

# WHO-Facts Sheet

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## 1. MENTAL HEALTH RESOURCES IN THE WORLD

### Initial results of Project ATLAS

Though considerable information has recently become available on the epidemiology and burden of mental disorders, very little known about the resources available for mental health care within countries. Accurate information is crucial for program development and serves as a baseline for monitoring changes.

Project ATLAS aims to meet this need by collecting basic information on mental health resources from all member states to construct global and regional databases, maps and profiles. Preliminary analysis of information collected during the initial study, from October 2000 to March 2001, from 181 countries covering 98.7% of the world's population is now available. The information was collected using a questionnaire completed by the mental health focal point within the countries.

The information shows that resources and services for mental and behavioral disorders are disproportionately low compared to the burden caused by these disorders in both developing countries and developed countries.

Of the countries studied

- 43% have no mental health policy
- 23% have no legislation on mental health
- 38% have no community care facilities.
- In 41%, treatment of severe mental disorders is unavailable in primary health care.

More than half of the beds for mental health care are in mental hospitals.

### Policies, Programs and Legislation

It is widely recognized that national policy, program and legislation on mental health are basic requirements for mental health care in any country. Out of the countries for which information is

available, only 57% have a mental health policy. Most national policies are recent, the majority having been developed during 1990s. About half of the WHO African and Western Pacific region countries do not have a mental health policy. Sixty-eight percent have a national mental health program. Nearly half of these programs have been initiated in the last five years.

Of the 160 countries providing information on legislation, 23% have no legislation on mental health. Nearly half of the existing legislation has been formulated in the last decade, whereas about 17% date back to a period before 1960, before most of the current treatment methods became available.

Serious disability caused by mental disorders is often not considered for state disability benefits. Out of the 174 countries where information about disability benefits is available, more than a quarter do not provide state or public disability benefits for mental illness. A large number of countries where benefits are available only provide very limited assistance in the form of a small monetary allowance or pension benefits for government employees.

### Mental Health in Primary Care and Community Care

While it is agreed that most mental disorders are best managed at the primary care level, this has proved difficult to achieve in practice. Eighty-five percent of countries report that mental health services are available at primary health care level, but actual treatment is reported to be available only in 59%. Forty-three percent countries have no regular program to train primary care personnel in mental health care.

Availability of essential drugs to treat mental and neurological disorders at primary care level is also crucial for providing effective care. A national therapeutic drug policy or a list of

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essential drug is present in most countries. However in many countries policies have been developed in the last five years, hence the benefits of this policy have not fully filtered down to the consumer level. Care of common mental and neurological disorders requires only a few drugs. More than 25% of the countries do not have the most commonly prescribed antipsychotic, antidepressant, and antiepileptic drugs considered essential for the treatment of common mental and neurological disorders at the primary health care level.

Community-based care is better than institutional care for chronic mentally illness. However, these facilities are not available in 38% of the countries. Even in countries that have community care, the coverage is far from complete.

### **Human Resources and inpatient Facilities**

About 71% of all people in the world have access to less than one psychiatrist per 100,000 people. Access to psychiatric nurses is also poor; 46% have access to less than one nurse per 100,000.

While the countries in the African region of WHO have only about 1,200 psychiatrists and 12,000 psychiatric nurses for a population of about 620 million, the European region has more than 86,000 psychiatrists and 280,000 nurses for a population that is only about 36% more (total population 840 million). The median number of psychiatrists for all the countries is 1/100,000 population, varying from 0.05/100,000 population in the African region to 9/100,000 population in the European.

Though mental hospitals with a large number of beds are not recommended for mental health care, a certain number of beds in general hospitals for acute care is considered essential. There is a wide variation in beds available for mental health care, median number for the world population being 1.5/10,000.

Across the different regions the median varies from 0.33 per ten thousand population in the South East Asian regions to 9.3 in European region. Nearly two-thirds of the world's population has access to less than 1 bed per ten thousand population. Even more disappointing, more than half of the beds are still in mental hospitals. These often provide custodial care rather than mental health care.

