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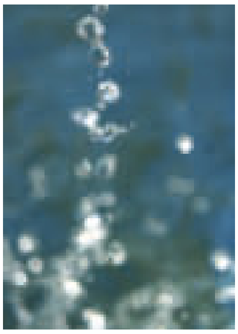

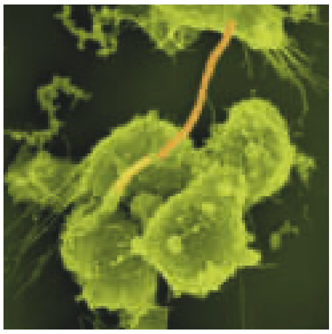

The Threat Posed by INFECTIOUS DISEASES

Need for Reform of Infection Control

Published on behalf of

RUDOLF SCHÜLKE FOUNDATION
in cooperation with the professional societies and medical associations for hygiene and public health

mhp Verlag GmbH Wiesbaden

Dedicated to the memory of Dr. Hans-Peter Harke, one of the initiators of this publication and of the previous memorandum and "spiritus rector" of the Future Hygiene Network, who passed away before this publication was completed.

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Published on behalf of RUDOLF SCHÜLKE FOUNDATION
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The author, Prof. Dr. Martin Exner, MD, is chairman of the Rudolf Schülke Foundation, since 1994 Director of the Department of Hygiene and Public Health of Bonn University as well as a member of the board of directors and member of several national and international scientific societies and committees in the field of hygiene and public health (www.meb.uni-bonn.de/hygiene).

The Rudolf-Schülke-Stiftung was founded in 1972. It promotes worldwide dialogue with representatives of science and research. Every two years the Foundation awards the Hygieia Medal to scientists who have found outstanding solutions to problems in the domain of hygiene, microbiology and preventive medicine. (Rudolf-Schülke-Stiftung, Robert Koch-Str. 2, 22851 Norderstedt, Germany; www.rudolf-schuelke-foundation.com).

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PREFACE

In 1996 the Schülke Foundation, then chaired by Prof. Dr. Knut Olaf Gundermann, compiled the *Memorandum on the Threat Posed by Infectious Diseases – Need for Reassessment and for a New Prevention Strategy in Germany* on behalf of the professional societies and medical associations in the field of infectious diseases. At that time the German Federal Epidemic Act (Bundesseuchengesetz) was amended, giving rise to a new structuring of the Robert Koch Institute, to extension of the notification obligation and to the creation of an exemplary epidemiological reporting system. In the opinion of the Scientific Council, the Robert Koch Institute has evolved into a reputable national and international institute for prevention and control of infectious diseases. The Memorandum published in 1996 has also helped drive this process, thus leaving its imprint on that period of time.

Despite this very positive development there are a number of demands that were outlined in the former Memorandum, and which are mainly the responsibility of the different federal states, which have not been addressed. On the contrary, in many respects there has been **further aggravation of the misguided developments seen in the domain of infection prevention**. In some federal states, despite urgent warnings, in-house scientific capacities and infrastructures relating to infection prevention and control have been virtually abolished and certain areas of the public health service have been severely weakened because of cutbacks on staffing. Today, it is no longer possible to assure the education of a new generation or the training of, in particular, physicians in infection prevention due to the closure of the hygiene departments at German universities.

Furthermore, the past 10 years have produced a plethora of novel scientific insights and epidemiological developments that have had a major impact on risk assessment and risk-minimising strategies. These include
– the sharp increase in the world population, with a commensurate increase in poverty worldwide,
– the increase in travel, facilitating the ever more rapid spread of microbial agents (e.g. SARS),
– the inadequate supply of safe water to more than 1 billion people and inadequate sanitary situation of more than 2 billion people.

This scenario also increases **the risk of a worldwide pandemic**. While, on the one hand, diseases that formerly posed a dangerous threat of epidemics such as cholera, typhoid fever, smallpox and plague are now of virtually no consequence or have been completely eradicated at least in the developed countries, there has been on the other hand a drastic increase in particular in contact-mediated as well as food- and waterborne diseases.

In its first epidemiological report published in 2007, the European Centre for Disease Prevention and Control (ECDC) identifies the **increase in antibiotic resistant microorganisms and nosocomial infections as the most important threat to health in Europe**. This also holds true in the case of Germany. Between 2000 and 2002 Germany witnessed a rise of more than 10 % in the MRSA rate, the highest in Europe. In contrast, in other European countries, e. g. France, it has been possible to achieve a major reduction in MRSA thanks to the astute allocation of priorities at a political level. A further example of the threat posed by nosocomial infections (also known as 'healthcare associated infections') is the salmonella outbreak that occurred in 2007 in the state of Hesse, the biggest salmonella outbreak seen anywhere in the world in the past 20 years and which needed more than a month to bring under control. There are also risks that are difficult to calculate with regard to bioterrorism and pandemics caused by, for example, influenza or SARS. All this must serve as a warning that the resilience needed to safeguard the health of the public against the threat of communicable diseases is by no means assured in Germany or worldwide.

There is thus an urgent need to face up to the health risks posed by communicable diseases as well as to focus on the **prevention potential to be realized by bolstering the infection control (hygiene) and public health infrastructures**, for which the various federal states are responsible, and to **reform hygiene and infection control in line with future needs**. This calls for a political committment and the setting of priorities, for the creation of well-trained human resources' capacities and an institutional infrastructure as well as for optimisation of training, in particular in medical disciplines by, among other things, establishment of chairs for hygiene and public health.

We hope that his present publication will lend impetus to new discussions, drive prioritisation and contribute to the creation of infrastructures for enhancement of health protection and, as such, will reinforce resilience in the face of the threat posed by emerging and re-emerging communicable diseases.

We would like to thank the following institutions and persons for their support and valuable constructive suggestions when compiling the manuscript: the professional societies and medical associations for hygiene and public health such as the German Society of Hospital Hygiene (Deutsche Gesellschaft für Krankenhaushygiene – DGKH) with its President Prof. Dr. med. Kramer, the Federal Association of Infection Control and Environmental Medicine Physicians (Berufsverband der Ärzte für Hygiene und Umweltmedizin), the Society of Hygiene, Environmental Medicine and Preventive Medicine (Gesellschaft für Hygiene, Umweltmedizin und Präventivmedizin – GHUP) with its President Prof. Dr. med. Eikmann, the Association for Applied Hygiene (Verbund für angewandte Hygiene – VAH) with its Chairman Prof. Dr. med. Hingst as well as the Federal Association of Public Health Physicians (Bundesverband der Ärzte des Öffentlichen Gesundheitsdienstes – BVÖGD) with its Chairman Dr. med. Walter; we also thank Dr. Hornei for her excellent contribution to diagnostics, Frau Ilschner for copy editing the text and the Rudolf Schülke Foundation for the trust placed in us.

Bonn, September 2007

Prof. Dr. med. Martin Exner
Chairman of the Rudolf Schülke Foundation

SUMMARY

Despite the enormous successes scored worldwide, infectious diseases continue to pose one of the greatest threats to mankind. This is borne out by their major contribution to morbidity and mortality, besides cardiovascular diseases as well as malignant and chronic degenerative diseases. They are characterized by **dynamics for which no prognosis can be ventured** and represent a major economic burden not only for the health services but also for the overall national economy. Hence combating them presents a **continual medical, political and social challenge**.

