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News and Notes

LEPRA in the 21st Century

On the occasion of the Annual General Meeting of LEPRA in London in July, 2001, copies of the *Report and Financial Statements* were available, describing in detail the income, expenditure, main activities and future plans of the Association. The Report included the following information on objectives, policies and activities.

OBJECTIVE OF THE ASSOCIATION

The main objective of the Association is to carry out the investigation of and promote research into the causes, treatment, cure and prevention of the disease of leprosy and any allied disease, and give and grant relief and assistance to any person suffering or believed to be suffering therefrom, or the family or dependants of such persons of any description, including financial assistance. (Extract from the Memorandum of Association).

This year 2000, the beginning of the new millennium, started with so much promise on the one hand, and concern on the other! There was certainly a widespread feeling of 'new beginnings' and a belief that there would be countless new opportunities. Such feelings certainly turned out to be correct for LEPRA. There was, of course, concern about the millennium 'bug' about which so much was written but did not in fact, appear to live up to expectation, and one wonders about the amount of resources that were used unnecessarily. Indeed, at the beginning of the year, we were talking about the forgotten 'bug' which causes leprosy and how much could be achieved towards the total eradication of the disease if only part of what was being spent on the millennium bug could be used in the fight against such a terrible disease.

The Director, Terry Vasey, in his role as President of the International Federation of Anti-leprosy Associations (ILEP), was deeply involved in the newly formed Global Alliance for the Elimination of Leprosy. The Alliance, launched in Abidjan in November 1999 consists of Governments of leprosy endemic countries, the World Health Organisation (WHO), the Nippon Foundation of Japan, Novartis, ILEP, the World Bank, and Danida. The Head of Programmes, Doug Soutar continued in his role as Chairman of the ILEP action group on Teaching and Learning materials in leprosy, and Tilak Chauhan, the Chief Executive of LEPRA India took on the role of Convenor of the ILEP representatives in India. Of course, it is India where the greatest number of new cases of leprosy is found and consequently where those suffering from the after effects of it are also found.

In India Dr K. V. Desikan, the Chairman of LEPRA India, won the prestigious Damien Dutton Award for his 50 years of service and dedication in the fight against leprosy. The end of the year saw the announcement that he would receive the International Gandhi Award in February 2001.

We believe that such high profiles and esteem in which LEPRA is held are the result of the quality of work that we undertake and support in the field. Our principal objective, written almost 80 years ago remains 'To carry out the investigation of and promote research into the causes, treatment, cure and prevention of the disease of leprosy and allied diseases...'. It is with pleasure we report therefore that once again our income increased by 22% over 1999 allowing us to plan further expansion and commence new initiatives.

Members of the Executive Committee met with members of its Medical Advisory Board and staff from England and India to plan our longer term strategies which resulted in a new commitment to growth and the broadening of our scope whilst retaining leprosy as our central focus. Vertical leprosy control programmes are at last being incorporated into general health services in many countries and general health care staff need training and support. In order to be cost effective in providing specialist services to those affected by leprosy we intend to follow our original mission to fight allied diseases such as tuberculosis, HIV infection, lymphatic filariasis, malaria and leishmaniasis wherever appropriate.

POLICIES OF THE ASSOCIATION

LEPRA's policies are that:

High quality services are given to patients through the running and support of leprosy control programmes.
Medical research into the causes and cure of the disease of leprosy and allied diseases is undertaken.
Governments are assisted to integrate services to leprosy patients into local health services or, at least, to combine them with TB control and HIV awareness raising programmes.
High priority is given to prevention of disability in all programmes.
Surgical and, where possible, socio-economic rehabilitation programmes are undertaken.
Medical Consultancy and Advisory Services are continued.
LEPRA continues to publish Leprosy Review, LEPRA's scientific journal.
High quality Training Programmes are run in all LEPRA supported programmes.
Education and Awareness Raising Programmes are run in all programmes which LEPRA supports, including the United Kingdom.
LEPRA will establish closer working relationships with Governments and Non Governmental Organisations at both local and international levels.
All assistance is monitored and evaluated to ensure the highest quality of service is maintained.
LEPRA will fight allied diseases, such as tuberculosis, HIV infection, lymphatic filariasis, malaria, and leishmaniasis wherever appropriate.