### **Non-governmental organizations (NGOs)**

NGOs can play a variety of roles in the area of mental health. These include advocacy, rehabilitation, treatment, prevention and promotion. More than 87% of the countries reported that some non-governmental agencies

were working in the mental health field, mainly involved in rehabilitation, advocacy and promotion. Only about half of them are involved in treatment. The presence of NGOs in a majority of countries is reassuring, since they serve an important function, especially where the governmental sector response has been slow and inadequate.

### **Monitoring and Data Collection System**

More than 27% countries have no system reporting mental health data in their annual health report. Those who have such system often lack any meaningful information. Often only the number of admissions and discharges from mental hospitals is recorded. This lack of monitoring makes detecting changes almost impossible.

Forty-five percent of countries have no facilities for collection of epidemiological or service data at the national level, though some of these have a few epidemiological studies covering a limited population.

### **Programs for special Populations**

Programs for special populations are present in a small number of countries. Programs for minorities and indigenous populations are not present in the majority of the countries. Programs for the elderly and for children are present in only 48% and 59% respectively.

Overall, the mental health resources in countries present a dismal picture of severe shortage, neglect and apathy. However, there are some rays of hope. A large number of countries have established policy, programs and new legislation in the last five years. NGOs have also started becoming active. These include consumer groups and family groups that have the capacity to bring about a change in the system. A concerted action by governments, professionals and the community is needed to improve the mental health resources situation in the world.

## **2. BOVINE SPONGIFORM ENCEPHALOPATHY (BSE)**

Bovine Spongiform Encephalopathy (BSE) is a transmissible, neuro-degenerative, fatal brain disease of cattle. The disease has a long incubation period for four to five years, but ultimately is fatal for cattle within weeks to months of its onset. BSE first came to the attention of the scientific community in November 1986 with the appearance in cattle of newly-recognized form of neurological disease in the United Kingdom (UK)

### Source of the Epidemic

- Epidemiological studies conducted in the UK suggest that the source of BSE was cattle feed prepared from carcasses of ruminants.
- Speculation as to the cause of the appearance of the agent causing the disease has ranged from spontaneous occurrence in cattle, the carcasses of which then entered the cattle food chain, to entry into the cattle food chain from carcasses of sheep with a similar disease scrapie.

### Cause

- BSE is associated with a transmissible agent. The agent affects the brain and spinal cord of cattle and lesion are characterized by sponge-like changes visible with an ordinary microscope.
- The agent is highly stable, resisting freezing, drying and heating at normal cooking temperatures, even those used for pasteurization and sterilization.
- The nature of the BSE agent is still a matter of debate. According to the prion theory, the agent is composed largely, if not entirely, of a self-replicating protein, referred to as a prion. Another theory argues that the agent is virus-like and possesses nucleic acids which carry genetic information. Strong evidence collected over the past decade supports the prion theory, but the ability of the BSE agent to form multiple strains is more easily explained by a virus-like agent.

### Causes of BSE

- Between November 1986 and April 2001 approximately 180-900 cases of BSE were confirmed in the UK.
- Since 1989 when the first BSE case was reported outside the UK, relatively small numbers of BSE cases (in total approximately 1900) have also been reported in native cattle in Belgium, Denmark, France, Germany, the Republic of Ireland, Italy, Liechtenstein, Luxembourg, Netherlands, Portugal, Spain and Switzerland. However, all but a couple of dozen cases have been reported in six countries ñ France, Germany, Ireland, Portugal, Spain and Switzerland.
- Since the introduction of monitoring programs to detect BSE in dead and slaughtered cattle some countries have found their first native case (Germany, Italy, Spain). Small numbers of cases have also been reported in Canada, the Falkland Islands (Islas Malvinas) and Oman, but solely in animals imported from the UK. The International Office for Epizootic Diseases (OIE) reports these cases on their web site: "<http://www.oie.int>"

