth century that a cure for leprosy emerged, but the real breakthrough came in the early 1980s with the introduction of multidrug therapy, or MDT. Around that time there were over 5 million registered leprosy patients in the world. By contrast, 210,758 new cases were reported in 2015. Three countries – India, Brazil and Indonesia – were responsible for 81% of all new cases of leprosy in 2015, and 14 countries accounted for 95%.

The Beginnings of our Efforts

The Nippon Foundation, of which I am the executive director, was founded in 1962. It is one of the biggest not-for-profits in Asia and is dedicated to finding solutions to social issues at home and abroad. One of the most important themes of the foundation, and a key area of its activities, is working for the elimination of leprosy.

In 1974, the foundation began its financial support for the WHO's efforts against leprosy. Since 1975, it has been the principal donor to the WHO's global leprosy program.

Following the introduction of MDT and its proven effectiveness in rendering patients non-infectious and curing them of the disease, the WHO resolved in 1991 to eliminate leprosy as a public health problem at the global level by 2000. It defined elimination as a disease prevalence rate of less than 1 case per 10,000 members of the population.

To give impetus to this effort, Yohei Sasakawa, who was then the president of the Nippon Foundation, pledged to underwrite the free distribution of MDT around the world for five years from 1995 to 1999 through the WHO. An estimated 5 million to 7 million people were treated with MDT during that period and an estimated 16 million people have been treated to date since MDT was first introduced.

We take pride in the fact that the free distribution of MDT initiated by the Nippon Foundation greatly changed the history of leprosy elimination. Since 2000, this drug donation has been guaranteed by the Novartis Foundation. From the 1980s through to the present, it is said that the global burden of leprosy has been reduced by 96%, thanks to MDT. Ensuring drug security is the first example of good practice that I will be mentioning today.€

Accompanying the introduction of MDT have been the collective efforts by governments of endemic countries, the WHO and other international organizations, NGOs and medical institutions, to detect and treat patients in order to work toward the shared goal of leprosy elimination. Following the elimination of leprosy as a public health problem at the global level in 2000, individual countries have continued to pursue this goal at the national and sub-national levels. Among these efforts by various stakeholders, I would like to commend the role of the Catholic Church and other religious faiths for the part they have played in leprosy work over the years. The collective efforts made by different stakeholders to work toward a common goal is a second example of good practice in addressing the challenge posed by an infectious disease such as leprosy.

The Role of the Goodwill Ambassador Yohei Sasakawa

Our chairman, Mr. Sasakawa, was appointed WHO Goodwill Ambassador for Leprosy Elimination in 2003. Since then he has made it his mission to visit countries that have yet to eliminate leprosy in order to see the situation for himself, meet with political leaders, enlist the support of the mass media, encourage frontline health workers, and, in particular, to meet with people affected by leprosy to hear directly from them about their day-to-day lives and the challenges they face.

His is not an empty title; he makes a point of going to see the situation for himself. I put forward this "boots-on-the-ground" approach as my third example of good practice.

Achieving a UN Resolution on the Elimination of Discrimination

As I mentioned at the outset, leprosy is not only a medical is-

sue; it is also a social issue. People affected by leprosy and their families must still grapple with stigma and discrimination. Unless both the medical and social issues are tackled at the same time, it will not be possible to achieve a truly leprosy-free world.

Mr. Sasakawa was the first private citizen to raise the issue of leprosy-related discrimination with the UN and seek a concrete solution. In July 2003, he approached the office of the UN High Commissioner for Human Rights and began a several-years-long drive to achieve this objective. Over time, he also received the understanding and support of the Japanese government.

In 2008, the Japanese government submitted a resolution on elimination of discrimination against persons affected by leprosy and their family members to the UN Human Rights Council. A version of this resolution was eventually adopted by the UN General Assembly in 2010, together with accompanying Principles and Guidelines, with the unanimous support of 194 countries.

The Human Rights Council Advisory Committee is now undertaking further research in order to promote the implementation of the Principles and Guidelines by governments of endemic countries.

In addition to this advocacy work through the United Nations, Mr. Sasakawa launched an annual Global Appeal in 2006 to call attention to leprosy-related discrimination. Over the past decade, the Global Appeal to end stigma and discrimination against people affected by leprosy has been endorsed by, among others, Nobel laureates, representatives of people affected by leprosy, human rights organizations, faith leaders, the heads of the world's leading universities, the World Medical Association, the International Bar Association and the International Council of Nurses.

Approaching the UN and launching an appeal calling for an end to discrimination make up the fourth example of good practice – advocacy work – that I offer you today.

Working toward a World without Leprosy Together with People Affected by Leprosy

For some years now, both the Nippon Foundation and its sister foundation, Sasakawa Memorial Health Foundation, have been providing support to communities and organizations of people affected by leprosy in such countries as India, Nepal, Ethiopia, Brazil, Indonesia and Ghana.

An initiative of Mr. Sasakawa through which we work with people affected by leprosy is the Sasakawa-India Leprosy Foundation, or S-ILF. This was established in 2007 with an endowment of $10 million to focus on welfare and education projects for residents of self-settled leprosy colonies. These are communities of people affected by the disease and their families who find it difficult to live in mainstream society because of stigma and discrimination.

The S-ILF's micro-financing operations have created opportunities for people who previously had no option but to beg for a living. It has given them a chance to strive for economic self-sufficiency. Since micro-financing operations began, the S-IFL has supported over 150 projects.

Another important activity of the S-ILF is to provide educational support for young people born in colonies through scholarships and vocational training. Through this support, people affected by leprosy and their families are gradually returning to society – and once-closed-off colonies are starting to interact with neighboring communities.

Another initiative started by Mr. Sasakawa in India is the Association of People Affected by Leprosy, or APAL. This organization was founded in 2006 to empower people affected by the disease to stand up for their rights and make their voices heard. Its membership focuses on India's 800 self-settled leprosy colonies.

An organization of and for people affected by leprosy, it works for social rehabilitation and the restoration of rights. In particular, it lobbies States and local authorities to increase the allowance given to people affected by leprosy, to improve the quality of the services they receive, to revise or abolish discriminatory legislation, and to make it possible for people affected by leprosy to acquire land ownership rights.

Looking ahead, we believe that the remaining medical and social problems posed by leprosy can only be resolved with the involvement of people affected by leprosy themselves. With direct experience of the disease and the discrimination it attracts, they are the real experts in what they need. We believe it is our mission to facilitate this involvement in finding the solutions. All these points I have made involving the empowerment of people affected by leprosy collectively form my fifth example of good practice: it is not our role to do something *for* people affected by leprosy, but *with* them. We need to work in genuine partnership.

Toward a World without Leprosy

Even though the number of patients has declined, leprosy is an ongoing issue. Because of the long incubation period, there are still many undetected patients. For that reason, it is important that leprosy control is firmly fixed in the healthcare agenda of endemic countries. Also essential are the unwavering commitment of political leaders and the existence of knowledgeable and experienced medical experts and caregivers. But realistically, with national budgets for leprosy control decreasing, we need to explore measures for tackling leprosy as part of measures against NTDs in general. This will allow synergies to emerge from campaigns for detection and disease elimination so that diagnosis and treatment can be carried out effectively and efficiently.

Lastly, I would like to talk about the preservation of history. The history of leprosy is a history of the alienation and suffering of those affected by the disease. But it is not exclusively a negative history, and it must not be allowed to fade. There is much to learn from the extraordinary spirit

of those who sought to find a way to live amidst the despairing circumstances in which they found themselves. The lessons to be learned from how they overcame suffering to find meaning in their lives must be passed on to succeeding generations.

In different parts of the world, various activities are underway to preserve leprosy history. In Japan, the National Hansen's Disease Museum is one such example. This museum was started by those who spent their lives isolated in leprosaria. Its purpose is to increase public awareness of leprosy and of the struggle waged by people affected by the disease for the restoration of their dignity. It also encourages respect for human rights in general and promotes an end to discrimination and prejudice.

The Nippon Foundation has been entrusted with the running of the museum by the Japanese government. Through the work of this museum, our aim is to convey through the history of leprosy, not just in Japan but throughout the world, the preciousness of human rights. This is the sixth and final example of good practice that I would like to introduce to you today: respect for human rights, because this must underpin everything that we do. On that note, I bring my presentation to an end. ■

3. The SAFE Strategy – Good Practice and Lessons Learnt from Ethiopia

DR. BABAR QURESHI
Director of the Programme of the C.B.M. for Neglected Tropical Diseases, C.B.M./Italy, Project Ethiopia

The SAFE Strategy is the approved strategy of the World Health Organisation to eliminate trachoma in endemic regions: *S*urgery of trichiasis, the advanced, blinding stage of the disease; *A*ntibiotics to treat the active trachoma infection; *F*acial cleanliness; and *E*nvironmental improvements to prevent re-infection in the long term

Ethiopia is the country with the highest prevalence of trachoma globally and the Province of Amhara has a very high trachoma prevalence in Ethiopia. The 'Amhara Trachoma Control Programme' (ATCP) is implemented by the CBM in the Amhara Region of Ethiopia, using the SAFE Strategy approach. It is funded by the Italian Development Cooperation Agency and will run from May 2014 to April 2017.