CHARITY ORGANIZATION

Her Majesty, Queen Elizabeth II, is Patron of the Charity and Sir Christian Bonington CBE, is President. Vice Presidents are HRH The Duke of Gloucester GCVO, The Secretary of State for Foreign and Commonwealth Affairs, Mr G. F. Harris, MC OLM, Baroness E. Nicholson of Winterbourne and Mrs N. K. Trenaman. The organisation of the Charity consists of a Chairman, Board of Trustees, Hon. Treasurer and Secretary who is the Director.

REVIEW OF ACTIVITIES

Based on our current available data we helped fund projects worldwide covering a total population of 270,474,319 and where 70,501 new cases of leprosy were detected. This means that LEPRA gives support to 10·4% of all projects supported by the International Federation of Anti Leprosy Associations (ILEP) and in those projects supported by us 19·9% of all new cases are found. (These figures exclude our assistance to the Prevention of Disability Programme in China which covers a population of 88 millions).

As planned our funding of the field activities we supported in 1999 continued in 2000 with increased expenditure in our direct programmes of India, Mozambique, Brazil and Bangladesh. In India we purchased 10 Health Education vans in order to broaden our coverage and efficacy in this area.

Funding to Mozambique included a £50,000 emergency grant, which was sent to assist after the terrible flooding there.

Our Social and Economic rehabilitation programmes were extended to all our projects in India and over 9,000 people affected by leprosy were helped.

Eye care was included in more projects and increased numbers of cataract operations were carried out as well as eye surgery inserting intra ocular lenses to restore sight.

We established technical support teams in the three Indian states of Andhra Pradesh, Bihar, and Madyha Pradesh. As an example two teams in Madyha Pradesh will cover a population of 5·2 millions and in Bihar a population of 11·7 millions will be covered.

The joint TB/leprosy programme in Orissa, India was extended to cover a whole district in conjunction with DANTB and Government and our new offices in Orissa opened as planned.

The Blue Peter Research Laboratory was equipped and research in TB, leprosy, and HIV started there in January 2000.

The Healthy Highway Project, which is funded by the Department for International Development, continued and will be further extended. This project is aimed at reducing the spread of sexually transmitted diseases, including HIV, amongst truck drivers and commercial sex workers in India.

The formal registration procedures of our offices in Brazil and Bangladesh were completed, and all staff in Bangladesh are now in post. Our representative in Brazil has been able to employ an administrator which will enable him to give more support to projects and seek out new initiatives. The registration also allows for easier transfer and utilisation of funds.

Our support to the National Leprosy Programme in Madagascar continued, however our French colleagues did not need the extra inputs we had anticipated.

A second World Bank loan to the Indian Government for leprosy control took longer than anticipated, and LEPRA India's accountant was asked to assist the Government in drawing up its budgets as well as working closely with the Government of Orissa to prepare its own future plans.

Our contribution to the research programme in the Karonga District of Malawi continued and the Wellcome Trust is considering funding a new programme of research to be carried out there.

We supported a programme in Tamil Nadu India, working with lymphatic filariasis.

Future activities

The focus of LEPRA's growth in 2001 will be the continued expansion of our activities in India, Brazil, Mozambique and Bangladesh.

In India we will be providing 15 technical Support Teams in four states and will begin work with three new partner NGOs in Andhra Pradesh, Bihar and Maharashtra. New work in Orissa will be facilitating the effective integration of leprosy work into the Primary Health care system and will include work in the Bargarh District, which is one of the most endemic districts in India. We will also provide support for a state level Sample Survey Assessment Unit in Andhra Pradesh which will help monitor the effective implementation of the national leprosy elimination programme in that state.

We will establish support for patient advocacy groups in four states in north eastern Brazil and consolidate our new programmes in Bangladesh.

We will support new leprosy and TB initiatives in Angola and investigate opportunities for supporting work in other priority countries such as Myanmar, Nepal and Madagascar.

The Executive Committee has carefully considered and is able to confirm the adequacy of the Charity's assets to fulfil its future obligations.