### Measures Taken to Prevent the Spread of BSE

- In July 1988, the UK banned the use of ruminant proteins in the preparation of animal feed. The use in the food chain of bovine offals considered to pose a potential risk to humans was also banned in the UK in 1989. The list of banned bovine offals was revised and expanded on several occasions as new information became available. In other countries, including those in Europe, measures taken, the date of implementation and the extent of enforcement vary from country to country.
- Starting in 1996, bans prevented the sale of food products containing beef from the UK to other countries. Other products (e.g. tallow, gelatin) derived from bovine tissue were also prohibited from sale from the UK to other countries. However, in 1999 the European Union (EU) lifted the ban for meat fulfilling specific requirements; for example; de-boned beef from animals from farms where there have been no cases of BSE and where the animals are less than 30 months of age at slaughter.
- Cattle are continuously monitored for BSE and BSE is decreasing in the UK. The number of reports of BSE in the UK began to decline in 1992 and has continuously declined year by year since then. New monitoring programs using newly developed tests for the diagnosis of BSE in dead and slaughtered cattle have been introduced throughout the EU.

### Transmissible Spongiform Encephalopathies (TSEs) in animals

TSEs are diseases characterized by spongy degeneration of the brain with severe and fatal neurological signs and symptoms. BSE is one of several different forms of transmissible brain disease affecting a number of animals species. Scrapie is a common disease in sheep and goats. Mink and North American mule deer and elk can contract TSEs. A neurological disease in household cats and in ruminant and feline species in zoos has been linked to BSE; most cases in such animals appear to have occurred in the UK.

### Creutzfeldt-Jakob Disease

- While several human TSEs exist, Creutzfeldt-Jakob disease (CJD) is the prototype human TSE. CJD occurs in a form associated with a hereditary predisposition (approximately 5-10% of all cases) and in a more common, sporadic form that accounts for 85-90% of cases.
- A small percentage of cases (less than 5%) are iatrogenic (resulting from the accidental transmission of the causative agent via contaminated surgical equipment or as a result

of cornea or dura mater transplants). It has also been shown that CJD can be transmitted humans as a result of treatment with natural human growth hormone. Replacement of natural human growth hormone by recombinant growth hormone has alleviated this risk.

#### **Variant Creutzfeldt-Jakob Disease (vCJD)**

- A newly recognized form of CJD, variant Creutzfeldt-Jakob disease (vCJD) was reported in March 1996 in the UK (cf. WHO Fact Sheet No. 180 on variant Creutzfeldt-Jakob Disease). In contrast to the classical forms of CJD, vCJD has affected younger patients (average age 29-years, as opposed to 65 years), has a relatively longer duration of illness (median of 14 months as opposed to 4.5 months and is strongly linked to exposure, probably through food, to BSE. Recent studies have confirmed that vCJD is distinct from sporadic and acquired CJD.
- From October 1996 to early June 2001, 101 cases of vCJD have been reported in the United Kingdom (UK) three in France and a case in the Republic of Ireland. Insufficient information is available at present to make any precise prediction about the future number of vCJD cases.
- Since few countries have surveillance systems, the geographical distribution of the incidence of vCJD cases is due to the same agent that caused BSE in cattle.

#### **World Health Organization (WHO) work on TSEs and advice on Research**

- Since 1991, WHO convened nine scientific consultations on issues related to human and animal TSEs; the ultimate goal of the meetings was to better to protect human and animal health. Experts who participated reviewed the possible human public health implications of animal TSEs, with special emphasis on BSE. The consultations also reviewed the evolving state of knowledge on these diseases, evaluated possible means of transmission and identified risk factors for infection.
- The group of independent experts assembled by Who is continually updating the state-of-the-art as more scientific information of BSE and vCJD becomes available. WHO provides a neutral scientific forum in which scientific questions related to BSE and vCJD can be reviewed, evaluated and debated.
- Research on all TSEs is promoted by WHO, especially on early diagnostic procedures and epidemiology. WHO has published a comprehensive priority list for new research.

One question which needs investigation is whether or not BSE has infected sheep populations. Advancing current knowledge about TSEs through research will permit the best possible decisions to be taken to safeguard public health, while securing consumer confidence so that national economies dependent on the beef industry can be maintained and developed.