The CBM works through its regional and country offices, with a wide range of partners in Ethiopia. The main implementing partner is the Organisation for Rehabilitation and Development in Amhara (ORDA) and the programme also works with the Amhara regional government, the local government, specifically the offices for Health, Water and Education, government hospitals, and the Regional Health Bureau.

The programme's overall objective is to reduce the prevalence of trachoma and all other water-related diseases, with its main focus on women and children, in the districts of Dessie Zuria and Raya Kobo. Two of the project's aims, among others, have been to provide access to clean water and appropriate sanitation systems for 22,000 people and to screen and treat 3,000 trachoma patients with surgery and antibiotics. In the first two years of the programme, the CBM already exceeded several of these targets: for example, 4,755 patients were screened, 1,074 received trichiasis surgery, and 2,155 received antibiotics, with a further 216,000 receiving antibiotics through government campaigns.

In May/June 2016, the CBM conducted a mid-term evaluation to determine the relevance, effectiveness, efficiency and sustainability of the ATCP and to collect evidence on the delivery of all four SAFE strategy components. In the past, trachoma programmes had been implemented in Ethiopia but with much less emphasis on the F&E components. The evaluation results will help the CBM to replicate and scale up the programme in other areas of Ethiopia and in other countries.

The evaluation's key findings were:

Relevance: key informants were unanimous in confirming the relevance of the programme to addressing the burden of trachoma at the national, regional and district levels, as well as the synergies with the Ethiopian government's national health policies. The programme's emphasis on the F&E preventative components of the SAFE strategy is a vital and complementary addition to the existing S&A activities that were and have been the focus of previous and ongoing programmes. The evaluation team found that the programme has been instrumental in strengthening the linkages between, and the capacity of, local non-government actors (ORDA) and regional and district level government partners in the region of Amhara, and has laid

the foundations for expanding the programme further in that region and elsewhere in Ethiopia.

Effectiveness: the programme is delivering well and is on track to deliver within the three-year plan. Project activities that have worked well include the strengthening of the diagnostic capacity of health extension workers to accurately screen, identify, treat (infection) or refer (trichiasis) patients at the community level; the establishment of Anti-Trachoma School Clubs in primary school to improve hygiene and sanitation practices (particularly face washing) at the school and community level; and the training of village hygiene educators to embed hygiene and sanitation behaviour change at the community level. A principle activity of the ATCP has also been the construction of community water-supply schemes and the evaluation team has seen evidence of good practice in the delivery of multi-scheme approaches to community water supply. The ATCP delivery approach is fully implemented through a multi-sectorial and multi-disciplined team of stakeholders at both the government and community levels and delivered though a fully participatory approach. There is evidence that strong collaborative systems have been established, as well as the demonstrable commitment of programme stakeholders. These approaches have been considered a key success of the programme.

Efficiency: resources have been used according to plan. Many elements of the programme have been delivered at zero cost, with significant elements delivered through in-kind contributions by programme partners. The modality for the capacity building and training of community level health staff and beneficiaries has been considered to be very cost effective. The inclusion of social workers has been responsible for the considerable levels of community mobilisation needed to achieve programme delivery.

Sustainability: ORDA and government partner staff feel that the programme has made considerable contributions in developing a viable model for comprehensive SAFE delivery and this approach can be effectively reproduced elsewhere in Amhara. Stakeholders have commented that the ATCP is showing a systems model approach to implementing comprehensive SAFE and the continuance of such approaches should be the responsibility of government. Trained staff in health facilities are already internalising the trachoma care services and mainstreaming them into the existing services. At the community level, the work of the anti-trachoma school clubs is considered to be embedded in the local schooling structure and village health educators are delivering hygiene education direct to households and at water schemes.

The main *recommendations for improvements*, produced by the evaluation, which the CBM will now incorporate into future trachoma programmes, as well as during the remainder of the current programme, as far as this is possible, are as follows:

1. To improve further the quality of TT surgery and place a greater focus on peer to peer recommendations for surgery. Often people are afraid to undergo surgery, but if they hear a positive story from a neighbour of a family member, they are much more likely to undergo surgery themselves.

2. To improve the availability of consumables and surgery sets at community health facilities.

3. To increase the number of schools involved in Anti-Trachoma School Clubs (ATSCs) and widen the training these clubs cover, provide basic supplies and facilitate experience sharing between clubs.

4. To address the presence of water and improved sanitation facilities in schools embracing the ATSCs as a priority, as this is of significance for effective community sensitisation and the adoption of changes in hygiene behaviour.

5. To invest in producing information, education and communication materials to strengthen the community education messages about water and sanitation.

6. To adjust water schemes more to local specificities, e.g. in drought affected areas and areas with especially low water tables, and to shift to shallow and deep well water schemes to increase the chance of success and to ensure the long-term sustainability of water points.

7. To cascade staff training to the field level more and encourage districts to share experiences and learning.

8. To improve the disaggregation of data to distinguish between active trachoma (TF) and trichiasis cases (TT) since they require different interventions that need to be measured separately. We also need to include information on gender, age and disability.

9. In future programmes, a Knowledge, Attitude and Practice (KAP) survey should be carried out into water, sanitation and hygiene practices, and trachoma knowledge, during the inception phase to make the programme more relevant to the local context.

4. Reaching the Most Vulnerable Through the Engagement of Civil Society and Faith-based Organisations: the WHO ENGAGE-TB model

DR. LANA SYED
DR. HAILEYESUS GETAHUN
DR. THOMAS JOSEPH
DR. GIULIANO GARGIONI
DR. MARIO RAVIGLIONE
Global TB Programme, the World Health Organisation, Geneva, Switzerland

Background

During the millennium development goals (MDG) era of 2000-2015, progress in the global fight against tuberculosis1 (TB) resulted in the reduction of the TB mortality rate by 47%. Despite this achievement, global TB incidence remains high. The World Health Organization (WHO) estimates that more than 10 million new cases of TB occurred in 2015, including 1 million among children and 3.5 million among women. In the same year, 1.8 million people died of TB, including over 200,000 children and half a million women. While globally only 11% of all TB cases were in people with HIV infection, in Africa, that proportion was 30%. The most drug-resistant forms of TB were estimated in 2015 at approximately half a million cases worldwide and 200,000 of these were fatal. Overall, Africa had the highest TB incidence rates per capita although the majority of cases (60%) were in Asia due to its larger populations. TB is present in every country worldwide. Six countries (India, Indonesia, China, Nigeria, Pakistan and South Africa) carry 60% of the global burden.2

The world has now entered the era of the United Nations (UN) Sustainable Development Goals (SDG) 2016-2030.3 The seventeen goals require a much larger perspective than the previous MDGs: they are indivisible and integrated, promote development of all nations through multidisciplinary approaches, aim at the reduction of inequities, and are universal since they apply to all countries. SDG 3 'ensure healthy lives and promote well-being for all at all ages', and relates directly to health. Other SDGs also propose targets that support the health of all people. Among the specific targets of SDG 3 is a clear call for ending the epidemic of TB by 2030, in addition to ending other major epidemics such as those due to HIV/AIDS and malaria. To respond to the threat posed by TB and align with the agenda of the SDGs, WHO launched the End TB Strategy,4 endorsed by the World Health Assembly in 2014. The Strategy builds on the need for a multisectorial and interdisciplinary approach to TB, as promoted within the SDG framework. The vision of the new Strategy is of a world free of TB with zero deaths, disease and suffering due to TB. It defines ambitious targets for the reduction of TB incidence and mortality. It requires that affected families should not bear any catastrophic costs due to TB, recognising that most of the 10 million people affected every year also suffer from poverty. The Strategy is composed of three pillars and four principles. These emphasise the need for a strong coalition with communities and civil society organisations (CSOs), including non-governmental and faith-based organisations (NGOs, FBOs) to achieve the ambitious goal of ending the TB epidemic (see table 1).

Evolution of the WHO Response in Engaging Communities, FBOs and other CSOs in TB Response

Being a classic disease of poverty, TB affects the most vulnerable people, such as those living in crowded settings, those with HIV infection, the malnourished, drug users, alcohol abusers, smokers, migrants, prisoners, minorities, displaced people, and women and children. Therefore, approaches and strategies designed to reach such marginalised and vulnerable populations are essential in the TB response.