There are myriad reasons underlying this continual potential threat: environmental factors, socioeconomic conditions, technical developments, the increase in travel and international ramifications, e. g. in the supply of foodstuffs, the growing number of population groups susceptible for acquiring infections as well as the **metamorphic and adaptability profiles being evidenced by microorganisms**. Set against that background, there has been a continual trend in the emergence of new communicable diseases. Infectious diseases that were deemed to have been brought under control have not yet been fully eradicated.

Novel virulent variants of known or hitherto unknown pathogens, such as HIV, are evolving and call for **→ continual adaptation of preventive and therapeutic approaches**. This is also borne out by, among other things, the danger of a pandemic spread of a new virulent influenza variant.

→
It must be expected that novel variants of known or hitherto unknown pathogens continue to emerge and pose a threat.

Despite the successful usage of available vaccines there are still considerable **vaccination gaps** in the population, in particular among adults, a fact that is also apparent in Germany. To date, there are no vaccines in sight against HIV/AIDS, hepatitis C or malaria.

As regards the treatment of communicable diseases, the **worldwide increase in antibiotic resistance among bacteria and fungi** continues to play a pivotal role. It is likely that soon there will be no antibiotics at all available against certain pathogens, thus ushering in the post-antibiotic era in which the antibiotics currently available against bacterial and mycological agents will no longer be effective.

Thanks to the insights gleaned from novel diagnostic techniques, there is growing evidence that a broad spectrum of microbial agents may be the cause of, or are cofactors in, **chronic degenerative diseases or malignant diseases**. The epidemiological role of microorganisms as the causative agents of such diseases by far exceeds that of chemical environmental pollutants with the exception of cigarette smoking.

In addition to those factors already mentioned in the summary to the Memorandum published in 1996, the existing threat has been drastically intensified by **bioterrorism** and by the **possibilities now available to humans to modify the virulence profiles of microorganisms**, something that could have major public health implications. In expert circles it is assumed that it is no longer a matter of *whether* but of *when* such genetically modified, and highly virulent, microbes will be deployed in bioterrorist attacks.

→
The majority of infectious diseases occuring in the developed countries are contracted in private households or in the workplace as well as in specific risk areas such as hospitals and nursing homes.

A fact often overlooked is that the majority of the infectious diseases occurring in the developed countries **→ are contracted in private households or in the workplace as well as in specific risk areas such as hospitals and nursing homes**.

However, the **risk perception** in the German population with respect to the importance of communicable diseases, and also as regards the requisite preventive and control measures that can be taken by each individual, is not sufficiently anchored. The possibilities for treatment of infectious diseases are considerably overestimated against the background of the increasing trend in antibiotic resistance.

Among the socioeconomic factors that contribute to the spread of infectious diseases is the estimated **increase in the world population** by up to 2 billion people in the next 20 years. It can be assumed that the **major deficits in the sanitary infrastructure**, in particular in the megacities, will be further aggravated. Even at present up to 1.1 billion people have no access to **safe drinking water** and 2.5 billion people are compelled to live under inadequate hygienic conditions. HIV/AIDS, tuberculosis and malaria have by no means been brought under control worldwide and in some African countries have contributed to a dramatic reduction in the average life expectancy.

In Germany, compared to the situation in 1996, it has been possible over the past decade to score major successes as regards the infrastructure for prevention and detection of infections. These include the enforcement of a modern **Protection Against Infection Act** (*Infektionsschutzgesetz*) and centralisation of tasks relating to infection prevention and control by the **Robert Koch Institut**.

Despite these resounding successes, there are still considerable **deficits in communication with the public** with respect to the importance of communicable diseases and of basic hygiene measures and the willingness to engage in immunisation to assure high vaccination coverage.

The **infrastructure** of well-functioning networks of hygiene and microbiology institutes at the universities is still endangered and to date it has not been possible to put a stop to their dismantling. This scenario gives rise to considerable risks both in terms of the **education, training and continuing professional development, research**, and public health services as well as of effective infection management.

Hence the partial successes scored over the past 10 years must be viewed as a baseline situation and as motivation for the further improvements urgently needed and must not be allowed to halt the train of developments.

But Germany, thanks to its historic experiences and accomplishments in the field of prevention and control of infectious diseases as embodied in particular by Robert

Koch, has a special **responsibility** to contribute on the world stage to the enhancement of infection prevention and control, to optimise education, training and continuing professional development programmes and to support development aid programmes, in its own interest too. The **UN Millennium Goals** serve as an orientational guide here, and each country should help to implement them.

There is also a need to **coordinate** the numerous experiences and scientific structures within Europe so that maximum benefit can be derived from them within Europe and also worldwide.

As such, today the main emphasis is no longer on discovering new microorganisms and characterising them with the help of molecular biology methods, as was the case a century ago. Rather, what is needed is to harness consistently the existing scientific insights while also acknowledging the pivotal role of other essential factors (political committment, social aspects, administrative structures, infrastructural prerequisites, historic, cultural, geographic circumstances, training, communication, inter alia in the various countries worldwide), so as to bring the threat posed by infectious diseases under control. In the → **holistic bundling of these activities** lie the scientific challenges of the next, possibly, 100 years. If this does not succeed, the threat faced can have existential implications once again, even for the developed countries.

→
In the holistic bundling of all activities relating to prevention and control of infection lie the scientific challenges of the next 100 years. If this does not succeed, the threat posed can have existential implications once again, even for the industralised countries.

The primary tasks for the coming years are as follows:

- **Enhancement of measures for health protection and health promotion**
- **Conductance of a different form of risk communication**
- **Further development of vaccines and increase of vaccination uptake rates**
- **Development of innovative diagnostic techniques and therapeutic agents**
- **Inclusion of the discipline of infection control (hygiene) in the education, training and continuing professional development of physicians and medical personnel**
- **Creation of networking systems between hygiene departments and microbiology institutes**
- **Expansion of public health infrastructures**
- **Promotion of a well-delineated infrastructure for human resources' and equipment capacities to meet everyday challenges as well as to deal with a crisis situation in Germany.**

1 INTRODUCTION

A 100 years ago, on 1 June 1906, the → **the German Society for Hygiene and Microbiology** (Deutsche Gesellschaft für Hygiene und Mikrobiologie – DGHM), formerly known as the "Free Association for Microbiology", was founded. In 1949 it was renamed as the German Society for Hygiene and Microbiology.

→
A 100 years ago, on 1 June 1906, the German Society for Hygiene and Microbiology was founded.

The centenary of the foundation of the first society, and parent association of several professional societies for hygiene and microbiology derived from it, is an occasion to review the successes, deficits and future challenges faced by hygiene and microbiology in the prevention and control of infectious diseases.

The year 1906 is linked not only to the foundation of the DGHM, whose founding fathers included leading scholars of that time such as Flügge, Ehrlich, Gaffky and Wassermann. One of the founding fathers was also → **Robert Koch** who, however, since April was on an expedition to German East Africa after sleeping sickness had begun to hover at the frontiers to that country. No other German researcher of the 19th or 20th century has exerted such a profound and global influence on hygiene (infection control) and microbiology to the extent that Robert Koch did.

→
No other German researcher of the 19th or 20th century has exerted such a profound and global influence on hygiene (infection control) and microbiology to the extent that Robert Koch did.