- Further data are urgently required from scientific studies on vCJD cases. More retrospective and prospective monitoring and surveillance studies on all forms of CJD, modeled on current European collaborative studies, are required throughout the world.
- WHO is helping to expand standardized surveillance of CJD and its variants in order to better understand the disease's geographic spread in the world and to better protect public health globally. From 1997-2000, WHO held a series of training courses worldwide, particularly in developing countries, with the intention of helping individual countries establish national surveillance of CJD and vCJD.
- WHO published guidelines for infection control of TSEs in 2000. The full text is available at [http://www.who.int/emc-documents/under\\_the\\_heading 'TSE'](http://www.who.int/emc-documents/under_the_heading_TSE).

#### **WHO Conclusions and Recommendations to Reduce Exposure to the BSE Agent**

- All countries must prohibit the use of ruminant tissues in ruminant feed and must exclude tissues that are likely to contain the BSE agent from any animal or human food chain. BSE eradication was recommended during a WHO consultation held in December 1999.
- All countries are encouraged to conduct risk assessments to determine if they are at risk for BSE in sheep and goats. It is advised that any tissue which may come from deer or elk with Chronic Wasting Disease (CWD, a transmissible spongiform disease of North American mule deer and elk) is not used in animal or human food; however, at this time there is no evidence to suggest that CWD in deer and elk can be transmitted to humans.
- No infectivity has yet been detected in skeletal muscle tissue. Reassurance can be provided by removal of visible nervous and lymphatic tissue from meat (skeletal muscle).
- Milk and milk products are considered safe. Tallow and gelatin are considered safe if prepared by a manufacturing process which has been shown experimentally to inactivate the transmissible agent.

- Human and veterinary vaccines prepared from bovine materials may carry the risk of transmission of animal TSE agents. The pharmaceutical industry should ideally avoid the use of bovine materials and materials from other animals species in which TSEs naturally occur. If absolutely necessary, bovine materials should be obtained from countries which have a surveillance system for BSE in place and which report either zero or only sporadic cases of BSE. These precautions apply to the manufacture of cosmetics as well.

### 3. VARIANT CREUTZFELDT-JAKOB DISEASE (vCJD)

Variant Creutzfeldt-Jakob disease (vCJD) is a rare and fatal human neuro-degenerative condition. Like Creutzfeldt-Jakob disease (CJD), vCJD is classified as a transmissible spongiform encephalopathy (TSE) because of characteristic spongy degeneration of the brain and its ability to be transmitted. vCJD is a new disease which was first described in March 1996.

Prior to the identification of vCJD, CJD was recognized to exist in only three forms. Sporadic cases, which have an unknown cause and occur throughout the world at the rate of about one per million people, account for 85-90% of CJD cases. Familial cases are associated with a gene mutation and make up 5-10% of all CJD cases. Iatrogenic cases result from the accidental transmission of the causative agent via contaminated surgical equipment or as a result of cornea or dura mater transplants or the administration of human-derived pituitary growth hormones. Less than 5% of CJD cases are iatrogenic.

In contrast to the traditional forms of CJD, vCJD has affected younger patients (average age 29 years, as opposed to 65 years), has a relatively longer duration of illness (median of 14 months as opposed to 4.5 months) and is strongly linked to exposure, probably through food, to a TSE of cattle called Bovine Spongiform Encephalopathy (BSE).

#### Total Cases

From October 1996 to early June 2001, 101 cases of vCJD have been reported in the United Kingdom (UK), three in France and a single case in the Republic of Ireland. Insufficient information is available at present to make any well-founded prediction about the future number of vCJD cases.

#### Epidemiology

The first person to develop symptoms of what turned out to be vCJD became ill in January 1994.

Most people who have developed vCJD have lived in the UK. Some of the patients had been long-standing residents in Wales, Scotland or Northern Ireland.

As of early June 2001, the CJD surveillance unit for the UK reported 95 cases of vCJD, including 88 confirmed and seven probable cases. In addition, there are six cases where vCJD is strongly suspected, but the diagnosis has not yet been definitively confirmed by post mortem analysis.