FBOs and other CSOs working in communities are in a unique position to contribute to community health.5 They are familiar with the community's culture and language, they can communicate with others about the community's needs, and they can mobilise people in the community to influence decisions made about the community. They are especially important for reaching people in isolated or neglected parts of the community when the formal health system cannot reach them. FBOs and other CSOs are also able to reach vulnerable and marginalised groups such as migrants, refugees, sex workers, people who use drugs and the very poor who are often unable or unwilling to access health services from the formal health system.

The WHO has a history of engaging FBOs and other CSOs as partners, starting with the Declaration of Alma-Ata in 1978,6 a true milestone in the history of global public health, where one can find a statement as strong as the following: 'The people have the right and duty to participate individually and collectively in

the planning and implementation of their health care'. Later, with the rise of the HIV/AIDS epidemic in the 1990s, there was renewed interest and increased resources to strengthen capacities of FBOs and other CSOs in provision of care, especially, but not exclusively, in African countries.7 In the same period, WHO started exploring community TB care through several projects in Africa.8 The projects were instrumental in demonstrating the usefulness and cost-effectiveness of engaging FBOs and other CSOs in providing community-based services for TB prevention, detection and treatment. The evidence garnered helped ensure the inclusion of civil society as a key partner in TB responses in the 2006 Stop TB Strategy,9 followed by the launch of a policy guidance document on community care in TB in 2008.10 This document emphasised the key concepts of social justice, human dignity, subsidiarity and solidarity as also articulated in the Social Doctrine of the Catholic Church.11 While social justice represents the definitive aim of all efforts to pursue better access to health for all, the universal concept of the dignity of each person was promoted and, within it, the basic principles of (i) the common good for which all must collaborate; (ii) subsidiarity, through which empowerment and support from higher level institutions foster development of communities; and (iii) solidarity, which incorporates the moral responsibility to share societal needs and pursue the common good in an inter-dependent world.

ENGAGE-TB Approach and Demonstration Projects

Aligned with these principles and developing them further, in

Table 1: THE END TB STRATEGY 2016-2035

VISION	**A world free of TB** – zero deaths, disease and suffering due to tuberculosis			
GOAL	**End the global TB epidemic**			
INDICATORS	**MILESTONES**		**TARGETS**	
	2020	**2025**	**2030***	**2035**
Reduction in number of TB deaths compared with 2015 (%)	**35%**	**75%**	**90%**	**95%**
Reduction in TB incidence rate compared with 2015 (%)	**20% (<85/100 000)**	**50% (<55/100 000)**	**80% (<20/100 000)**	**90% (<10/100 000)**
TB-affected families facing catastrophic costs due to TB (%)	**0**	**0**	**0**	**0**
PRINCIPLES				
1. Government stewardship and accountability, with monitoring and evaluation 2. Strong coalition with civil society organisations and communities 3. Protection and promotion of human rights, ethics and equity 4. Adaptation of the strategy and targets at country level, with global collaboration				
PILLARS AND COMPONENTS				
1. INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION A. Early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups B. Treatment of all people with TB including drug-resistant TB, and patient support C. Collaborative TB/HIV activities, and management of co-morbidities D. Preventive treatment of persons at high risk, and vaccination against TB				
2. BOLD POLICIES AND SUPPORTIVE SYSTEMS A. Political commitment with adequate resources for TB care and prevention B. Engagement of communities, civil society organisations, and public and private care providers C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control D. Social protection, poverty alleviation and actions on other determinants of TB				
3. INTENSIFIED RESEARCH AND INNOVATION A. Discovery, development and rapid uptake of new tools, interventions and strategies B. Research to optimise implementation and impact, and promote innovations				

* Targets included within the United Nations 'Sustainable Development Goals'

2012 the WHO launched the ENGAGE-TB Approach to facilitate the integration of community-based TB services into the work of FBOs and other CSOs.12 Its purpose is to provide guidance on the implementation of community-based TB prevention and care activities; collaboration between governments, FBOs and other CSOs based also on the principles of solidarity and subsidiarity; and integration of TB care into the existing community-based work of those organisations, especially where TB care was not previously being provided. Following requests from interested stakeholders and based on the initial experience acquired in the projects, in recent years WHO has produced an implementation manual13 and training materials14 (see box 1) to support the implementation of the ENGAGE-TB approach.. The guidance available today targets a wide spectrum of organisations working in areas such as primary health care; HIV; maternal, newborn and child health (MNCH); education; agriculture; livelihood development programmes; and water, sanitation and hygiene initiatives.

In 2012, demonstration projects were initiated in the Democratic Republic of the Congo, Ethiopia, Kenya, South Africa and the United Republic of Tanzania, over a period of 30 months. Actions at a national level targeted policies and programming while the services were delivered at a community level. At a national level, ministries of health in collaboration with FBOs and other CSOs, and with support from the WHO, set national policies to facilitate the engagement of FBOs and other CSOs in integrated community-based TB activities. These were subsequently included in the national strategic TB plans. At the community level, 24 FBOs and other CSOs received seed funding to pilot integration of TB care into their ongoing programmes, covering a population of eight million persons collectively; 2 FBOs in Ethiopia and South Africa covered nearly half a million persons collectively. In the focus countries, innovative models were developed by FBOs and other CSOs that integrated TB services into MNCH, cervical cancer screening, livelihood development programmes and HIV/AIDS programmes (see table 2).

Key Achievements

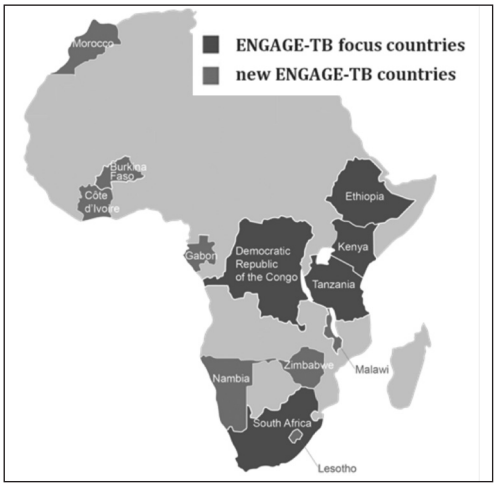
The achievements of the demonstration projects included the creation of more conducive policy and programme environments for the engagement of FBOs and other CSOs in community-based TB activities at national and local levels. The integrated community-based TB activities led to finding those with TB early and improving their adherence to treatment, resulting in better outcomes, particularly among the most vulnerable groups. Furthermore, coordination mechanisms among hundreds of FBOs and other CSOs were established. During the period 2013-14, a total of seven thousand persons with presumptive TB were referred for diagnosis – nearly a thousand were identified through the two FBOs – and more than a thousand cases were identified and supported at community level for treatment adherence. A total of thirteen countries have since included the ENGAGE-TB approach in national strategies and policies and secured funding for implementation (see figure 1).

Another key area has been the standardisation of the global core indicators for community engagement and related monitoring and evaluation guidance provided as part of the ENGAGE-TB approach. These indicators include the contribution of community referrals to notified TB patients in the catchment area, and treatment success of persons who benefited from any form of community-based treatment support. Standardisation is essential to ensure continuity in the years to come. It also facilitates documentation of comparable data from the implementing countries as part of the WHO routine yearly data collection, analysis and publication.

To take stock of the engagement of FBOs and other CSOs and the implementation status of the EN-

Box 1. ENGAGE-TB implementation tools by year of publication

Figure 1. ENGAGE-TB expansion: from demonstration projects to countries newly adopting the model



GAGE-TB approach, the WHO held a consultation with 90 FBOs and other CSOs from 35 countries worldwide in 2015 in Addis Ababa, Ethiopia.15 The outcome was a Statement of Action16 which contained twenty recommendations for FBOs, NGOs and other CSOs, national TB programmes, ministries of health and other line ministries, the Global Fund and other bilateral and multilateral donors as well as for the WHO. The implementation of these recommendations will be crucial to ensure enhanced engagement of FBOs and other CSOs in TB care and prevention efforts.

Conclusion

Lessons learned from emerging evidence of the ENGAGE-TB demonstration projects identify close collaboration between the national TB programme, FBOs and other CSOs in planning, implementation, and monitoring and evaluation as a minimum requirement for achieving bold results in partnering with FBOs and other CSOs. The integration of TB into the existing community-based work of FBOs and other CSOs has proven feasible and effective and this approach needs to be strengthened and scaled up in all the highest burden countries; more research on the impact of FBO and other CSO engagement in TB response will help strengthen the evidence base and facilitate resource mobilisation for scale-up.17

Other features of successful demonstration projects include the multi-sectorial collaboration which enabled formulation of important policies on social protection. These built on the synergy and complementarity experienced in partnering with the non-state sector using the principle of subsidiarity. Finally, the solidarity in relationships experienced within communities is paramount in order to achieve integrated patient-centred TB care and prevention.