In addition to the foundation of the Society, the year 1906 also marked two other important developments that had profound implications for infection control and microbiology. It was in 1906 that the **Implementation Provisions of the Prussian State Epidemic Act**, based on the Prussian State Epidemic Act published in 1905, were introduced. These Implementation Provisions underline the paramount importance of bacteriological investigations for the detection of infectious diseases. As such, microbiological diagnostics was granted a legal mandate, serving in turn as an important prerequisite for the establishment of infection control and microbiology institutes.

On 16 June 1906 the **Guide to establishment, operation and supervision of public water supply systems** was published by the German Federal Council (Bundesrat). This conferred a legal basis to the monitoring of drinking water and was, at the same time, a precondition for a major improvement in the hygienic condition of drinking water. In this way it was possible to bring almost completely under control or eradicate the most important waterborne diseases prevailing at that time in Germany such as cholera, typhoid fever and Shigella dysentery. The incidence of the most important notifiable diseases of that time per 100,000 inhabitants in the Ruhr-Kohlen district (with 2,869,674 inhabitants) is given in **Table → 1.1**. In 1956, 50 years later, while infectious diseases that were of epidemiological significance were not yet brought under control, there was a marked decline in their incidence.

Over the next years, thanks to **improved hygienic structures and measures** as well as **improved microbiological diagnostics** and consistently applied **immunisation strategies** under the direction of the public health offices, there was a continual decline in infectious diseases **Table → 1.2**.

→
Tables 1.1, 1.2:
Incidence (%) of reported infectious diseases in the *Ruhr-Kohlen District* per 100,000 inhabitants in 1906 (Tab. 1.1) and based on data from the Robert Koch-Institut in Germany 2006 (Tab. 1.2).
Sources: Verein zur Bekämpfung von Volkskrankheiten 1907, RKI 2007.

Incidence of Infectious Diseases in the Ruhr-Kohlen District 1906	
Diphtheria	189.9
Meningitis	20.4
Scarlet fever	202.1
Shigella dysentery	9.9
Tuberculosis	70.4
Typhoid fever	37.6

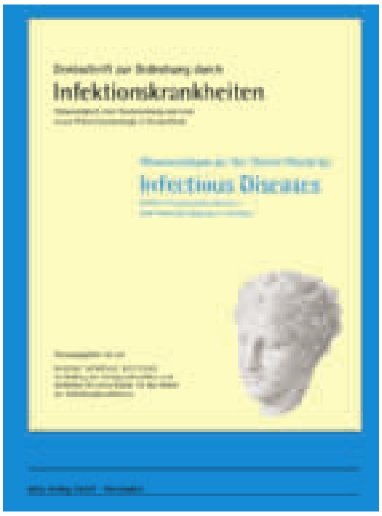
Table 1.1

Incidence of Infectious Diseases 2006 (RKI)	
Campylobacter	63
Diphtheria	0
Dysentery (*Shigella*)	1
Meningitis (invasive)	0.7
Norovirus	92
Pertussis	ca. 12.3
Poliomyelitis	0
Rotavirus	81
Salmonellosis	64
Scarlet fever	no data
Tuberculosis	6,6
Typhoid/paratyphoid fever	<1

Table 1.2

In 1980 the World Health Organisation (WHO) announced that the world was free of smallpox, one of the most deadly epidemics ever visited upon mankind. The enormous successes scored in eradicating smallpox and the large-scale eradication of polio (poliomyelitis) as well as the ability to control bacterial infections through antibiotics led to the belief in scientific and political circles that **"the book of infectious diseases could be closed"**. As a result of this, the financial resources needed for prevention, detection and surveillance of infectious diseases were continually reduced worldwide and public institutions for diagnosis and prevention of infectious diseases were to a large extent dismantled.

In October 1992 the Institute of Medicine under the direction of *J. Lederberg* published a position paper on the topic of **"Emerging Infections – Microbial Threats to Health in the United States"**, which portrayed the assessment of the epidemic and infection control situation hitherto as a fatal misconception of global proportions. The extent of the threat, as emphasised in this report, could be contained only by continual worldwide joint efforts on the part of both the underdeveloped and developed countries. This, however, called for a willingness to uphold the organisational infrastructures underpinning the prevention, detection and control of infectious diseases. Only in that way could public health duties be discharged to contain the existing risks posed by infectious diseases.



Based on that document, in 1996 the Rudolf Schülke Foundation published the **"Memorandum on the Threat Posed by Infectious Diseases – Need for Reassessment and for a New Prevention Strategy in Germany"** on behalf of the professional societies and medical associations in the field of infectious diseases. That Memorandum focused on the epidemiology of infectious diseases as well as on the risks and socioeconomic burdens in Germany, Europe and the world. Misguided developments and deficits were identified and recommendations and strategies formulated. That Memorandum made a decisive contribution to a reappraisal process, giving rise to exemplary developments such as the new structuring of the Robert Koch Institute, the establishment of surveillance and publication of the Epidemiology Bulletin. This meant that Germany was once again able to integrate, especially with developments in the English-speaking countries, and today it is even ahead of these in certain areas such as in the prevention and control of nosocomial infections.

At that time it was primarily → **the AIDS epidemic** – which has not been brought under control up to the present day – that led to the awareness that communicable diseases cannot always be safely controlled even in the modern age. Since then a number of new infectious agents such as **SARS (severe acute respiratory syndrome) associated coronavirus**, the henipavirus ((Hendra and Nipah viruses) as well as **avian influenza virus** have been identified, and which pose the risk of a pandemic spread. Infectious diseases that have been around for a long time such as West Nile fever, human monkeypox, dengue, tuberculosis and malaria have by no means been brought under control. Once again this attests to the fact that the dynamics and multifaceted nature of infection epidemiological processes call for continual reassessment and adaptation of prevention and control strategies.

→
The AIDS epidemic and the failure to develop a preventive vaccine against this disease to date has led to the awareness that communicable diseases cannot always be safely controlled.

Apart from the newly emerging problem areas, one must not lose sight of the existing local risks. While, for example, back in 1996 the increasing spread of **antibiotic resistant microorganisms** had already been identified as posing a threat, it has continued to grow since that time. The worrying trend of an increasing prevalence of **methicillin-resistant** *Staphylococcus aureus* **(MRSA)** in Germany and Austria compared with all other European countries elicited much attention especially between 1999 and 2002. **Inadequate vaccination uptake** rates are reflected in the growing number of measles cases in German in 2006.

The **increase in risk populations** in Germany, composed mainly of elderly persons, has in the meantime shown that it is not only hospitals but also homes for the elderly that pose an equal risk of nosocomial infections. On the world stage, the **increase in the world population** by up to 2 billion people, with a commensurate increase in urbanisation, entails a considerable risk for **pandemic spread** of epidemic diseases with dramatic economic and epidemiological implications.

Microbiological diagnostics has made enormous progress but has also led to the identification of new risks emanating from communicable diseases, such as their relationship to malignant diseases and other chronic ailments.

Nonetheless, the **risk perception** in the general population in respect of preventive measures is insufficiently anchored. Accordingly, among other things the **"Hygiene Hypothesis"**, which postulates that having experienced infectious diseases confers protection against atopic diseases, has fostered the common public belief that good hygiene practices are unnecessary or even dangerous and that, furthermore, because of the fear of underpinning resistance, selective and justified disinfection procedures have not been carried out to the extent needed. There are also shortcomings in the teaching of **hygiene (infection control) as part of the medical curriculum** following the combination of the disciplines of hygiene, microbiology and virology to a single topic in the German medical licensure regulations.