Some of these patients have donated blood. However, to date vCJD has never been known to have developed in a recipient of this blood; study of possible transmission through blood transfusion continues. The UK no longer sources plasma from its inhabitants, and as a further precautionary measure, has instituted leukocyte reduction (removal of white blood cells) from blood transfusions. Some countries have prohibited donations of blood from persons who have resided in the UK for longer than six months; or (as France has done) for one year.

#### Clinical Features

Early in the illness, patients usually experience psychiatric symptoms, which most commonly take the form of depression or, less often, a schizophrenia-like psychosis. Unusual sensory symptoms, such as "stickiness" of the skin, have been experienced by half of the cases early in the illness. Neurological signs, including unsteadiness, difficulty walking and involuntary movements, develop as the illness progresses and, by the time of death, patients become completely immobile and mute.

#### Diagnosis

The clinical presentation, progressive nature of the disease and failure to find any other diagnosis are the hallmarks of vCJD.

There are no available, completely reliable diagnostic tests for use before the onset of clinical symptoms. However, magnetic resonance (MRI) scans, tonsillar biopsy and cerebrospinal fluid (CSF) tests may be useful diagnostic tests.

The brainwave pattern observed during an electroencephalogram (EEG) was abnormal in most of the vCJD patients, but the wave forms characteristic of sporadic CJD do not occur.

Currently the diagnosis of vCJD can only be confirmed following pathological examination of the brain. Characteristically, multiple microscopic and abnormal aggregates encircled by holes are seen, resulting in a daisy-like appearance described by the term "florid plaques".

#### Probable Cause

vCJD is strongly linked with exposure to the BSE agent. BSE is a transmissible spongiform

encephalopathy (TSE) affecting cattle and was first reported in the UK in 1986. Since that year, about 180,900 cases have been reported in the UK. The number of reports of BSE in the UK began to decline in 1992 and has continuously declined year by year since then.

The most likely route of exposure was through bovine-based food, although infectivity is mainly found in the brain and spinal cord of clinically ill animals over two years of age.

Since 1989 when the first BSE case was reported outside of the UK, relatively small numbers of BSE cases (in total approximately 1900) have also been reported in native cattle in Belgium, Denmark, France, Germany, the Republic of Ireland, Italy, Liechtenstein, Luxembourg, Netherlands, Portugal, Spain and Switzerland. However, all but a couple of dozen cases have been reported in six countries – France, Germany, Ireland, Portugal, Spain and Switzerland. Since the introduction of monitoring programmes to detect BSE in dead and slaughtered cattle some countries have found their first native case (Germany, Italy, Spain). Small numbers of cases have also been reported in Canada, the Falkland Islands (Islas Malvinas) and Oman, but solely in animals imported from the UK. The International Office for Epizootic Diseases (OIE) reports these cases on their website: [www.oie.int](http://www.oie.int)

The nature of the TSE agent is being investigated and is still a matter of debate. According to the prion theory, the agent is composed largely, if not entirely, of a self-replicating protein, referred to as a prion. Another theory argues that the agent is virus-like and possesses nucleic acids which carry genetic information. Although strong evidence collected over the past decade supports the prion theory, the ability of the TSE agent to form multiple strains is more easily explained by a virus-like agent.

#### **Evidence of vCJD-BSE Link**

The hypothesis of a link between vCJD and BSE was first raised because of the association of these two TSEs in time and place. More recent evidence supporting a link, includes identification of pathological features similar to vCJD in brains of macaque monkeys inoculated with BSE. A vCJD-BSE link is further supported by the demonstration that vCJD is associated with a molecular marker that distinguishes it from other forms of CJD and which resembles that seen in BSE transmitted to a number of other species. Studies of the distribution of the infectious agent in the brains of mice artificially infected with tissues from humans with vCJD and cows with BSE showed nearly identical patterns.

The most recent and powerful evidence comes from studies showing that the transmission characteristics of BSE and vCJD in laboratory mice are almost identical, strongly indicating that they are due to the same causative agent.