Bombay Leprosy Project

Reports are available on two Silver Jubilee Year commemorative functions held by the Bombay Leprosy Project.

Computer training for the disabled

Bombay Leprosy Project started its computer training courses on 3rd July in collaboration with the Sion branch of St Angelo's Computer Ltd. The course was inaugurated by Mr Mangesh D. Karangutkar, a handicapped individual, at a simple but meaningful function organized to commemorate the Silver Jubilee Year of BLP.

The first batch of five trainees, which includes a leprosy disabled person from Dharavi slum, is being fully sponsored by BLP, through funds raised from the public for the 3-month course. BLP plans to recruit many more handicapped individuals for future training courses, depending on the level of public donations.

Seminar on pathogenesis of early leprosy lesions

As a consequence of the country-wide efforts to identify at the earliest possible stage when the disease takes root, the National Leprosy Eradication Programme is confronted by problems related to diagnosis of early leprosy, which is the commonest form of the disease currently encountered in leprosy endemic regions in the world.

How does the pathogen causing leprosy gain a foothold in the skin and nerves? How does the human host react to invasion by this pathogen? How can leprosy be diagnosed with certainty at the earliest stage?

These questions were debated on Tuesday 3rd July at the Sion Medical College by a team of experts from the Bombay Leprosy Project and the faculties of dermatology and pathology, following an elaborate and painstaking review of the subject by postgraduates of K. J. Somaiya Medical College. The seminar was organized by BLP in commemoration of its Silver Jubilee Year.

The animated discussions revealed the need for focused research on early leprosy by collaborative efforts to try and find satisfactory answers to the questions raised in this seminar.

Gandhi Memorial Leprosy Foundation, India

We are grateful to Dr V. V. Dongre, Director, GMLF, Wardha 442001 Maharashtra, India for a copy of The Annual Report 2000–01, 'Golden Jubilee Year'. His Epilogue reads as follows:

> On 6th December, 2000, GMLF has entered its 50th year of existence. Longevity is a curse for an organization that works for controlling a communicable disease. Nonetheless, continuation of efforts to control the disease is noteworthy.
>
> In the last 49 years, the Foundation has paved the way towards elimination of leprosy. It has done pioneering work in the initial years when NLEP was born. It has influenced the lives of hundreds and thousands of leprosy patients and leprosy workers. The genesis of Survey, Education and Treatment (S.E.T.) pattern, involvement of General Medical Practitioners in the programme, training of Paramedical Workers, concept of Referral Hospitals, realizing importance of Health Education in the programme, motivation for political will and advocacy for the allied organizations and relatively late included Social Science Research are some of the landmarks of the Foundation's work.
>
> This was possible because of the devotion of a band of staff members and the foresight of the earlier path-finders.
>
> As it happens in almost every very well established organization, the output of good work of GMLF remained on a plateau for some time and then declined rapidly. The organization that was a grantor became a grantee organization. Good workers deserted the Foundation due either to its step-motherly attitude towards them or for green pastures. The result naturally was not unexpected in this situation. An organization does not consist of brickbats and walls alone. The workers are the soul of it. When that is at stake, providence is in peril!

Outside the Foundation, the circumstances have changed drastically. Leprosy has not remained a priority from many points of view. Foundation did not mould its policies accordingly. However, today, it is heartening to know that those workers who left the Foundation, are coming forward actively to rejuvenate its activities. This will happen as long as it is needed. Therefore, needless to say, the Foundation will bear the torch for leprosy elimination as long as it is required to be carried out.