Table 2: Summary of ENGAGE-TB demonstration projects in the five focus countries

Country	Name of implementing FBO or other CSO	Primary focus of FBO or other CSO *	Population covered	Number of health facilities covered by the project
Democratic Republic of the Congo	Fondation Femme Plus	HIV/AIDS, women and orphans	4,709,007	33 diagnostic and/or treatment centres
Ethiopia	AMREF	Malaria and MNCH	107,912	17 treatment and/or diagnostic centres
	CUAMM**	Cervical cancer screening and MNCH	181,877	8 treatment and/or diagnostic centres
	Save the Children	Immunization and livelihood development programme	100,619	4 treatment and/or diagnostic centres and 6 health posts
Kenya	CHAP	Health, immunization, sanitation and breastfeeding	3,.000	2 treatment centres
	GAPP	HIV, OVCs, agriculture and livelihoods, social justice and human rights	337,960	22 treatment and/or diagnostic centres
	TALAKU	TB	174,408	1 treatment centre
South Africa	Bambisanani	HIV/AIDS	801,344	10 treatment and/or diagnostic centres
	CPC	HIV/AIDS	706,000	16 treatment and/or diagnostic centres
	MAP**	HIV/AIDS	216,149	20 treatment and/or diagnostic centres
	Thabo Mwale	HIV/AIDS	85,000	N/A
United Republic of Tanzania	Pathfinder International	Home based HIV/AIDS care	713,736	19 treatment and/or diagnostic centres

* Health or development theme that TB was integrated into
** Faith-based organisation

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5. Research, Solidarity and Medicines

DR. LELIO MARMORA
Executive Director UNITAID, Switzerland

1. Unitaid – Who are we?

The global health paradigm has gone through a triple shift, from a donor driven agenda to more national ownership, from a government-centric to a multi-stakeholder approach and from budgetary to performance-based funding. Unitaid was created during this paradigm shift and within the momentum of increased development assistance for health in the early years of this century that led to the creation of a number of organisations in the health sector.

Unitaid was created in 2006 through a unique partnership to invest in new ways to prevent, diagnose and treat HIV/AIDS, tuberculosis and malaria more quickly, more cheaply and more effectively. Unitaid has a unique role, connecting those responsible for developing innovations with the people who will most benefit from them – notably, people in resource-limited settings who are affected by the diseases on which Unitaid focuses. By working with those 'upstream' – that is, researchers, academics, product development partnerships, the private sector, and others involved in research and the development of new technologies – Unitaid helps identify promising, close-to-market products that offer innovative health solutions. Unitaid then works with 'downstream' partners – for example, national governments, funding partners, implementing partners, NGOs and others who directly serve those in need – to ensure that access to innovative health solutions becomes a reality and serves the needs of people most affected by these diseases.

By bridging the 'upstream' and the 'downstream', Unitaid catalyses access to innovative health solutions for greatest impact. Unitaid overcomes the various market barriers that prevent access to innovative health products, such as affordability, quality, supply and delivery, and demand and adoption.

Unitaid translates global goals into concrete projects by using a systemised approach:

As a starting point, Unitaid examines the public health needs and the goals agreed to by the global health community.

Unitaid then analyses the context for each disease, reviewing: the disease characteristics (including burden, key health products, access to these); challenges that threaten the

achievement of the global goals; and finally, Unitaid's potential role in addressing specific challenges, as part of a coordinated global response. This analysis is referred to as the Disease Narrative and is based on consultations with partners and input from multiple sources.

From the Disease Narrative, Unitaid develops Areas for Intervention, reflecting Unitaid's ability to add value on challenges related to health products. Unitaid uses four criteria as filters to identify a shortlist of challenges that represent the highest potential for Unitaid's interventions. This final list of challenges provides the basis for the identification of Areas for Intervention, which are proposed to the Executive Board for endorsement.

In order to prioritise Areas for Intervention between health topics, Unitaid relies on a number of strategic and pragmatic criteria, including – but not limited to – public health impact, fit with the Strategy, portfolio balance across diseases, synergies with other projects, secretariat capacity, etc.

Based on endorsed Areas for Intervention, Unitaid issues calls for proposals. To select the proposals for funding, Unitaid leverages a Joint Review Committee composed of independent reviewers and the Secretariat.

Partner engagement is key through the entire process. At all stages, Unitaid engages with a variety of partners at the technical, scientific and political levels. Unitaid pilots promising solutions and engages with countries, major funders and health partners such as the Global Fund, PEPFAR, PMI, USAID and civil society to ensure that these are deployed on a full-scale. Unitaid spotlights critical challenges and plays an important role in raising awareness and commitment among global health actors, including countries, technical partners, implementers, funding partners, the private sector, and civil society.

Unitaid has a fast growing portfolio with expected number of 36 grants in 2016 and estimated 48 grants in 2017. The majority of grants are in HIV/AIDS, followed by Malaria, TB and cross-cutting projects.

2. Our Analysis of the Global Health Landscape

The global health agenda is continuously evolving and expanding. Previously, out of the 8 Millennium Development Goals (MDGs), three were specifically focused on health, with the fight against HIV/AIDS, malaria and other diseases being a goal in its own. The Sustainable Development Goals (SDGs), agreed in 2015, are much broader and encompass a variety of tropics, ranging from poverty, education, sanitation, infrastructure, economic growth, climate change and development to global health. Of the 17 SDGs, only one goal is focused on health with a variety of sub-areas on HIV, tuberculosis, malaria, non-communicable diseases, maternal health, child health, universal health coverage etc.

Remarkable progress has been made in the fight against HIV/AIDS, tuberculosis and malaria over the past two decades, yet pressing needs remain. New investments and effective partnerships hold the key to achieving ambitious global health goals. It took 15 years to put 18 million people on ARV therapy. To get 15 million more people on treatment in the next five years, we will have to work harder and faster. Many critical gaps also persist in tuberculosis and malaria. In 2015, more than 4 million tuberculosis cases still escaped detection, and fewer than 40% of people infected with malaria received appropriate care.

With increasing public health needs as the population grows and within the context of rising resource constraints, innovative solutions are needed to avoid a kick-back of gains achieved so far.

The funding needs to reach the Sustainable Development Goal 3 (Ensure healthy lives and promote wellbeing for all at all ages) are increasing with an estimation of $50-80 billion per year needed. Yet, we are observing a plateau in international financing, which means that we need more effectiveness to tackle the needs. *Unitaid is contributing to greater effectiveness in the global health response*, in particular by promoting access to better health products, by spending smarter and by fostering integration and coordination.

3. Draft strategy 2017-2021

Unitaid has developed a new strategy for the next five years (2017-2021), underpinned by technical strategies – i.e., Disease Narratives on HIV/AIDS and co-infections (e.g., hepatitis C), tuberculosis, malaria, a Thematic Narrative on Reproductive, Maternal, Newborn and Child Health (RMNCH), and approaches to specific topics, such as Intellectual Property. Unitaid's mission for 2017-2021 is to '*maximise the effectiveness of the global health response by catalysing access to better health products*'. Indeed, Unitaid plays a role at three critical moments, from when a product is available, to when a product is adopted and finally when a product is scaled up.

To deliver on its mission, Unitaid has identified *three Strategic Objectives*: Innovation, Access, and Scalability. Unitaid's projects are designed to promote innovation, to catalyse equitable access to these products, and to create the conditions for scale up to reach all people in need.

Unitaid has defined a set of commitments, which underpin the way in which it invests in projects, to ensure its investments generate maximum impact for the global response: We strive for equity, we maximise value for money, we succeed in partnership, we invest in products, which impact health systems.

Going forward, Unitaid's portfolio will evolve towards projects supporting better integration, as a response to the need for increased effectiveness of the global health response and for higher value for money of Unitaid's portfolio. This focus on integration follows the global trend to evolve towards more holistic approaches to global health, initiated with the SDGs. This will translate into a higher share of the grants in the portfolio supporting a more integrated approach to health.