Intensive surveillance in 17 European countries has confirmed the high incidence of vCJD in the UK, the country with the largest potential exposure to BSE. France (with three reported cases) imported relatively large quantities of cattle products from the UK. The one case in the Republic of Ireland lived in the UK. Australia, Canada and the United States of America (all with extremely low potential exposure) have no confirmed reports of vCJD. For the final opinion of the European Union's Scientific Steering Committee on the Geographic Risk of BSE, please see: [http://www.europa.eu.int/comm/food/fs/sc/ssc/out113\\_en.pdf](http://www.europa.eu.int/comm/food/fs/sc/ssc/out113_en.pdf)

In conclusion, the most likely cause of vCJD is exposure to the BSE agent, most plausibly due to dietary contamination by affected bovine central nervous system tissue.

#### **Other Human TSEs**

Other human TSEs include kuru in Papua New Guinea, which is believed to be transmitted in the course of funerary rituals involving brains of corpses; Gerstmann-Sträussler-Schenker (G.S.S.) syndrome (occurring in persons with an apparent hereditary predisposition) and fatal familial and sporadic insomnia. CJD is the most common of all the human TSEs and is the disease most commonly mistaken for vCJD.

#### **Measures Taken to Protect Public Health**

Due to strong suspicions of a linkage between vCJD and BSE, the British government made BSE a notifiable disease in June 1988. Shortly afterwards, a statutory ban on the feeding of protein derived from ruminants (e.g., cattle, sheep and goats) to any ruminant was introduced. The use in the food chain of bovine offals considered to pose a potential risk to humans was also banned in the UK in 1989, and the list of banned bovine offals was revised and expanded on several occasions as new information became available. In other countries, including Europe, measures taken, the date of implementation and the extent of enforcement vary from country to country.

#### **World Health Organization (WHO) Involvement**

Since 1991, WHO has convened nine scientific consultations on issues related to animal and human TSEs. These meetings have made wide-ranging recommendations aimed at protecting human and animal health.

As exposure to the BSE agent may extend to populations outside Western Europe, it was

recommended that to ascertain the number and distribution of any future cases, global surveillance of CJD and its variants would be required.

From 1997-2000, WHO held a series of training courses worldwide, particularly in developing countries, with the intention of helping individual countries establish national surveillance of CJD and its variants. The first workshop, for West African countries, was held in Dakar, Senegal in June 1997. Similar workshops were held in Bangkok for Southeast Asian countries (October 1997), in Cairo for North African countries (February 1998) and in China for countries of the Western Pacific (July 1999) and for Eastern and Central European countries in May 2000. Another is planned for Mediterranean countries.

### WHO Recommendations

To protect human health, WHO has also recommended the following:

No part or product of any animal which has shown signs of a TSE should enter any (human or animal) food chain; Countries should not permit tissues that are likely to contain the BSE agent to enter any (human or animal) food chain.

In 1999, a review was conducted of the known information about a number of animal TSEs to try to proactively determine if there are any new TSE threats. Their principle recommendations were to eradicate BSE and to find out if BSE has infected sheep populations. The recommendations are available at <http://www.who.int/emc-documents/> under the heading 'TSE'.

WHO published guidelines for infection control of TSEs in 2000. The full text is available at <http://www.who.int/emc-documents/> under the heading 'TSE'.

## 4. RABIES

### Disease

Rabies is a viral infection transmitted in the saliva of infected mammals. The virus enters the central nervous system of the host, causing an encephalomyelitis that is almost always fatal. Definitive diagnosis of rabies infection in humans or suspected animal vectors depends on the detection in infected brain tissue of specific rabies antigen, inclusions (Negri bodies), or of rabies nucleic acid by the PCR reaction, on the presence of antibodies in the CSF, and on the isolation and identification of the virus from the brain or the saliva. The infection is widely distributed throughout the world and present in all continents. The number and size of rabies-free countries, territories or areas are small compared to those of

rabies affected areas. Only 46 out of 153 countries and territories reported no cases of rabies in 1996. World-wide, a large number of mammalian animal species are involved in rabies maintenance and transmission. In a given area, one animal species is usually both host and transmitter of the disease. The rabies host species consists mainly of wild terrestrial animals (e.g. red, arctic and grey foxes, racoons skunks, coyotes, mongooses). Also many bat species are involved either as hosts, transmitters or victims of rabies (e.g. in the USA, certain South American countries, some European countries, and more recently Australia). Dogs, however, remain the principal host and transmitter of rabies to humans. It is estimated that more than 2.4 billion people, about half the world's population, are living in countries/territories where dog rabies still exists and are potentially exposed to rabies.