Leprosy: the case of the missing genes

The following is taken from Issue 26 Q1 2001 of *Wellcome News* (Research and Funding News from the Wellcome Trust), 183 Euston Road, London NW1 2BE, England (Fax +44 (0)20 7611 7288):

> Scientists at the Wellcome Trust Sanger Centre and the Pasteur Institute in Paris have published the genome sequence of *Mycobacterium leprae*, the cause of leprosy. They have also compared the sequence, published in *Nature*, with that of its relative, *Mycobacterium tuberculosis*, which causes TB.
>
> The comparison threw up some startling differences. *M. leprae* has just 1600 genes (*M. tuberculosis* has 4000) and many of these are non-functional 'pseudogenes'. *M. leprae* also seems to have lost most of a large family of *M. tuberculosis* genes that direct its interaction with its human host. The genetic differences between the two species are reflected in their differing biologies, as *M. leprae* survives in a much more narrow environmental niche—it lives only in the human peripheral nervous system.
>
> The sequence should open up new ways of tackling leprosy, a disease that affects more than a million people a year. As with all projects at the Sanger Centre, DNA sequence information is released onto the Internet without restriction or charge to users. The project was funded by the Heiser Trust (Heiser Program for Research in Leprosy and Tuberculosis of The New York Community Trust), l'Association Francaise Raoul Follereau, the International Federation of Anti-Leprosy Associations (ILEP, which includes LEPRA in the UK), the Pasteur Institute and the Wellcome Trust.

The relevant article is entitled 'massive gene decay in the leprosy bacillus' by S. T. Cole *et al.* in *Nature*, Vol 49, 22 February 2001, www.nature.com and the summary reads:

> Leprosy, a chronic human neurological disease, results from infection with the obligate intracellular pathogen *Mycobacterium leprae*, a close relative of the tubercle bacillus. *Mycobacterium leprae* has the longest doubling time of all known bacteria and has thwarted every effort at culture in the laboratory. Comparing the 3·27-megabase (Mb) genome sequence of an armadillo-derived Indian isolate of the leprosy bacillus with that of *Mycobacterium tuberculosis* (4·41 Mb) provides clear explanations for these properties and reveals an extreme case of reductive evolution. Less than half of the genome contains functional genes but pseudogenes, with intact counterparts in *M. tuberculosis*, abound. Genome downsizing and the current mosaic arrangement appear to have resulted from extensive recombination events between dispersed repetitive sequences. Gene deletion and decay have eliminated many important metabolic activities including siderophore production, part of the oxidative and most of the microaerophilic and anaerobic respiratory chains, and numerous catabolic systems and their regulatory circuits.

A Commemorative Issue, Supplement 4, of *Wellcome News*, entitled 'Unveiling the human genome', first draft 2001, was published earlier this year, providing (to quote from the Director's covering letter) '... brief descriptions of the human genome and some of its more fascinating features, the history of the Human Genome Project, how sequence data can be used and the ethical and social implications of the research.

The contribution of dermatological clinics to leprosy control in the People's Republic of China

In this issue an article by Chen Shumin and colleagues will be published on the prevention of disability in leprosy patients in Shandong Province, the People's Republic of China. This includes mention of the continuing cooperation between the leprosy services and the dermatologists working in dermatological clinics. In fact, over one-third of all new cases in PR China have been detected in such clinics in recent years, underlining the very considerable contribution of dermatology to leprosy diagnosis and control in this country—an unusual situation in other leprosy-endemic countries, even when dermatologists are available. See recent contributions on this subject on the *Leprosy Mailing List*, Cefpas, Caltanisetta, Italy. E-mail: noto@cefpas.it

Leprosy mailing list (e-mail) from Cefpas, Caltanisetta, Italy

Dr Salvatore Noto at the Centre for Research and Training in Public Health (Cefpas), Via G. Mulè, 1, 93100 Caltanisetta, Italy, has established a 'Leprosy Mailing List' for the exchange of information between people working with this disease, using e-mail. From a modest beginning, the list now has dozens of names from correspondents in control, research, public health, communications, dermatology, charities, tuberculosis and publishing, etc. We congratulate Dr Noto on this potentially very valuable initiative. *Further information*: Cefpas: fax +39 0934 594310. http://www.cefpas.it e-mail: cdf@infoservisi.it

OCEDUS: observatory of the European citizenship for human rights, Caltanisetta, Italy

Within Cefpas (Centre for Training and Research in Public Health), OCEDUS is being launched, with the following objectives:

- To develop a European culture for the promotion of human rights and health conditions and, thus, to ensure peoples' welfare through the understanding and respect of the fundamental rights sanctioned by the UN and the EU.
- To create a Permanent International forum to discuss and find solutions to the serious problems of human, animal and environmental health caused by human rights violation.