SATURDAY 12 NOVEMBER

Precision Medicine in Rare and Monogenic Diseases

PROF. GIUSEPPE NOVELLI
University of Rome 'Tor Vergata', Italy

Monogenic or Mendelian diseases are defined as such because they are determined by the presence of a single mutated gene that segregates in line with the laws discovered by Mendel. In addition, these diseases are seen as rare because they are present with a prevalence lower than a certain threshold within the general population. In Europe this corresponds to 0.05% of the population, that is to say 1 case in every 2,000 inhabitants. Genomic medicine is an approach of medicine whose goal is to create targeted diagnostic and therapeutic pathways that are constructed on the basis of what is by now extensive knowledge of the human genome. Personalised medicine is a model that in general emphasises the 'customisation' of care, according to which all decisions and practices are tailored to individual patients and not groups of patients. Present at the base of personalised medicine is a systematic use of genetic information with an individual patient to select or to optimise preventive or therapeutic treatment for that patient himself or herself, taking into consideration the genetic variability of individuals within a population. Thanks to the implementation of the techniques of next generation sequencing (NGS), as well as bio-information and computational techniques, it is possible to identify a pathology at the molecular level by characterising its pathogenic nucleotide variants. The identification of these variants also allows us to establish the risk of recurrence of the disease in future generations and therefore to plan diagnoses, prognoses and in some cases therapy as well. The priorities of research into, the discovery, and the development of new medical products by pharmaceutical companies and the academic world are directed towards meeting needs that are currently outstanding in the case of orphan diseases or neglected diseases, and residual needs, in the case of patients who do not respond to the therapies available for a specific disease.

Today new medical products are experimented with, and programmes of innovative treatment such as gene therapy are assessed, for about two hundred rare diseases. The success of these research programmes, which prevalently concern totally unmet therapeutic needs, increasingly depends on cooperation between the interested parties: pharmaceutical companies, private research agencies and companies, the academic world, research foundations and charities, and the regulatory system. From a therapeutic point of view, knowledge of molecular defects has allowed the development of personalised protocols of gene therapy that envisage the targeted correction of a molecular defect and the synthetic production and approval of medical products aimed at the specific correction of that defect. These approaches, in addition to an in-depth knowledge of facts about a molecule, also envisage a full understanding of the pathogenic mechanism that leads to the pathological phenotype. Gene therapy thus has the task of correcting a genic disease through the transfer of gene material inside the cell nucleus. The principle is to use DNA as a 'medical product' to remove in a permanent way an alteration of the genome, or to express in a temporary way functional copies of a 'therapeutic gene'.

The European Agency for the Evaluation of Medical Products defines a product of gene therapy as 'a biological medicinal product that meets the following characteristics: it contains an active substance (a recombinant nucleic acid) that is administered to a human being with the aim of regulating, repairing, replacing, adding or eliminating a genetic sequence. In addition, its therapeutic or diagnostic effect is directly connected with the DNA or RNA sequence that it contains or with the product which is the expression of its sequence'. Gene therapy can be applied to somatic cells, in which case the defect is treated exclusively in the patient who receives therapy.

Gene therapy today is becoming an important reality thanks to new technologies such as Clustered Regularly Interspaced Short Palindromic Repeats (CRISP) which allow a direct correction of the sick gene, repairing it with absolute precision. CRISP technology is based upon the use of artificial endonucleases, that is to say proteins constructed in a laboratory that are used to induce a modification of a specific sequence of DNA which cut the DNA at a specific place and thus set in motion the normal reparative mechanisms of a cell. These recopy in the site of the excision a correct sequence that is provided by us to the same cell. CRISP exploits a system of bacterial defence which

is activated when they encounter a virus, break its DNA and place it in inside the right place in areas that are called 'leader sequences'. In this way, when a bacterium is exposed to a virus that has already been encountered it is able to destroy its DNA by eliminating it. This is the result of a protein called *Cas* which cuts all of the DNA identical to the 'leader sequences'. By modifying the DNA contained in the leader sequence, it is possible to make the bacterium acquire a resistance to a target sequence of DNA.

In parallel with gene therapy, even though more recently, protocols for cell therapy have been developed that envisage the use of progenitor stem cells or cells derived from them in order to replace or repair damaged organs or tissues. Cell therapy involves the insertion of cells that are able to differentiate into different types or sub-types within specific target tissues or organs, thereby helping to recover the lost or damaged functions of tissues. This protocol also envisages a stimulation of the regenerative endogenous capacities of the organism or alternatively the transplanting of cells or tissues reconstructed *ex vivo*. The cells can be autologous (the same person is the recipient and donor), allogeneic (the recipient and donor are different people), or xenogeneic (the cells of the donor come from an animal). Cell therapy constitutes the final therapeutic frontier for the treatment of those pathologies that are caused by the malfunctioning of a specific cell type. In addition to being useful in relation to monogenic diseases, it has also been shown to be useful with tumors during the treatment of toxicity induced in tissues by therapeutic treatment such as chemotherapy or radiation in childhood leukemia or where there are deficiencies of the immunity system.

Conclusions and Recommendations Treating Everyone to Achieve True Fraternity

FATHER MICHELE ARAMINI
Professor of Theology at the Sacred Heart Catholic University of Milan, Italy

1. Rare Diseases

1.1. The situation

From the point of view of classification, there is still not complete agreement on the definition of what a rare disease is. In some countries and regions only the level of prevalence is taken into account, whereas in others criteria involving genetic origins and difficulties in achieving a diagnosis are also included. Side by side with the classification of a rare disease, some authors also use the classification of an 'ultra-rare disease'. We may cite some examples of these diseases: hypothyroidism, phenylketonuria, cystic fibrosis and the adrenogenital syndrome. These diseases are a grave problem in countries with advanced medicine and are an authentic drama in countries that do not have adequate health-care systems.

Although rare diseases afflict a small portion of the total population, the absolute number of these people is indeed notable. In particular, however, people with individual pathologies constitute a niche and often they do not receive sufficient medical care and treatment. Governments and societies do not pay sufficient attention to these people who thus, in addition, do not have opportunities at the level of instruction and jobs, and thereby remain marginalised.

This situation is also present in countries with advanced medicine although these countries in recent decades have witnessed notable improvements above all else in relation to the more frequent rare diseases.

We will briefly describe some advances that are required in all countries and thus are goals of both rich systems and poor health-care systems. Neonatal genetic screening must become routine. In this way, rare diseases can be identified on a genetic basis. At the present time, the tests that are carried out look for about forty such diseases. This is a number that is destined to increase. A second fundamental point is the creation in every region of centres of reference specialised in rare diseases that can support the parents of children and work with associations of patients and their families. Without these centres, there will be isolation and hopelessness.

In Western countries, the centres of reference are not to be found everywhere and not all groups of rare diseases are covered by them. De La Riva presented us with the Spanish case. In Spain about a half of the groups of rare diseases do not have a centre of reference. And support is not provided by the state for those that do exist: there is the commitment on a voluntary basis of medical doctors and other personnel. This lack has political causes, as a result of which there is no sensitivity and agreement between the seventeen regional governments into which the country is divided. There are also organisational causes involving competition between hospital institutions, as a consequence of which large hospitals do not foster the specialisation of some small hospital institutions. Lastly, there are economic reasons: the Ministry of Health does not grant funds for the creation of centres of reference. Therefore, family associations, helped by volunteer medical doctors, create support networks for patients and their families – the hope networks.

Very recently in Italy another 118 diseases have been placed at the essential levels of health care and this allows therapies and medical products to be obtained from the National Health Service in that country. But this confirms the fact that many other diseases remain outside these levels of health care. Thus we can say that in Western countries, as well, there are league A and league B rare diseases.

Side by side with these observations, which bring out the organisational and economic aspects, one should also remember that the treatment of patients with rare diseases is more than a medical problem. It requires an interdisciplinary team with a medical staff, social assistants, specialist psychological consultants and consultants in pastoral care, in order to assure holistic care for patients and those who look after them, in particular their nuclear families and close relatives.

Here we can refer to the painful question of the time that is needed to obtain a correct and accurate diagnosis. If we exclude genetically-based diseases that are covered by the various kinds of neonatal screening, and which are discovered at birth, as regards all the others the objective of diagnosis is reached often after many years, the average period of time being about five years. It is easy to understand the difficult pathways that have to be faced up to by the families of these very young patients. A large proportion of medical personnel are not trained to recognise rare diseases and do not refer patients to centres of reference, even when these last exist. Therefore, a major problem of training exists as regards health-care personnel and their being able to have the competence and sensitivity that are needed to take

responsibility for people with rare diseases and for recognition of their pathologies.

Prevention

This is work that must be developed because it is overly neglected. One can act in a way that respects environmental conditions, with the prevention of particular infections. In addition, treatment must not stop at medical products alone. Therapies for the treatment of symptoms are also required and these are often able to help patients to secure a good quality of life (Taruscio).