### Epidemiology

Most of the 33,209 human deaths reported to WHO for the year 1996 occurred in Asian countries: India officially reports 30,000 deaths and Bangladesh, 2,000. On that basis and considering the level of under-reporting (e.g. in Pakistan estimates range from 2,000 to 10,000 deaths annually), it is estimated that 40,000 rabies deaths are occurring in Asia alone. Therefore between 35,000 and 50,000 persons may die of rabies each year and most of these deaths are taking place in developing countries. In addition to mortality due to rabies, some 50 million doses of vaccines are used in 10 million human post-exposure treatments world-wide. About 8 million people receive rabies vaccine in developing countries annually and again most of these treatments are administered in Asia (e.g. 1 million in India, 5 million in China) and Latin America.

In countries such as China and Thailand, an improved post-exposure treatment and a vaccine delivery system, associated with a major shift in the type of vaccine produced from brain tissue towards cell culture based products, has played a major role in drastically reducing the number of human deaths due to rabies.

Prompt and thorough cleansing of the wound, together with administration of purified equine or human rabies immunoglobulin (ERIG or HRIG) and modern vaccines immediately after exposure virtually guarantee complete protection, and the risk of post-exposure treatment complications is much lower than with brain tissue vaccines.

### Vaccines

There are two main types of vaccine:

- i) Brain-tissue vaccines. First used by Pasteur in 1885, they are prepared from the nerve tissue of

adult or neonate animals, inactivated by phenol, ultraviolet radiation or, more recently, betapropiolactone (BPL) and at best purified by centrifugation. Repeated inoculation of homogenates of brain tissue may induce immune responses to some neural antigens. In the case of sheep-brain-tissue vaccine (Semple vaccine), these neurological complications are attributed to myelin basic protein and some of the ganglioside and phospholipid constituents. Though properly prepared suckling-mouse brain vaccines contain virtually no myelin, neurological complications still occur, but at much lower rates than with adult nerve-tissue vaccines.

- ii) Modern vaccines. These second-generation vaccines consisting of highly purified vaccines prepared on primary and continuous cell lines, and in embryonating eggs.

Only the following vaccines meet WHO's safety, potency and efficacy requirements when used for post-exposure intradermal treatment of rabies: - human diploid cell vaccine (HDCV): Rabivac<sup>TM</sup> - purified vero cell vaccine (PVRV): Verorab, Imovax, Rabies vero, TRC Verorab<sup>TM</sup> - purified chicken embryo cell vaccine (PCECV): Rabipur<sup>TM</sup> - purified duck embryo vaccine (PDEV): Lyssavac N<sup>TM</sup>.

The quantity of vaccine produced on nerve tissue and administered to patients is still much higher than that of modern vaccine produced on cells or embryonating eggs. There is however a tendency to replace the former with cell-culture vaccines, partly from public demand, partly from a public health point of view and partly from commercial interests.

For all modern vaccines that meet WHO requirements, the Essen regimen consists of five injections of one dose intramuscularly on days 0, 3, 7, 14 and 28. In addition, three reduced-treatment regimens have been developed to reduce the cost of rabies post-exposure treatment:

- The "2.1.1." regimen, consists of two intramuscular doses on day 1, and a single-dose booster on days 7 and 21. This regimen is particularly recommended when no immunoglobulin is required i.e. when contact consists in nibbling of uncovered skin, minor scratches or abrasions without bleeding, licks on broken skin.
- The "2.2.2.0.1.1." regimen for use with purified vero cell vaccine (PVRV), purified primary chick embryo cell vaccine (PCEC) and purified duck embryo vaccine (PDEV). It consists of intradermal injections of one fifth of the intramuscular dose (0.1 to 0.2 ml according to vaccine type) at two locations on days 0, 3 and 7, and at one location on days 30 and 90.
- The "8.0.4.0.1.1." regimen for use with human

diploid cell vaccine (HDCV) and purified primary chick embryo cell vaccine (PCEC). ) It consists of an injection of 0.1 ml intradermally at 8 different intradermal sites on day 0, four sites on day 7, and one site on days 28 and 90. This regimen is particularly recommended for severe exposure (single or multiple transdermal bites or scratches, contamination of mucous membranes with saliva) when no immunoglobulin is available.