→
More than 5 % of all deaths are directly attributed to infectious diseases. Millions of other deaths are caused by the secondary effects of infectious diseases.

After cardiovascular diseases, infectious diseases continue to be the most common cause of death worldwide. Of the estimated 57 million deaths each year worldwide, some 15 million, i.e. → **more than 25 % of all deaths are directly attributed to infectious diseases**. Millions of other deaths are caused by the **secondary effects** of infectious diseases. Infectious diseases lead to compromised health and account for approx. 30 % of all Disability Adjusted Life Years (DALYs) worldwide (a Disability Adjusted Life Year is the loss of one healthy year of life). Each year infectious diseases are responsible for the loss of almost **1.5 billion total DALYs worldwide**. Set against that background, the European Parliament decided in 2004 to set up the **European Centre for Disease Prevention and Control**, which has its headquarters in Stockholm. The European Centre for Disease Prevention and Control is a new EU centre aimed at coordinating European efforts to combat communicable diseases such as influenza, SARS and HIV/AIDS.

→
Table 1.3:
The 8 UN Millenium Development Goals and their indicators based on the Millenium Declaration of 2000.

In view of the worldwide implications of infectious diseases, the 2006 G8 Summit in St. Petersburg focused in depth on the fight against AIDS, tuberculosis, malaria and vaccine-preventable diseases, thus underlining the pivotal and topical role played by communicable diseases in the world economy. Major efforts are needed to help the United Nations reach the **UN Millennium Goals**, which are also aimed at prevention and control of major infectious diseases (→ **Table 1.3**).

The aim of this present publication in 2007 is to engage in risk assessment of the current and future threats posed by infectious diseases and, on that basis, to formulate and present the necessary risk-minimising strategies.

8 Health Goals in the Millenium Development Goals

Goal 1:

Eradicate extreme poverty and hunger.

Target 1: Halve, between 1990 and 2015, the proportion of people whose income is less than $ 1 a day.

Target 2: Halve, between 1990 und 2015, the proportion of people who suffer from hunger.

Goal 2:

Achieve universal primary education.

Target 3: Ensure that, by 2015, children everywhere, boys and girls alike, will be able to complete a full course of primary schooling.

Goal 3:

Promote gender equality and empower women.

Target 4: Eliminate gender disparity in primary and secondary education, preferably by 2005, and in all levels of education no later than 2015.

Goal 4:

Reduce child mortality.

Target 5: Reduce by two-thirds, between 1990 and 2015, the under-five mortality.

Goal 5:

Improve maternal health.

Target 6: Reduce by three-quarters, between 1990 and 2015, the maternal mortality ratio.

→ *Indicators*: Maternal mortality ratio, proportion of births attended by skilled health personnel

Goal 6:

Combat HIV/AIDS, Malaria and other diseases

Target 7: Have halted by 2015 and begun to reverse the spread of HIV/AIDS.

Target 8: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases.

→ *Indicators*: HIV prevalence among pregnant women aged 15–24, condom use rate of the contraceptive prevalence rate, condom use at last high-risk sex, percentage of population aged 15–24 years with comprehensive correct knowledge of HIV/AIDS, contraceptive prevalence rate, ratio of school attendance of orphans to school attendance of non-orphans aged 10–14 years, prevalence and death rates associated with malaria, proportion of population in malaria-risk areas using effective malaria prevention and treatment measures, prevalence and death rates associated with tuberculosis, proportion of tuberculosis cases detected and cured under DOTS (internationally recommended TB control strategy)

Goal 7:

Ensure environmental sustainability.

Target 9: Integrate the principles of sustainable development into country policies and programs and reverse the loss of environmental resources.

Target 10: Halve, by 2015, the proportion of people without sustainable access to safe drinking water and basic sanitation.

Target 11: Have achieved by 2020 a significant improvement in the lives of at least 100 million slum dwellers.

→ *Indicators*: Proportion of land area covered by forest, ratio of area protected to maintain biological diversity to surface area, energy use (kg oil equivalent) per $ 1 GDP (PPP), carbon dioxide emissions per capita and consumption of ozone-depleting CFCs, proportion of population using solid fuels, proportion of population with sustainable access to an improved water source, urban and rural, proportion of households with access to secure tenure

Goal 8:

Develop a global partnership for development.

Target 12: Develop further an open, rule-based, predictable, nondiscriminatory trading and financial system (includes a committment to good governance, development, and poverty reduction, both nationally and internationally).

Target 13: Address the special needs of the Least Developed Countries (includes tariff- and quota-free acess for Least Developed Countries, exports, enhanced program of debt relief for heavily indebted poor countries and cancellation of official bilateral debt, and more generous official development assistance for countries committed to poverty reduction).

Target 14: Address the special needs of landlocked developing countries and small island developing states.

Target 15: Deal comprehensively with the debt problems of developing countries through national and international measures in order to make debt sustainable in the long term.

Target 16: In cooperation with developing countries, develop and implement strategies for decent and productive work for youth.

Target *17:* In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries.

Target 18: In cooperation with the private sector, make available the benefits of new technologies, especially information and communication technologies.

2 RISK EVALUATION

2.1 Epidemiological implications of infectious diseases

2.1.1 Epidemiological implications of infectious diseases in Germany

Several sources have to be evaluated to identify the epidemiological implications of infectious diseases in Germany. These include:

– The presentation of notifiable diseases as published each year in the Infection Epidemiology Yearbook by the Robert Koch Institute,

– The mortality cause statistics compiled by the German Federal Office of Statistics *(Statistisches Bundesamt)*,

– Sentinel investigations of non-notifiable infectious diseases such as pneumonia, diarrhoea, nosocomial infections,

– Reports on pandemics and imported infections *(RKI, ECDC, WHO)*.

On 7 June 2007 the European Centre for Disease Prevention and Control (ECDC) published its first Epidemiological Report on Communicable Diseases in Europe, outlining the trends manifested by 49 of the most important infectious diseases in 25 Member States of the EU and in three EEA/EFTA countries (Iceland, Liechtenstein and Norway (Amato-Gauci 2007).

2.1.1.1 Notifiable diseases in Germany

The Memorandum on the Threat Posed by Infectious Diseases of 1996 noted that the procedures in place at that time for diagnosis and reporting of infections did not lend themselves to the pooling of valid data in an international network.

With the amendment of the Protection against Infection Act *(Infektionsschutzgesetz)* and its enforcement in 2001, the reporting system and the scope of notifiable microbial agents was expanded to serve as a model even at international level and, as such, the deficits pinpointed in 1996 were fortunately eliminated to a large extent.

At European level, together with Finland, Germany has the highest number of individual microorganisms defined as notifiable in its Protection against Infection Act → **Table 2.1** (Medema 2006). The most important notifiable pathogens and infectious diseases are presented on the basis of the cases reported since 2001, inter alia in the Infection Epidemiology Yearbook published each year. The results are based on intensive cooperation with and between physicians in public health offices and corresponding state institutions, laboratories as well as the hospitals and doctors' surgeries participating in this system.