The main objectives are:

- To collect data, to develop research and training activities and to disseminate knowledge for the promotion of human rights.
- To organize meetings, debates, discussions at international level so as to find concrete answers to the problems regarding human rights violations and their effects on health.
- To create a world-wide telecommunication network for the rapid exchange of information on the subject.

Further information: Cefpas, Citadella Sant'Elia, Via G Mulè, 1, 93100 Caltanisetta, Italy. E-mail: ocedus@cefpas.it

WHO 'Leprosy Elimination Kit'

We have recently received copies of the following three documents from WHO:

1. Guide for Health Professionals to Eliminate Leprosy as a Public Health Problem who/CDS/CPE/

CEE/2000.14. Developed in collaboration with the Global Alliance for Elimination of Leprosy: member States of the World Health Organisation, Danish International Development Assistance (DANIDA), International Federation of Anti-Leprosy Associations (ILEP), Nippon Foundation, Novartis Foundation for Sustainable Development and World Health Organisation. 38 pages, A5 format.

2. Guide for Information, Education and Communication for Elimination of Leprosy. Communication Concepts and Support Material. 36 pages, A3 format. Highly illustrated in colour. Wide range of '... templates for approaches to communication about leprosy ... for modification and adaptation to local conditions and cultures ...'
3. How to Monitor Leprosy Elimination in your Working Area. WHO/CDS/CEE/2001.19. Main headings—The Final Push to Eliminate Leprosy; Why do we Monitor?; Elimination Indicators, Patient Care Indicators; Managerial Indicator.

Further enquiries: Leprosy Elimination Group, World Health Organisation, CH-1211 Geneva 27, Switzerland. Internet: www.who.int/lep E-mail: ee@who.int Fax +41 22 791 48 50.

TDR: A massive effort against diseases of poverty: What role will research play?

This is the title of the Keynote Article in the February 2001, Number 64 issue of *TDR News*, written by David Heymann, Executive Director of the Communicable Diseases Cluster at WHO and David Nabarro, Executive Director In the Director General's Office. It reads as follows:

> A WHO-led massive effort against diseases of poverty (announced in October 2000) is a process that is primarily about prosperity and strengthened health delivery systems, not about diseases. It is about people and how to improve their health, about health systems and how they respond to poor people. It is about getting well-tested and effective control interventions to the people who need them, whether by reducing their costs, improving their distribution, increasing their efficacy, or slowing down the development of antimicrobial resistance. Such a massive effort would involve a whole range of partners from public, private and not-for-profit sectors, bringing focus to the disconnection in what we actually do and what we would like to do in terms of controlling the diseases of poverty.
>
> A massive effort would eventually make available a sustained high level of resources that would make possible both increased access to existing drugs, vaccines and diagnostic tests, and research to better use these existing goods and develop the new ones necessary.
>
> What is the place of research in this effort? Disease control today depends on cost-effective strategies to best use the many drugs, vaccines and diagnostic tests that, when used properly, are capable of reducing mortality. But, today these strategies don't reach all who need them, and maybe we can develop better strategies. So the massive effort will, in part, be about developing better strategies to make existing drugs, vaccines and diagnostic tests more accessible to those in need (e.g. the use of bednets in Africa would need to be scaled up 20 times using strategies that ensure better access and increase demand). Operational research is therefore required in a massive effort.
>
> With evidence in the form of data from well-designed operational research and its analysis and synthesis, we can demonstrate that existing interventions get drugs, vaccines and diagnostic tests to where they are needed in a way such that they can be maximally used.
>
> At the same time, research in a massive effort is also required to develop new tools—new drugs and vaccines, and easier-to-use diagnostic tests. Adaptations of existing products, such as better fixed-dose combinations of drugs for tuberculosis and malaria, simplified for field use, are also required.
>
> TDR, with its broadened disease mandate and new emphasis on operational research, is well placed to ensure the research necessary for a massive effort. As increased funds for a

> massive effort become available, the balance between funds used to make existing vaccines, drugs and diagnostic tests available, and funds for operational and more basic research and development, will be a great challenge. TDR has successfully maintained the correct balance between research and implementation in the past, and will surely rise to the task of doing the same as a massive effort continues to evolve.