Orphan drugs and the economic management of treatment and care

The term 'orphan' refers to a medical action. The terms 'rare' or 'ultra-rare' refer to a medical condition or a disease. The clinical definition of an 'orphan' intervention says that orphan treatments are those initiatives that are of proven efficacy for rare or ultra-rare diseases. However, orphan treatment and orphan medical products are subject to legal regulations. Thus, the definition of an orphan treatment and an 'orphan medical product' depends on a complex of factors.

The greatest problem as regards the refunding of orphan medical products is their high price. However, the prices of orphan medical products can differ significantly and thus the assessment procedures must be accurate. If an orphan drug is a real innovation at the level of therapy, a high price in many cases becomes acceptable, but if the innovative character of the drug is limited or uncertain, a high price for this product is not justified.

From the point of view of health-care policies, one should not apply to orphan treatment the criterion that is used for common diseases, that is to say the utilitarian criterion of the cost/benefit ratio. In the case of orphan drugs, the correct approach must be an egalitarian one. In this case, to the foreground is the right of a person to care and treatment and the decision to refund the cost of orphan treatment is of vital importance. The budgets for the refunding of the costs of treatment of rare and ultra-rare diseases must be adequate in order to allow better access to innovative therapies for patients with rare diseases.

1.2. Action to be taken

Some papers clearly indicated the steps that should be taken to activate a modern service for the treatment of rare diseases.

1.2.1. Organisational aspects

As regards the organisational aspects, we can take some indications from the Spanish case as described in the paper by Santiago de la Riva and which can be applied to every country.

First of all, the creation of centres of reference for rare diseases should be promoted in every country and in every region of the world so that people with these diseases have a real opportunity to obtain a diagnosis and, if possible, treatment as well.

Secondly, one should proceed to the drawing up of a protocol to shorten the long pilgrimages of people who do not have a medical diagnosis of their condition. An early diagnosis must be achieved.

Thirdly, research should be promoted with suitable projects and funding.

Lastly, an element that can never be sufficiently emphasised is the training and sensitisation of health-care personnel: the present state of affairs often leads to an unacceptable situation of abandonment of people with rare diseases. This training cannot be limited to aspects that are exclusively medical in character. It should be extended to psychological and religious aspects as well. One understands the urgent need for action when some authentically bare statistics are taken into consideration: only 10% of rare diseases are currently the subjects of research projects and only 0.4% of rare diseases can count on effective therapeutic responses.

1.2.2. An experience to be imitated

An important paper described to us the journey of a country that has become aware of the problem and can become a model for many other countries – Taiwan. When discussing rare diseases, the paper given by Dr. Han demonstrated to us in detail how one can improve the situation of a country through suitable laws and funding. Over the last two decades, progress has been achieved through the union of the efforts of the government and those of non-profit-making organisations operating in Taiwan. An integrated network has been created for social assistance, medical care, legal aid, and scientific research into rare diseases in order to safeguard human life and the dignity of those people who have rare diseases. The approaches of the action plan relate to legislation, social and financial resources, research funds, clinical diagnosis, genetic screening, prevention, and future prospects as regards the treatment of people with rare diseases. At the present time, the total number of cases of uncommon diseases registered by the Authority for the Promotion of Health of the Ministry of Health is 10,620. From the point of view of diagnosis, neonatal screening has been introduced and this has been adopted in twenty-two centres of reference spread throughout the country. Of interest is the plan for social and financial assistance for families with children who have rare diseases. These families find themselves in conditions of grave economic and social malaise, and on this front, as well, an attempt is made to act. Subventions are provided for medical products the cost of which is not refunded by the National Health Service; special milk is provided to breast-feeding mothers with neonates with rare diseases; and, in addition, support medical equipment is supplied. A specific Foundation for rare diseases offers various kinds of financial help in order to contribute to relieving the burdens of care and treatment for patients and their families. In the year 2015, the sums of money paid over to 1,830 people amounted to US $1,566,181.

The Foundation for rare diseases also seeks to develop and strengthen academic research in Taiwan, granting research grants and study scholarships to encourage advanced research amongst

medical professionals and scholars, as well as university students. The Foundation accepts research projects relating to diagnosis, clinical treatment, medical products, long-term care, psychological needs, case studies, and the analysis of large-scale data on rare diseases. Starting in the year 2014, thirty-seven research projects have been approved for an overall expenditure of US $493,870. Eighty-five degree theses have also been sponsored, involving an overall sum of US $101,612. This research has concentrated on rare diseases to be found in Taiwan and for these the Taiwan Biobank was founded. It should also be observed that one task of the Foundation is improving and facilitating the legislation of the government.

Last but not least, clinical diagnosis and genetic screening have been introduced and these constitute an essential element in diagnosis. To achieve this, in addition to the creation of twenty-two centres of reference, cooperation with international laboratories for genetic screening operating in Europe and the United States of America has also been developed.

2. Neglected Tropical Diseases

2. 1. The situation

The second subject that the international conference addressed was neglected diseases. The recommendations of the World Health Organisation as regards NDTs (neglected tropical diseases) are well known.

The World Health Organisation has listed certain characteristics which these diseases share. They constitute an indicator of the poverty of populations; above all afflict sections of the population with a low level of visibility and with little political power; they tend not to spread geographically; they cause stigma and discrimination, above all to the detriment of girls and women; they have an important impact on illness and mortality rates; they are neglected by research because the sections of the population that are afflicted by them do not have a sufficient income to create a remunerative market; and they can be controlled, prevented and probably eliminated by using strategies that are effective, practicable, and have moderate costs.

Neglected tropical diseases afflict the poorest people of the world, above all in the continents of Africa and Latin America. Most of these diseases are caused by contagion and are widespread in geographical areas that have a tropical climate where the drinking water is not safe, hygiene is scarce, housing conditions are poor, and access to health-care services is of a low level or does not exist. Environmental deterioration also has a major effect and, as is known, this particularly afflicts poor countries. The World Health Organisation calculates that over a billion people, of whom a half are children – a sixth of the population of the world – suffer from one or more neglected tropical diseases. These diseases have effective therapies involving low-cost medical products. However, these reach only a half of their targets.

The challenge from an epidemiological, scientific and clinical point of view is very great because this is a matter of managing to provide adequate care and treatment to a very large number of people. This challenge involves responsibilities and commitment at a global level by all the players – international and national political and health-care authorities; health-care workers; the biomedical industry; associations of citizens/patients; and lay and religious volunteers.

The concept of neglected tropical diseases was born with the Millennium Development Goals (MDGs) which were launched in the year 2000 when infectious diseases were highlighted as Goal 6: 'to combat AIDS, malaria and other diseases'. Although AIDS and malaria have benefited from massive aid for research and treatment, what are called 'other diseases' have been ignored or neglected (Hotez).

To respond to this situation, philanthropic institutions such as the Sabin Vaccine Institute have created an NTD system to work with a group of 13-14 chronic and debilitating diseases caused by infections provoked by parasites.

Some papers instructed us as to the reality of these diseases, and here we may cite only some of them: leprosy, filariasis, malaria, the Zika virus, tuberculosis, etc.

The paper by Raviglione described the good practices of the work of the World Health Organisation in relation to a disease which, although it is the most widespread, is completely neglected. Here we are speaking about tuberculosis which today is receiving a little more attention, even if the support for the fight against this disease is still far from global requirements. The contents of this paper allowed many of those listening to become familiar with an infectious disease that kills an enormous number of people throughout the world.

An important question emerged from this paper: who bears the gravest damage and burden caused by tuberculosis? The answer is terribly simple: the most vulnerable people, those who live in crowded poor environments, those infected by the HIV virus, the malnourished, drug addicts, alcoholics, smokers, migrants, people in prison, displaced persons, and women and children. These are the parts of populations that must be prioritised with respect to any initiative that seeks to prevent or treat tuberculosis and other diseases that are common amongst the poorest and most marginalised people of the world.

This paper went on to emphasise that in the fight against tuberculosis a multi-sectorial approach is essential given that tuberculosis is a disease linked to poverty. In this fight all the players should be committed to cooperating and building networks. The good practice of the 'Engage TB' initiative promoted by the World Health Organisation can be used as a model to demonstrate that in difficult circumstances, as well, one can act and communities and civil society can be involved in addition to government institutions and non-governmental organisations. Naturally, one must intensify efforts in the field of research and increase funding for

pharmacological innovations, working with pharmaceutical companies. The WHO should be more intensely activated to move in this direction.

2.2. What is being done to combat neglected tropical diseases?

The signs of hope are notable, even if the journey has not yet come to an end. Some papers successfully informed us about current realities and the methodology that should be followed in the fight against NTDs (the papers by Luparello, Kapepela, Raviglione and others). The fight against neglected tropical diseases involves the commitment of a broad range of partners who for some time have worked together, offering donations, funding, resources, expertise, time and energy to develop, implement and broaden adequate strategies for action. Amongst these, there are government agencies, private foundations and pharmaceutical multinationals.