Analysis of notifiable diseases in Germany for 2004 and 2005, while taking account of earlier developments, reveals the following fundamental trends in notifiable communicable diseases compared to 2004:

1. The widespread, epidemic infectious diseases that still instilled fear at the beginning of the 20th century such as cholera, diphtheria, epidemic typhus, measles, anthrax, paratyphoid fever, plague, poliomyelitis, rubella, rabies as well as abdominal typhoid fever are virtually of no importance anymore. Isolated occurrences of such diseases are mainly due to importation from other countries. The achievements in prevention and control of these diseases are mainly due to:

   - **Improvement of the hygiene and sanitary preconditions in Germany** (primarily drinking water and effluent-disposal facilities: (cholera, Q fever, anthrax, paratyphoid fever, plague, and abdominal typhoid fever).
   - **Specific immunoprophylaxis** (diphtheria, measles, plague, rubella, rabies).

   – Another group of epidemic diseases that were of relevance in the past such as **tuberculosis** or **hepatitis A** have shown a continual **decline** thanks to improvement of general hygiene conditions, improvement of drinking water and effluent-disposal facilities as well as, in the case of hepatitis A, due to immunisation and better monitoring of risk patients.

   – In the case of **bloodborne infections** such as hepatitis B there has been a **slow continual decline**, attributable, inter alia, to intensified efforts and the availability of hepatitis-B-specific immunisation. There has also been a reduction in the number of hepatitis C cases despite the fact that there is no preventive vaccination; this is due to, among other things, **improved diagnosis**, including monitoring of blood products.

2. Conversely, there has been no satisfactory reduction in another group of pathogens, causing mainly *gastroenteritis*.

→
Table 2.1:
Comparison of mandatory notification of pathogens causing gastroenteritides in Europe.
Finland (2005), Germany (2001),Netherlands (1999, 2005), Sweden (2001, 2004, 2005), UK (2005), France (2007).
Source: modified as per Medema 2006.

Pathogen	Country					
	Finland	France	Germany	Netherlands	Sweden	United Kingdom
Campylobacter	●	❍	●	❍	●	❍
Cryptosporidium	●	❍	●	❍	●	❍
E. coli 0157:H7	●	●	●	●	●	❍
Giardia	●	❍	●	❍	●	❍
Norovirus	●	❍	●	❍	❍	❍
Salmonella	●	●	●	❍	●	❍
Shigella	●	●	●	●	●	❍
*Acute gastroenteritis**	●	❍	●	●	❍	●
Outbreak	●	●**	●	●	●	❍

*linked to food processing or food poisoning. **All infections are notifiable after outbreak with the exception of campylobacter
● Notifiable ❍ Data registration based on voluntary reporting

→

Trends in infectious diseases in Germany (examples):

Marked declining trend:

– "Classic epidemics" such as cholera, polio, typhoid fever, anthrax, plague, rubella

Slowly declining trend with fluctuations:

– Tuberculosis as well as hepatitis viruses A, B and C

Increase

– Norovirus infections, EHEC, influenza, legionellosis

Marked increase:

– Campylobacter and rotavirus infections, new HIV infections.

– Conversely, there has been a marked increase in **campylobacter enteritis** and in the meantime this has also overtaken salmonellae as the main cause of bacterial gastrointestinal infection.

– Equally unsatisfactory is the situation of norovirus gastroenteritis, rotavirus infections and salmonellosis which account for a high proportion of the notifiable diseases. A common aspect of all these diseases is that they are infectious diseases spread through poor personal hygiene practices and, in particular, involve foodborne transmission and direct person-to-person contact transmission. This is also true in the case of giardiasis and cryptosporidiosis, which can also in some cases cause severe intestinal infections but with an essentially lower incidence. However, here too no decline can be discerned.

– Another worrying trend is the increase in **enterohaemorrhagic *E. coli* (EHEC) diseases.** These diseases are spread, in some cases very effectively, through foodstuffs or as contact or waterborne infections (drinking water, bathing water). Both campylobacter infections and norovirus infections are additionally known to have a very low infective dose. When interpreting these figures it must be borne in mind that a large number of notifiable diseases involving campylobacter, norovirus and rotavirus as well as salmonellosis are not diagnosed.

3. **Legionellosis** has also grown in importance. The Robert Koch Institute has noted in this respect that it is likely that there is considerable underreporting of legionellosis and that instead of the 475 and 554 reported cases in 2004 and 2005, respectively, the actual figures could be as high as 30,000 community-acquired pneumonia cases caused by legionellae. Legionellosis is transmitted to humans only through water-conveying technical systems; there is no person-to-person transmission. For that reason **prevention strategies for water supply systems** as well as, on the other hand, improved diagnosis are urgently needed.

4. Viral haemorrhagic fevers which have caused much consternation did not occur in Germany in either 2004 or 2005. But in 2006 there was one case of Lassa fever in Münster.

5. In recent years there has been an increase in **new HIV infections** and in other sexually transmitted infections in Germany and in other industrialised countries, in particular among men who have sex with men (MSMs). In Germany, there was a 13 % rise in the number of new diagnoses of HIV in 2005 compared with the previous year (RKI Annual Report 2005).

Overall, analysis of notifiable diseases shows that the classic diseases causing epidemics in Germany in the past have been kept under control by **optimising the sanitary hygiene preconditions** as well as thanks to **immunisation strategies**. However, there continues to be a high rate of notifiable bacterial, viral and parasitic diseases transmitted mainly through direct contact.

Therefore strategies devised to change his situation as well as to develop specific vaccines must be aimed at improvement of hygiene conditions at individual and population level.

In other cases, e. g. hepatitis C infections, there is a need for → **improvement of hygiene measures in the medical setting** as well as in areas dealing with potentially blood-contaminated invasive systems (piercing, tattooing, shaving, etc.) and **enlightenment of the population groups at risk.**

→

Based on risk assessment of the trends in notifiable diseases in Germany, the principle goals are identified:

- **Development of specific vaccines**
- **Improvement of immunisation strategies**
- **Improvement of hygiene conditions at an individual and general-population level**
- **Improvement of hygiene measures in the medical setting**

In view of the ongoing worrying situation of HIV infections close monitoring and, in particular, education to inculcate low-risk sexual practices is needed.

The fight against influenza as one of the world's most dangerous respiratory infectious diseases demands unrelenting efforts. A high **vaccination uptake rate** in the population is of paramount importance. In this respect, depending on the infection epidemiological situation, the appearance of **new variants of influenza viruses** must be expected. These variants are responsible for the annual influenza prevalence of 3,486 cases in 2004 and 12,734 cases in 2005.

2.1.1.2 Infections as the cause of death in Germany

A further source for characterisation of the epidemiological implications of infectious diseases is the presentation of the "Causes of Death in Germany" compiled by the Office of Statistics (Specialist Series 12/Series 4).

The mortality cause statistics are recorded on a single-cause basis in line with WHO regulations, i. e. as per the entries on the death certificate, which as a causal chain work backwards from the immediate cause of death to the underlying disease, and only this underlying disease is taken into account for statistical purposes.

In this present publication the situation as prevailing in 2004 is presented by way of comparison. In 2004 there were 818,271 deaths in Germany. The most common cause of death in 2004, too, was cardiovascular diseases, which were responsible for almost one out of every two deaths (45 %). Almost one out of every fourth death (25.6 %) was attributable to a malignant tumour. Respiratory diseases accounted for 6.4 % of deaths and digestive tract diseases for 5.2 %.