TDR increases its efforts in social, economic and behavioural research

This article, under the heading of Basic and Strategic Research, appears in the latest issue, No 64 of TDR News, February 2001:

The new Steering Committee on Strategic Social, Economic and Behavioural Research (SEB) issued its first call for grant applications in October 2000. Over the next 2–3 years, SEB will focus on supporting research that increases understanding of:

- how large-scale social and economic forces affect inequality of access to treatment, prevention and information related to infectious diseases;
- the implications of globalization on the persistence, emergence and resurgence of these diseases.

Studies of this nature will require innovative research methods, involving multi-level analyses that allow for investigation of the effects of large-scale forces on local level processes and outcomes. An important aspect of the Committee's work will be to support capacity building to conduct such analyses.

From the beginning, TDR has placed considerable emphasis on the social and economic aspects of tropical infectious diseases and their control. From 1979–94, TDR supported social science research through its Steering Committee on Social and Economic Research (SER), and since 1994, applied social science research has been supported by the Intervention Development and Implementation Research team (formerly the Applied Field Research team).

In June 1999, TDR's Joint Coordinating Board (JCB) approved the creation of a new Steering Committee on Strategic Social, Economic and Behavioural Research (SEB). As mentioned in *TDRnews* No. 63, SEB is located within the Basic and Strategic Research team (STR) to reflect its focus on basic social, economic and behavioural research issues of trans-disease and global importance.

A Scientific Working Group (SWG) of experts from a range of social, economic and policy sciences met in Geneva in June 2000 to set the overall direction for SEB. In September, the SEB Steering Committee met for the first time, and developed a vision for the next five years and a detailed workplan for the coming two years.

The focus of SEB reflects WHO's growing interest in the complex relationship between poverty and health. On a worldwide scale, infectious and parasitic diseases disproportionately affect populations living in poverty. Social, political and economic inequalities are central to the persistence and spread of these diseases, and the performance of health systems in protecting vulnerable populations from the impact of these diseases often falls far short of potential. Over the next several years, the SEB Steering Committee will examine these issues within the context of globalization, the changing role of the state, and the emerging role of non-state actors (the private sector, NGOs and civil society).

Repositioning of leprosy in TDR: notice to leprosy researchers

From TDR News (UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases) No 64, February 2001:

> In December 2000, Carlos Morel, Director TDR, and Bjorn Melgaard, Director WHO Department of Vaccines and Biologicals, agreed that leprosy research previously under the purview of the TDR Steering Committee on Immunology of Mycobacterial Diseases

(IMMYC), will in future be integrated into each of the four functional areas of TDR: Basic and Strategic Research (STR), Product Research and Development (PRD), Intervention Development and Implementation Research (IDE), and Research Capacity Strengthening (RCS). This move brings leprosy into line with all the other diseases in TDR's mandate, which have been addressed by the functional units since 1994, and it will make TDR leprosy research more sustainable. Dr Paul Nunn, in his position as TDR Leprosy Disease Coordinator, will coordinate TDR activities with each of these area. Researchers are invited to submit proposals directly to each areas according to their deadlines.

Additional information on research grants as well as application forms: www.who.int/tdr/grants

INASP-Health, UK

INASP-Health is a cooperative network created by health information providers, for health information providers. Its goal is to facilitate co-operation across the health information community towards universal access to reliable information for health professionals in developing and transitional countries.

The network currently involves more than 600 participants. North and South, representing non-governmental organizations, international agencies, library services, publishers (print and electronic), and others. Visit our website at: www.inasp.org.uk for further information about our range of services and activities.

We welcome all those who are willing to share their experience and expertise with others to improve access to reliable information. Participation is free of charge and without obligation. Please write to:

Dr Neil Pakenham-Walsh
Programme Manager
INASP-Health
27 Park End Street
Oxford OX1 1HU, UK

Please note, new telephone number for INASP-Health!