The World Health Organisation has given itself a general objective for the years 2014-2020: to accelerate the reduction of the 'burden' of NTDs through the control, elimination and eradication of specific NTDs and through contributing to the reduction of the poverty of people with these diseases, as well as to their productivity and quality of life.

The concrete objectives of the WHO in Africa to be achieved by the year 2020 are: to eradicate the Guinea worm disease and framboesia in all the countries of the continent; to sponsor the elimination of leprosy and further reduce the grave disabilities produced by leprosy; to eliminate lymphatic filariasis, onchocerciasis, schistosomiasis and tracoma; and to control morbidity caused by Buruli ulcer, human African trypanosomiasis, leishmaniasis, helminthiasis transmitted from soil, and rabies in the region

This plan of the World Health Organisation for the control of NTDs envisages the integrated use of different strategies which strengthen each other: the development of the capacities of national health-care systems; improving the planning, the mobilisation of resources for, and the financial sustainability of, national programmes to combat NTDs; improving monitoring, assessment, surveillance and research (this principally concerns action to interrupt the transmission of Guinea worm disease in Chad, Ethiopia, Mali and the South Sudan); supporting the social and physical rehabilitation of people with NTDs (improving cooperation with other sectors such as the services of social assistance, instruction, and good practices in agriculture), and contributing to their participation in the socio-economic development of their communities.

Action in relation to national health-care systems takes place through various initiatives. The first is preventive chemotherapy. The second is the diagnosis and intensive treatment of cases. The third is the control of vectors. The fourth is improvement in conditions of hygiene and health care. The fifth is action involving veterinary public health.

The sustainability and efficacy of initiatives in relation to NTDs increase when they are implemented inside national health-care systems, coordinated with other existent health-care programmes, and contribute to improvements in health-care systems. The empowerment of people and communities is also important. The involvement of populations with NTDs or at risk to them is important for the success of these initiatives. Communities should thus be authorised to take action through, and be involved in, activities involving the prevention and control of neglected tropical diseases.

Special attention should be paid to programmes that support women, for whom access to health-care services is more difficult, in particular in rural areas where neglected tropical diseases are highly endemic.

All initiatives should intentionally address or prevent problems of this kind and other inequalities. It is clear, therefore, that the management of neglected tropical diseases requires a multidisciplinary approach.

2.3 Examples of good practices that offer hope

An example connected with malaria provides us with hope (the paper by Drabek). Twenty years ago malaria had become one of the most neglected diseases in the world. The availability of new anti-malaria medical products was practically inexistent because of the low economic returns on investments in the development of anti-malaria medical products. As a result, the cases of malaria increased, with more than a million deaths caused by this disease every year. To counter this grave situation, in the year 1999 the 'Medicine for Malaria Venture' (MMV) group was created and since that date the panorama of research in this field has totally changed. Partnerships have been activated for the development of new medical products. This research has had, and has, as its goals the discovery, development and supply of new, effective and cheap anti-malaria medical products. The MMV has managed to bring together pharmaceutical researchers and academics to defeat this disease. Its partnership model is unique and has been emulated by many other entities. In this activity, public, private and philanthropic funds are brought together. The best projects are then selected and they are supported both financially and scientifically, and a portfolio of research into promising anti-malaria medical products is constructed.

2.3.1 A shared element at the level of method

One is dealing here with the essential involvement of patients in research and treatment.

This criterion applies to both rare diseases and neglected tropical diseases in different ways, although it is always essential in both cases.

This criterion was strongly referred to in all the papers (see the paper by Lasko): patients must be more closely involved in all the areas of research. Fortunately, in the world, by now, there are many initiatives that involve this closeness of patients and medical doctors and researchers. We may refer to the PCORI group in the

United States of America, other groups in Canada and Great Britain, Uniamo in Italy, and others. Many of the most recent developments in diagnosis and therapy have come from an agenda of shared research. But not only this, because these associations are involved in raising the funds that are needed for research and they work to create a network for the sharing of the most up-to-date data so that these can be at the service of all people with these diseases in the world. Of particular importance as a model for associations is the International Rare Diseases Research Consortium (IRDiRC) which works intensely to develop diagnostics for rare diseases, to support about two hundred new therapies for rare diseases, and to achieve the goal of being able to treat these diseases by the year 2020.

One of the policies of the IRDiRC is the Matchmaker Exchange and the Global Alliance for Genomics and Health. This is a large database in which the genome of many patients, which has been sequenced for diagnostic purposes, is obtained, with special attention being paid to unique genetic variants. These variants cannot be connected in a certain way with the disease of the carrier unless the variant itself is found in one or more other patients who belong to families that do not have kinship ties. The Matchmaker Exchange provides a systematic instrument by which to find such matches and to study genetic and phenotypical variants.

The task of associations of patients, family relatives and medical doctors should be extended to the training of workers in social communications. A banal article in diabetes finds space in newspapers and the television whereas a scientific article of value on a rare disease is not even published in the mass media.

The task of associations also extends to the political world to call for suitable attention and legislation. Naturally enough, these associations must operate according to a regime of transparency, cooperation, and assessment of the needs for justice of other patients.

From Raviglione's paper we learnt that the work of these associations helps in the implementation of concepts of social justice, human dignity, subsidiarity and solidarity, which, indeed, are an integral part of the social teaching of the Church and are well mirrored in the Compendium of Social Teaching of the Church.

3. The Role of the Catholic Church

The efforts of the international community are intensely supported by the Catholic Church. Speaking at the World Assembly of Health in Geneva last May, Msgr. Mupendawatu emphasised the role of Catholic health-care institutions 'in the fight against AIDS, tuberculosis, malaria and neglected tropical diseases, as well as against other transmissible diseases'. In February 2015, in his speech on access to medical products on behalf of the Holy See to the Social Forum of the Council for Human Rights, Msgr. Tomasi, the permanent observer of the Holy See, called the attention of those taking part in this forum to two obstacles to access to medical products: 'the weak incentive to so called 'non-market' or 'low investment return' forms of treatment, such as those for neglected tropical diseases, rare diseases or even those diseases with a greater incidence in low-income populations', and the difficulties that come from the fact that 'many essential medical products have not been developed with appropriate formulations or specific dosages for paediatric use'.

These two speeches offer us a key by which to read the activities of the Catholic Church to combat neglected tropical diseases. On the one hand, we encounter a 'glorious' history of commitment and sacrifice on the part of numerous men and women missionaries who, often in difficult conditions, took care of sick people, offering, at times, more the help of compassion and essential measures of hygiene than the help of medical products which did not exist or were still not available, as well as a history of commitment to creating wells, the health-care education of mothers…which still continues, above all in areas that are furthest away from large populated centred. On the other hand, we see sensitisation and/or denunciation, in large assemblies as in the communities from which these men and women missionaries came, in relation to these diseases…or, to put it better, of the lives of so many brothers and sisters who were sorely tested and deprived of the most elementary rights.

It is possible to affirm that at the present time the health-care institutions that belong to the Catholic Church, or which work in mixed regimes with national governments, are called to place their activity within the framework of the health-care programmes of such governments, thereby offering space, institutions and personnel to the implementation of the initiatives described above. This cooperation, which today we call 'networking', is as necessary as ever before in order to avoid the waste of energy and resources and the scandal of division as regards serving the human person. However, this role is not without its difficulties because powerful international organisations often impose on governments, and these governments impose on those who work with them, measures that do not always conform to Catholic morality. These measures can create embarrassment, perplexity, and at times preclude the pathway of real cooperation.

On 25 May 2013 Pope Francis received the members of the *Centesimus Annus Pro Pontifice* Foundation on the occasion of its international conference on 'Rethinking Solidarity for Employment: the Challenges of the 21st Century'. A part of his message is an invitation to '"to rethink solidarity" no longer as simply assistance for the poorest, but as a global rethinking of the whole system, as a quest for ways to reform it and correct it in a way consistent with the fundamental human rights of all human beings… We have forgotten and are still forgetting that over and above business, logic and the parameters of the market is the human being;

and that something is due to men and women in as much as they are human beings by virtue of their profound dignity: to offer them the possibility of living a dignified life and of actively participating in the common good'.

4. The Role of the Mass Media

The mass media are playing an increasingly important role because they are the principal institutions of information and communication. Thus they have a great responsibility as regards the construction of the common good. Without wanting them to become didactic instruments at the service of some power group, the wish is that they should turn their attention to all the men and women of this world and especially the weak and marginalised. Their task is to denounce injustice and to reject indifference. We all know that such is not always the case and that the realities of the situation are very different. The problems of poor people are never on the front pages and often these people do not have any voice at all.