When vaccine is administered intradermally, proper staff training is needed in correct storage, reconstitution and administration of the vaccine. A 1ml syringe and short hypodermic needle are used. If proper sterile technique is used in drawing the vaccine up from the vial, the remaining doses may be kept in the vial in a refrigerator at 4-8 °C for another patient within 6 to 8 hours after reconstitution if there is no preservative.

### Public health strategies

The three principal control strategies for the prevention of rabies in human are the increased supply and administration of appropriate vaccine for pre and post-exposure use; and the elimination of rabies in its animal host(s). Due to increasing awareness and a subsequent increasing trend in demand for safer and efficacious products from exposed people, there is a tendency to favor the first strategy over the second. This is in spite of relatively high costs of human biological products, and despite the indication in developing countries where most human cases result from contact with rabid dogs, that rabies elimination by vaccination of the dogs might be the most cost-beneficial strategy in the long term.

### WHO policy

Each of the following strategy has its place in the prevention and control of rabies in humans and animals:

- Vaccination of humans before exposure. Pre-exposure prophylaxis is currently mainly recommended for those individuals at increased risk of infection by nature of their occupation.
- Post-exposure treatment: the combination of local treatment of wounds, passive immunization with rabies immunoglobulins (RIG) and vaccination is recommended for all severe exposures to rabies. New recommendations on the use of immunoglobulin were issued by WHO in 1996 and supplement/supersede the relevant recommendations of the 8th report of the Expert Committee on Rabies published in 1992.

Factors that should be taken into consideration when deciding whether or not to initiate post-exposure treatment are:

- the nature of the contact,
- the presence of rabies in the area where the contact occurred or from which the animal came from,
- the species of the animal involved;
- the vaccination and clinical status of the animal involved, the type of vaccine used and the availability of the animal for observation;
- the results of laboratory testing of the animal for rabies, if available. In areas where either wildlife or dog rabies prevails, dogs should be vaccinated. WHO promotes the implementation of mass vaccination campaigns for dogs using inactivated potent veterinary vaccines injectable by the subcutaneous or intramuscular routes. For dog sub-populations that are difficult or impossible to reach, WHO promotes research on (live) vaccines for use in bait. In areas where there is wildlife rabies, in those animal species host for which oral vaccines have been shown to be safe and efficacious, WHO promotes the use of rabies vaccine-loaded bait for oral immunization. Such techniques have led to the elimination of fox rabies in many areas in Western Europe.

#### **Special issues**

Cost: Reduction in the cost of each effective course of treatment remains an essential

objective. Costs of a full rabies post-exposure treatment (currently US\$ 30 to 35 on average for vaccine and US\$ 50 to 160 for immunoglobulin) remains prohibitive for most people particularly those living in countries affected with canine rabies.

**Supply of vaccine:** A significant reduction in the price of these would help reduce the cost of treatment and make it more acceptable to poor people who are often the most at risk. Rabies vaccines have been added to the WHO list of essential drugs and should be made available at the lowest price possible within a country.

**Supply of immunoglobulins:** The current WHO definitions for certain categories of exposure call for more frequent passive immunization in association with vaccination. The increased production and use of highly purified horse immunoglobulins that are safer than the heterologous products of the previous generation should be promoted to provide at least a partial solution to the problems of supplies of human immunoglobulin and the cost involved.

**New post-exposure regimens:** None of the existing regimens is entirely satisfactory. As no new vaccine or delivery system will be available soon, continued research into new vaccines and reduced regimens and associations with other EPI vaccines is a priority.