The diseases are classified using different ICD codes (International Statistical Classification for Diseases and Related Health Problems). In Germany a total of 11,062 persons died from diseases classified as "Certain Infectious and Parasitic Diseases" (ICD Codes A00 to B99). Flu and pneumonia cases are listed separately (ICD Codes J10–J18). 19,094 persons died from these diseases → **Table 2.2.** Overall, it can be said that the **proportion of infections implicated as the cause of death has markedly declined** compared with the beginning of the 20th century and compared with cardiovascular diseases and malignant tumours.

→
Table 2.2:
Mortality cause statistics in Germany for 2004: selected infectious diseases.
Source: Office of Statistics 2005.

Certain Infectious and Parasitic Diseases	Deaths
– Infectious intestinal diseases (not further specified)	942
• Other salmonella infections	54
– Tuberculosis	350
– Other bacterial diseases, including:	6,445
• Meningococcal infections	63
• Other sepsis	5,956
• Erysipelas	131
– Infections transmitted mainly through sexual practices	7
– Viral infections of the central nervous system	184
– Atypical viral infections of the central nervous system	156
– Creutzfeldt-Jakob disease	144
– Viral infections with skin and mucosal lesions, including:	104
• Herpes zoster	73
– Viral hepatitis, including:	1,156
• Acute viral hepatitis B	74
– HIV disease, including:	507
• Infectious and parasitic diseases secondary to HIV infection	114
• Malignant tumours secondary to HIV infection	43
– Other viral diseases	151
– Mycoses	125
– Protozoal diseases	23
– Sequelae of tuberculosis	91
– Other, not further specified infectious diseases	726
Flu and pneumonia (ICD Codes J10–J18)	
– Pneumonia, causative agent not further specified	18,395
– Flu due to diagnosed influenza viruses	9
– Flu, viruses not diagnosed	116
– Viral pneumonia, not classified elsewhere	42
Other acute infections of the lower respiratory tract (J20–J22)	629
Infections specific to the perinatal period (P35–P39)	78
Total	30,863

→
Overall, infectious diseases play a minor role as the cause of death in Germany. Among the infectious diseases resulting in death pneumonia is the most important, ranking eighth as the most common cause of death.

Noteworthy is, however, the pivotal role played by certain infectious diseases as the cause of death: in the order of the → **most common causes of death, pneumonia infections rank eighth.** Among the "Certain Infectious and Parasitic Diseases", sepsis occupies a leading rank, accounting for more than half (5,956) of the 11,062 deaths.

The proportion of malignant tumours and chronic diseases triggered by infectious agents has not been taken into consideration or is to be studied in greater depth at a future date. These include, for example, hapatocellular carcincoma caused by hepatitis B and hepatitis C viruses or gastric carcinoma caused by *Helicobacter pylori (see Chapter 2.2 and 2.3.2).*

As such, the actual proportion of infections implicated cannot be exactly inferred from the mortality causes.

2.1.1.3 Non-notifiable infections in Germany

Analysis of notifiable infectious diseases and mortality cause statistics shows only **a partial aspect** of the epidemiological implications of infectious diseases in Germany.

The actual significance of infectious diseases can be elucidated only through in-depth analysis, as impressively borne out in the case of pneumonia, gastrointestinal and nosocomial infections.

Pneumonia cases

In the case of pneumonia infections a distinction must be made between

- **nosocomial** pneumonia and
- **community-acquired** pneumonia.

Community-acquired pneumonia (CAP) includes any lung infection in an immunocompetent person, i. e. anyone with a healthy immune system, contracted in a non-healthcare setting, such as in the home or workplace. This is also true in the case of pneumonia first diagnosed within the first two days of admission to hospital.

The epidemiology of community-acquired pneumonia is investigated by the **Competence Network for Community-Acquired Pneumonia) (CAPNET),** which is sponsored by the Federal Ministry of Education and Research.

Community-acquired pneumonia is the **most commonly recorded infectious disease worldwide** and accordingly of major sociomedical importance. CAPNET data reveal that in the USA 2–3 million cases are diagnosed each year, giving rise to up to 10 million visits to general practitioners and around 0.5 million hospital admissions. There are no comparable epidemiological data available for Germany, especially to identify how many CAP cases are treated exclusively in the community.

The → **incidence** (number of new cases of disease) in the total population is estimated to be in the range **1–11/1,000 inhabitants per year, and even as high as 68–114/1,000 persons among the residents of homes for the elderly.** More than 30 % of patients are admitted to hospital due to the illness, with 10 % being treated in the intensive care unit (i. e. approx. 2 % of all patients suffering from community-acquired pneumonia). As such, community-acquired pneumonia results in more frequent admissions to hospital than does myocardial infarction (132,000 admissions) and apoplexy (162,000 admissions). Based on CAPNET data, the costs incurred each year due to this disease are estimated to be more than 500 million euros.

→
The incidence of pneumonia in Germany is estimated to be in the range 1–11/1,000 inhabitants per year. More than 30 % of patients are admitted to hospital due to the illness, with 10 % being treated in the intensive care unit. The most common aetiological agent worldwide is *Streptococcus pneumoniae*.

Predisposing factors for disease, or for a severe course of disease, are implicated in more than two-thirds of cases. Apart from the main risk factor, i. e. chronic obstructive pulmonary disease, other factors include an advanced age (> 65 years), smoking, cardiac insufficiency, chronic liver and kidney diseases, diabetes mellitus, previous influenza infection as well as diseases involving a predisposition to aspiration. Chronic obstructive pulmonary disease predisposes to infection due to, first, a disrupted local immune function with damage to the mucous membranes conducive to bacterial infection and, second, due to the malnutrition or undernutrition often seen in advanced stages of disease. Smoking with inhalation increases the risk of legionellae and chlamydiae infection as well as pneumococcal infection with bacteraemia (sepsis).

The following **bacteria** are responsible for more than 90 % of cases of community-acquired pneumonia,

- *Streptococcus pneumoniae* (pneumococci),
- *Haemophilus influenzae* and
- *Mycoplasma pneumoniae.*

In severe courses of disease *Staphylococcus aureus, Klebsiella pneumoniae* and *Legionella pneumophila* are often implicated. *Enterobacteria* and *Pseudomonas aeruginosa* may be detected with increasing age and are associated with a high mortality rate.

→ **In 40–60 % of cases of community-acquired pneumonia no causative agent is identified.**

It must be borne in mind, however, that in → **40–60 % of cases** (in reality more than 70 %) **no causative agent** is identified for several reasons (difficulty with sample collection, delicate microbial agent, contaminants, co-infection, etc.). Investigation of the frequency of the pathogens implicated shows on the whole a homogeneous pattern in many countries despite national peculiarities (e. g. a high legionellae prevalence in Spain): *Streptococcus pneumoniae* (25–45 % of all cases) continues to be the most important agent worldwide, followed by *Haemophilus influenzae* (10–20%) as the most common Gram-negative bacterial species. *Mycoplasma pneumoniae* (10–12 %) plays a minor role, especially in younger patients. The prevalence of *Chlamydia* spp. and *Legionella* spp. is unclear. A virus is detected in around 10–25 % of cases, often involving co-infection with bacteria (especially with pneumococci and *Staphylococcus aureus*). Apart from influenza viruses, RSV-, adeno-, corona- and enteroviruses play a certain role. Since the majority of the findings available are for hospitalised patients it remains unclear to what extent such biased data reflect the infection epidemiology of community-acquired pneumonia. Bridging this lacuna in infection epidemiology so as to be able to draw conclusions reflecting the reality is a particular aim of CAPNET, which in the meantime has presented preliminary data on this topic.