5. A Look at the Future: treating in a Way that Respects Life and the Dignity of Patients and the Environment

When looking at future action, we cannot neglect the need for the close integration of treatment and health and care for the environment according to the approach strongly emphasised by the encyclical *Laudato Sì'*: 'In this universe, shaped by open and intercommunicating systems, we can discern countless forms of relationship and participation'. Living beings are therefore 'open systems', that is to say they are in constant and unceasing interchange with the environment in which they live.

The environment and health constitute an indissoluble tandem. A living organism cannot be healthy if it is 'immersed' in an unhealthy environment (or, at the least, its state of good health cannot last for a long time).

At number 20 of *Laudato Sì'* we find strong emphasis on the connection between the environment and health: 'People take sick, for example, from breathing high levels of smoke from fuels used in cooking or heating. There is also pollution that affects everyone, caused by transport, industrial fumes, substances which contribute to the acidification of soil and water, fertilizers, insecticides, fungicides, herbicides and agrotoxins in general. Technology, which, linked to business interests, is presented as the only way of solving these problems, in fact proves incapable of seeing the mysterious network of relations between things and so sometimes solves one problem only to create others'.

We should then consider that modern science, thanks above else to epigenetics, has provided us with a way of understanding how our genetic inheritance (or at least its way of expressing itself phenotypically) is also dependent on external influences connected with the environment. That is to say, it has by now been demonstrated that so-called 'environmental overload' (*Laudato Sì'* n. 20) also damages a genome that is exposed to it, causing negative consequences that are transmitted to subsequent generations.

In the light of these observations, medical doctors and healthcare workers should perform their work and their mission, in the sense of prevention and care and treatment, through action directed towards 'strengthening' the natural systems of defence and disintoxication that we received as a gift when we were born in order to reduce to the utmost the so-termed 'disturbance factors', all of which are closely connected with environmental deterioration. The fundamental element from which we must start is awareness of what has been described hitherto. A medical doctor must know that very many pathologies, and in particular chronic diseases (including rare and neglected diseases) and functional disturbances have as their principal cause (or joint cause) factors that have an environmental origin. This should be explored and also demonstrated given that today we have available to us internationally recognised laboratory analyses to engage in a monitoring of the environment and bio-monitoring.

6. A Culture of Health that is Welcoming and Supportive

We can affirm that the approach of service that should characterise the art of medicine in every situation becomes even more urgent and necessary in the case of rare and neglected diseases. As has already been observed, the treatment of patients with rare diseases is more than a medical problem. It requires an interdisciplinary team to assure holistic care for patients and their caregivers, and in particular their families. For Christians, the words of Jesus are decisive for this kind of service: 'Truly I say to you, as you did it to one of the least of these my brethren, you did it to me' (Matthew 25:40). It is in giving and in caring for patients that we live our true identity as Catholics and as disciples of Jesus. In *Ex Corde Ecclesia* St. John Paul II taught us the dual role of a Catholic university to be found its identity of educating and evangelising. In the same way, a Catholic hospital can best embody its identity if the medical staff and the support team can heal in a way that allows patients to believe in the love of God. In his prayer for the jubilee year, His Holiness Pope Francis prays to the Lord Jesus and says: 'You are the visible face of the invisible Father, of the God who manifests his power above all by forgiveness and mercy: let the Church be your visible face in the world, its Lord risen and glorified'.

To employ the words of Pope Francis, we could say that the world of rare and neglected diseases is also 'the outermost fringes of society… fringes which modern society itself creates. How many uncertain and painful situations there are in the world today! How many are the wounds borne by the flesh of those who have no voice because their cry is muffled and drowned out by the indifference of the rich! During this Jubilee, the Church will be called even more to heal these wounds, to assuage them with the oil of consolation, to bind them with mercy

and cure them with solidarity and vigilant care. Let us not fall into humiliating indifference'.

Many papers provoked in us thought about the subject of the humanisation of the relationship of patients and those who provide them with care and treatment. The word 'humanisation' leads us to affirm that 'being' with a patient can be more important than 'doing'. To encounter the sick means to listen to them, to welcome them with their cares and worries, their hopes and difficulties, their personal histories, their fears and their anxieties; it means establishing a relationship of nearness with them, centred on the person, reaffirming their dignity and greatness. It means not passing over the situations that patients and their families are experiencing; it means offering complete care that is able to meet their needs at a physical, emotional, intellectual, social and spiritual level, and not dealing solely with their specific pathology.

The humanisation of care relationships is a matter of a personal approach, a lifestyle that goes beyond norms, an ideology or a philosophy; one moves from a functional relationship to an empathetic relationship centred on the person.

'No institution can by itself replace the human heart, human compassion, human love or human initiative, when it is a question of dealing with the sufferings of another' (*Salvifici doloris*, n. 29).

'Yet, while professional competence is a primary, fundamental requirement, it is not of itself sufficient. We are dealing with human beings, and human beings always need something more than technically proper care. They need humanity. They need heartfelt concern… Consequently, in addition to their necessary professional training, these charity workers need a "formation of the heart"' (*Deus caritas est,* n. 31a).

Voluntary service is a concrete expression of the love of God and it is the duty of every person and in particular of Christians. Through their approach of love and free and unconditional service, volunteers promote the culture of life on the basis of the values of solidarity and fraternity.

This service can also be performed with the support of associations of sick people. They should be recognised and accompanied in their efforts so that they can transmit great human and Christian values to the community.

7. Recommendations

A. As Regards Rare Diseases

1. Primary prevention

As regards rare diseases, the primary prevention of diseases with an environmental component must be spread throughout the world, both by increasing protection factors in pregnancy (for example through the taking of folic acid which reduces the risks of spina bifida and other congenital defects) and by decreasing or eliminating teratogenic risk factors (for example diabetes, alcohol, or smoking during pregnancy, as well as some medical products, environmental pollutants, and infectious diseases).

2. Secondary prevention

Secondary prevention has to be spread through neonatal screening in order to achieve a swift identification of diseases in neonates that respond to effective treatment and to diagnose rare diseases as early on as possible, thereby assuring effective (both pharmacological and otherwise) treatment and rehabilitation. In addition, there should be an identification of diagnostic-clinical centres of high quality that are connected with each other through national and international networks in order to share good clinical practices and expertise. Medical, psychological and social support should be provided to patients and their families.

3. Formation and research

A plan for the formation of health-care personnel in all rich and poor countries must be planned so that they have the capacity, on the basis of a diagnostic suspicion that a disease is present, to refer patients to centres of excellence that belong to care-providing diagnostic-clinical networks.

Scientific research must be funded in a regular way by States but one can also launch the idea of asking, on a voluntary basis, for an allocation of a part of the profits of the pharmaceutical industry. The World Health Organisation must activate itself in this direction.

The involvement of the population of patients in taking part in planning their treatment and their rehabilitation, as well as support for families, must be seen as ordinary practice.

B. As Regards Neglected Tropical Diseases

1. Cooperation in a network

There is an urgent need to develop strong commitment to cooperation so as not to have a dispersal of energy and resources. It is crucially important that research plans in relation to neglected tropical diseases, as well as their results, be shared and disseminated as rapidly as possible through a connecting network. Ministries of Health and the World Health Organisation have an important role to play in this area. Donating countries must ask that the resources that are made available become help for the progress of all poor populations.

2. The health of migrants

Especial attention must be paid to the health of migrant people. Migration increases poverty and aggravates its health-care conditions.

The destination countries, if they are poor, must be supported in their commitment to accepting sick people and to care and treatment for the most widespread tropical diseases.

C. As Regards Both Fields

1. Justice

The richest States of the world should engage in a transfer of medical technology and adequate means both for rare diseases and neglected diseases. It is surprising that this is done rapidly in the case of the transfer of military technology and capabilities but

is not done in the field of health care.

2. The environment and health

The environment and health constitute an indissoluble tandem. Governments and health-care workers should work with this great awareness towards a harmony between human beings and the environments in which they live. Medical doctors must above all else have the knowledge and the instruments to enable them to engage in prevention because very many pathologies, and in particular chronic diseases (including rare diseases and neglected diseases) and functional disturbances, have as their primary cause (or joint cause) factors with environmental origins. Therefore, in acting to improve the quality of the life environment (in which food is also a determining part) one works for the health and the dignity of the present generation and future generations.

3. The role of the mass media

We need to work for an involvement of the mass media at all levels. Today, the subjects of rare and neglected tropical diseases are truly marginalised by the press, radio and television, whereas true professional ethics should lead the professionals of the various sectors to deal with the weakest strata of the population in order to sensitise governments and public opinion to implementing support policies. ■