Tel: +44 (0)1865 248 124
Fax: +44 (0)1865 251 060
E-mail: ⟨INASP_Health@compuserve.com⟩
WWW: ⟨www.inasp.org.uk⟩

'INASP-Health in association with WHO, runs the HIF-net at WHO' which links 500 people worldwide-health professionals, librarians, publishers, technologists, policy-makers on an e-mail list dedicated to the improvement of reliable, relevant information for health professionals in developing and emerging countries.

The Wellcome Trust, London, UK: Grants Handbook 2000

The Grants Handbook 2000 (70 pages) begins with following Introduction:

With an asset base of £13 billion and an annual expenditure of more than £450 million, the Wellcome Trust is the world's largest medical research charity. Its mission is 'to promote and foster research with the aim of improving human and animal health'. The Trust funds most areas of biomedical research, although its support for cancer research is limited.

The Trust supports basic, 'blue skies' research as well as studies of direct medical relevance. Its funding schemes are similarly diverse, covering support for research centres, individual programmes and projects, scientific equipment, international collaboration and exchange, and research infrastructure.

It runs personal support schemes covering all stages of the research career, from PhD studentships to Principal Research Fellowships (which are reader professional-level fellowships).

The Trust is committed to providing scientists with the resources and support they need to carry out world-class research. As well as investing in the UK university research infrastructure, it has been increasing its long-term support—for example, through programme grants and long-term fellowships. The Trust is also committed to improving the salary conditions of academic researchers and has always striven to facilitate the development of scientists whose careers have needed, for a variety of reasons, to be flexible. The Trust is willing, in all its schemes, to accept applications from individuals wishing to work part time, returning to science or undergoing career reorientation.

The Trust supports excellent science all over the world, and is a major supporter of research in the developing and restructuring world. Its activities there focus on the diseases of the tropics (infectious and noninfectious), the medical impact of population change, and international collaboration and exchange. It funds research in its own Overseas Units, in Kenya, South-East Asia and South Africa, and in other overseas centres of excellence.

The Trust has made a substantial investment in genome sequencing, primarily at the Sanger Centre on the Wellcome Trust Genome Campus at Hinxton, near Cambridge. The Sanger Centre is one of the largest single contributors to the Human Genome Project, the global collaborative venture to sequence the 3 billion nucleotides of the human genome. It is also one of the world's leading centres for the sequencing of genomes of microbial pathogens, having sequenced *Mycobacterium tuberculosis* (TB), *Campylobacter jejuni* (food poisoning), and *Neisseria meningitidis* (meningococcal septicaemia), among others.

The Wellcome Trust is committed to developing partnerships with other governmental and nongovernmental bodies that share its commitment to biomedical research. The £750 million Joint Infrastructure Fund, a partnership with the UK Government, was launched in 1998 to alleviate the research infrastructure crisis in UK universities. The Trust has entered into several other joint funding agreements with the governments of other countries and with other charities in the UK and overseas.

The Trust also makes other significant investments in the biomedical science base. Most notable is a £110 million commitment to a new synchrotron facility in the UK. Moreover, the Trust's funding policies are continually being assessed, to ensure that the Trust remains responsive to scientific opportunities and medical priorities. It is currently developing major new funding initiatives arising from the Human Genome Project.

While research can provide profound insights into the natural world, its full worth is gained when it is applied to improve human health more directly. The Wellcome Trust has established a business subsidiary, Catalyst BioMedica Ltd, to help ensure that promising lines of research do lead to medically useful products or services. Catalyst works in partnership with Trust-funded researchers, university technology transfer staff, financial institutions and the pharmaceutical industry to identify and exploit research opportunities. It advises on the protection of intellectual property, helps to negotiate commercialization agreements and has a development fund for progressing applied research with the potential for improving healthcare.

The Wellcome Trust's Medicine, Society and History activities provide a historical and social counterpoint to its medical research funding work. Founded on the principle that today's medical research is poised to have a significant impact on society, the programme aims to engage the public in informed debate about biomedical research and its medical application, inform public policy making in this area, and to ensure that the valuable lessons of history inform and influence current debate.