Streptococcus pneumoniae was also the most commonly detected causative agent, followed by viruses identified in 15–20 % of throat swabs using PCR (polymerase chain reaction). The most commonly detected virus in 2005 was influenza virus, which occurred in particular in the months from January to March. Atypical pneumonia cases were responsible for around 20 % of pneumonia cases for which the causative agent could be identified. The high rate of legionellae infections, amounting to almost 8 %, was a surprising discovery. Infections caused by this bacterium were associated with the highest mortality. However, one problem is that it appears to be difficult to conduct diagnosis of *Legionella* infection since there were disparities between the results produced by the legionellae antigen test in urine, PCR-based bronchoalveolar lavage (BAL) and other respiratory tract specimens and serum antibody tests. Another surprising finding was the low number of chlamydia infections detected (< 1 %).

Despite the availability of appropriate standards for treatment of community-acquired pneumonia **therapy failure** is often seen; this is something that must be concluded if after 48–72 hours no clinical improvement is seen or if there is evidence of progression of lung infiltrates on X-ray. Therapy failure was noted in 5–10 % of outpatients, and in 20–30 % of inpatients.

As regards the → **prognosis**, the **overall mortality** for community-acquired pneumonia was **less than 6 %.** In the case of treatment administered in the outpatient setting the mortality rate is < 2 %. If the patient has to be admitted, mortality rises independently of age and risk category to 2–10 %, depending on co-morbidity and age up to 20 %. Noteworthy is the fact that even today mortality associated with bacteraemic pneumococcal pneumonia is still 20 %. *Legionella* pneumonia, too, has an overall poor prognosis, with 10 % of immunocompetent patients dying even on optimal treatment regimens, otherwise this rises to more than 20 %. If a patient contracts a severe form of community-acquired pneumonia, a mortality rate of between 15 and 50 % can be expected.

→

Pneumonia cases have very different prognoses. Whereas the mortality rate is <2 % for outpatient treatment, severe community-acquired pneumonia can also have a mortality rate between 15 and 50 %. In the meantime up to 30 % of pneumococci are resistant to macrolide antibiotics.

In terms of hygiene, **legionellosis** is of special significance since its infection reservoir is restricted to water-conveying technical systems. The principle infection sources are the **piping systems used for hot water distribution** (e. g. sanitary facilities, showers, whirl pools) and cooling towers. There continues to be widespread underreporting of legionellosis in Germany, since apparently not all cases of legionelloses are diagnosed as such. This is especially true in the case of Pontiac fever. Furthermore, when pneumonia is diagnosed only relatively rarely is testing conducted to identify a specific causative organism, hence in all probability only very few of the legionellosis cases are identified. Based on data from the Robert Koch Institute it is assumed in line with the findings from CAPNET that in Germany **6–8 % of all cases of community-acquired pneumonia are caused by legionellae.** With an annual rate of some 500,000 cases of community-acquired pneumonia around 30,000–40,000 of cases would be attributable to legionellae. This figure is at least 3–4 higher than that hitherto thought. This underscores the need for prevention of this important cause of community-acquired pneumonia.

Likewise the possibilities for **preventive vaccination**, in particular against pneumococcal and influenza infections must be exploited in a much more consistent manner than has been the case hitherto.

→
Gastrointestinal infections are responsible for the biggest proportion of notifiable infectious diseases. In Germany, a total of over 5,921 potential foodborne outbreaks involving 70,530 persons were reported to the Robert Koch Institute in 2006. Of these, 1,319 outbreaks affecting 7,217 persons were confirmed as being attributable to foodstuffs.

Gastroenteritides

Gastrointestinal infections are responsible for the → **biggest proportion of notifiable infectious diseases.**

The most important causative agents of gastrointestinal infections are:

- *Salmonella*
- *Campylobacter*
- *Yersinia*
- Enterohaemorrhagic *Escherichia coli* (EHEC)
- *Clostridium perfringens and Bacillus cereus*
- *Shigella*.

The most important viral infections include:

- Rotavirus infections
- Norovirus infections
- Human caliciviruses and small round structured viruses (SRSV)
- Astroviruses.

They are also of enormous significance in terms of health policies because of the costs incurred, including for hospital stays. Based on the data published on hospital diagnostics by the Office of Statistics from 1994–1999 between 110,000 and 130,000 cases were reported, involving hospitalisation of patients with gastrointestinal infectious diseases.

The average hospital stay was 6 days. In 1999 more than **750,000 nursing days** were invoiced. Half of the hospital stays and nursing days involved **children under the age of 5 years and adults above the age of 65 years.** Children under the age of 5 years accounted for one-third of both patients as well as of nursing days.

With costs of around 300 euros incurred per nursing day in 1999 for inpatient treatment, a total of **225 million euros** (751,194 nursing days) were charged for inpatient treatment of patients with gastrointestinal tract infections. Children under the age of 5 years accounted for around 65 million euros (218,239 nursing days).

In addition, there are the costs incurred for outpatient treatment and incapacity to work for inpatients, outpatients and for those persons who stay home for 1–2 days without consulting a doctor as well as for those who have to take time off from work to look after sick children or relatives.

It is not possible at present to estimate exactly how many foodborne infections occur in Germany each year since there is still a lack of suitable population-based representative studies. In 2006 a total of 5,921 outbreaks of potential foodborne infections were reported to the Robert Koch Institute. However, the reported data are incomplete and have not been systematically evaluated.

Further **epidemiological studies** similar to the CAPNET study are therefore urgently needed **for diarrhoea.**

Nosocomial infections (healthcare-associated infections)

Pursuant to the German Protection against Infection Act *(Infektionsschutzgesetz),* **nosocomial infections** (also known as **healthcare-associated infections**) are understood to mean infections showing local or systemic symptoms of infection as a reaction to the presence of pathogens or their toxins which are temporally or causally related to inpatient or outpatient medical interventions, assuming that the infection did not exist prior to the latter.

Just as in all other industrialised countries, so in Germany, too, nosocomial infections are among the most common infections and the most frequent complications associated with medical treatment. While nosocomial infections are notifiable if they give rise to an **outbreak, only around 2 to 10 %** of all nosocomial infections are manifested as outbreaks.

The **prevalence** of nosocomial infections is high in Germany too. Between **3.5–4 % of all patients treated in Germany contract a nosocomial infection.** Within the framework of the "NIDEP Study" (Nosocomial Infections in Germany – Registration and Prevention - Rüden et al.1997) an average nosocomial infection prevalence of 3.5 % was observed in hospitalised patients enrolled in the NIDEP Study. Since at the time of the study some 15 million persons were being treated each year as inpatients in Germany, it was estimated that around 500,000 patients could have contracted a nosocomial infection each year. Apart from the personal suffering and prolongation of medical treatment, such infections are also associated with considerable costs. It has been estimated that nosocomial infections give rise **each year to costs in the region of 1.5 billion euros.** Included in this figure are the consequential costs, e.g. resulting from lost earnings due to a prolonged incapacity to work.