The Trust's grant-giving activities in this area include a comprehensive range of schemes for support of research in the history of medicine—the Trust is the UK's biggest funder of historical medical research. The Medicine in Society funding programme is exploring the social, ethical and public policy implications of developments in medical science; its areas of interest encompass biomedical ethics and public engagement with science, and it provides support both for academic research in this area and for public communication projects.

The Handbook carries detailed information on policy and funding decision making: grant decision-making processes: applying for support: information for applicants: overview of funding opportunities. *Apply* Grants Information Department, The Wellcome Trust, 183 Euston Road, London NW1 2BE. E-mail: grantenquiries@wellcome.ac.uk

Susceptibility to infection

This is the title of a Clinical review in the *British Medical Journal*, volume *321* of 28 October 2000, pages 1061–64.

The opening paragraphs read as follows.

Genetic factors explain, at least in part, why some people resist infection more successfully than others. Rare gene disruptions cause fatal vulnerability to specific microbes, but more subtle differences are common and arise from minor variation in many genes. Recent advances in the human genome project and in high throughput genotyping technology will make it feasible within the next decade to screen the whole genome for genetic factors that determine susceptibility to HIV and AIDS, malaria, and tuberculosis. This will help to identify critical pathways of host defence and generate novel strategies for disease prevention. Understanding the evolutionary impact of infectious disease on the human genome may shed light on the origins of other common diseases, particularly those with an atopic or autoimmune component.

Historical accounts of the plague tell of individuals who survived unscathed in households where almost everyone else died. Each winter, British hospital wards are full of infants requiring oxygen therapy for bronchiolitis, but most infants infected with the same virus have little more than a runny nose. Over a million African children die each year of malaria, but many more remain in relatively good health despite being continually infected with the parasite.

To what extent does our genetic make up determine the different ways that we respond to the same infectious agent? This is difficult to answer because of the many other contributory factors involved, such as previous health, acquired immunity, and variability in the pathogen. Epidemiological analysis of the genetic component is confounded by environmental factors that cause familial clustering and is further complicated by the many different genes that are likely to be involved. Nevertheless, there is compelling evidence for a genetic component, including twin studies of tuberculosis, leprosy, malaria, and *Helicobacter pylori* infection and a large survey that found that individuals adopted in childhood had a markedly increased risk of death from infection if a biological parent had died prematurely of infection.

Unravelling the genetic and environmental determinants of infectious disease will soon be feasible. The human genome sequence provides the starting point for a systematic analysis of human genetic diversity (www.wellcome.ac.uk/en/genome). The most common form of DNA variation is a direct swap of one nucleotide for another, such as adenine for guanine, known as a single nucleotide polymorphism or SNP (pronounced 'snip'). Polymorphisms that are present in at least 1–2% of normal individuals are found on average once in every 300–600 nucleotides, suggesting that some 10 million may be present across the whole genome. Although only a small proportion of these polymorphisms may be of functional relevance—by causing disruption or structural alteration of the protein encoded by a gene or by altering neighbouring regions of DNA that control gene regulation—all are of potential value as genetic markers for mapping regions of DNA that determine disease susceptibility. Much work is going into the development of DNA chips and other novel technologies for high throughput typing of single nucleotide polymorphisms that will make it feasible to screen many thousands of these markers in large study populations, with the ultimate goal of mapping disease associations across the whole genome. Efforts are being made to assemble the large DNA collections that will be required for this complex exercise.

What is the practical purpose of understanding the molecular genetic basis of susceptibility to infection? Efforts to develop vaccines and improving treatments for major diseases such as tuberculosis,

HIV infection and AIDS, and malaria are hindered by our poor understanding of the molecular and cellular mechanisms that determine clinical outcome. Genetic epidemiology may identify hitherto unknown molecular mechanisms and improve understanding of critical events in the evolution of disease. For example, if an infectious disease is associated with high levels of a factor X in the blood, it is often difficult to know whether this is of pathogenic importance or simply an epiphenomenon of the disease process. But if the production of X is known to be determined by a genetic polymorphism, and if this polymorphism is shown to predispose to the disease in question, then there is a much stronger case for X playing a causal role.

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