Analyses conducted by Harbarth et al. (2003), based on a systematic review of 30 interventional studies, identified that there was considerable scope for minimising the scale of nosocomial infections, ranging from 10 % to a maximum of 70 % depending on the specific circumstances and features of the respective studies. Based on these data, the authors believe that **→ in general at least 20 % of all nosocomial infections can be prevented.**

→
It is estimated that 500,000 patients per year in Germany contract a nosocomial infection. At least 20 % of these infections could have been prevented.

Nosocomial infections are also thought to have major implications for health policies in other countries. Based on data presented by Burke (2003), between 5 and 10 % of all patients admitted to acute care hospitals in the USA contract one or more infections, with the infection risk continually rising over the past few decades.

It is estimated that each year around 2 million patients suffer such complications in the USA, giving rise to approx. 90,000 deaths and additional costs to the tune of 4.5–5.7 billion dollars.

According to a report issued in 2004 by the National Audit Office in the United Kingdom, around 9 % of patients in that country contract a nosocomial infection. It is difficult to put a figure on the costs incurred for treatment of nosocomial infections, including the prolonged hospital stay, but the report estimates them to be in excess of 1 billion GBP. That publication also presupposes that around 30 % of nosocomial infections could be avoided through better implementation of the existing body of knowledge and through appropriate infection control practices.

Only in recent years have detailed analyses been published on the additional costs incurred because of nosocomial infections (Exner et al. 2004). Here it was revealed that they are largely determined by

- prolongation of hospital stay,
- increased nursing expenditure,
- additional investments for diagnosis and treatment,
- restriction of bed capacities which, because of isolation requirements to curtail the further spread of nosocomial infections, cannot be utilised.

→ **Intensive care units and wards used for immunosuppressed patients are at increased risk for nosocomial infections.**

In a prospective Dutch study (Kamp-Hopmans 2003), 648 nosocomial infections were observed on a **surgical ward** of a university hospital over a 5-year period in a total of 50 (14 %) out of 3,854 patients. The **→ incidence density was 17.8 infections per 1,000 patient days.** Patients suffering from a nosocomial infection were hospitalised for an average of 19.8 days while, conversely, this was only around 7.7 days for patients without such an infection. Prolongation of hospital stay led to a 664 reduction in patient admissions due to the lack of beds because of isolation requirements.

Studies conducted by Gastmeier et al. (2004) showed that out of approximately every 6.4 million operations, 2 postoperative wound infections could be expected for each 100 patients undergoing surgery. This gave rise to 7–8 additional days in hospital, and in turn to **around 1 million extra hospital days per year**. Moreover, there was a 2–3fold increase in the mortality rate.

According to the NIDEP Study the proportion of different types of infection observed in 14,966 patients was as follows:

- 8 % sepsis
- 15 % wound infection
- 17 % other infections
- 40 % urinary tract infections
- 20 % lower respiratory tract infections.

The most common nosocomial pathogens are endogenous microbes that belong to the patient's resident flora of the skin or mucous membranes or are spread exogenously through contact, water, the air or foodstuffs. The most important nosocomial pathogens include, in addition to *Staphylococcus aureus* and coagulase-negative staphylococci, enterococci. Among the Gram-negative bacteria are *Escherichia coli,* *Pseudomonas aeruginosa, Enterobacter, Proteus, Klebsiella,* and in rising numbers *Serratia marcescens* and *Acinetobacter* spp, as well as the fungus *Candida albicans.* The five most common agents of nosocomial infections on intensive care units are *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella, Enterobacter, E. coli* and *Candida albicans.* The **highest risks** are posed by **invasive systems** such as intravascular catheters.

Comparison of nosocomial infection rates at international level provides interesting insights. In 2004 the National Audit Office published data comparing the estimated prevalence rates of nosocomial infections contracted in hospitals in different European countries.

In a comparison at international level → **Table 2.3,** Germany, with an estimated prevalence rate of 4 %, ranks first before all other European countries. While these findings are based on national surveillance data, they must be further corroborated. Based on the data from the NIDEP Study, if one takes these figures as a basis, costs to the tune of 3.87 billion euros (compared with 1.5 billion in Germany) will have been incurred for a 9 % nosocomial infection rate as given for the United Kingdom.

The markedly lower prevalence of nosocomial infections in Germany compared with other European countries has also been recently confirmed by the HELICS *(Hospital in Europe Link for Infection Control through Surveillance)* Study (2005).

The comparatively positive performance in respect of nosocomial infections is possibly attributable to the following factors:

– Since 1976 Germany has national regulations that are being continually updated and provide information to the public health service as well as to all hospital-based healthcare workers on consensual hygiene measures. These have been given a legal mandate with the coming into force of the **Protection against Infection Act** in 2001. Other European countries, with few exceptions, do not have such consensual national guidelines with corresponding high levels of acceptance. For example, the United Kingdom only has recommendations by specialist societies which, however, do not have the same level of acceptance as the German regulations governing nosocomial infections.
– The German **hygiene regulations have been conceived in a comprehensive and holistic manner.** They include operational / organisational and structural / functional criteria and give detailed information on cleaning, disinfection and sterilisation.
– Moreover, over the past decade the **National Reference Centre for Hospital Hygiene (Referenzzentrum für Krankenhaushygiene)** has developed, by international standards too, an excellent **surveillance system**. This publishes clear strategies for management of nosocomial infections.
– There is specially trained **infection control personnel** such as hospital epidemiologists, infection control physicians and infection control nurses who are assigned clearly designated tasks; this has major implications for infection control management and offers important support to the hospital-based doctors.

Country	Prevalence Rate of NI
Denmark	8 %
England	9 %
France	6–10 %
Germany	4 %
The Netherlands	7 %
Norway	7 %
Spain	8 %
Australia	6 %
USA	5–10 %

→ **Table 2.3:**
Estimated prevalence of nosocomial infections (NIs) in different European countries, Australia and the USA.
Source: UK National Audit Office 2004.

	USA	United Kingdom	Germany	Netherlands
Total population	290 million	60 million	82 million	16 million
Over 65 years of age	35.6 million	9 million	13 million	2 million
Living with cancer: significant proportion in the community, and undergoing chemotherapy	2 million	1 million	–	160,000
Under 1 year of age	35.6 million	600,000	800,000	100,000
Discharged from hospital within previous 2 weeks	1.25 million	200,000	–	60,000
Hospital outpatients at home	–	–	1,270,000	–
AIDS cases*	40,000	15,000	–	91
People in home care	0.5 million	–	–	–
Total number of persons at higher risk for infection	>1 in 7	>1 in 6	>1 in 5,6	>1 in 6,3

*This does not include those who are HIV positive, who may also have lowered resistance to infections.

→
Table 2.4:
Proportion of persons <1 year, persons >65 years and immunosuppressed persons in the entire population in different European countries.
Source: IFH 2007.

– In the meantime, in some cases such guidelines are already incorporated into the **curriculum** for **medical students**. They can also be easily accessed by anyone on the internet.
– The guideline has a clear **preventive orientation** and, as such, differs from certain European countries, especially the United Kingdom where the main focus is on infection control, i.e. based on detection and control of nosocomial infections that have already occurred.

→
Due to demographic changes and the increasing shift of patient care to the outpatient domain, a greater proportion of patients at risk for infections is to be expected in the hospital setting.

In view of the → **changing demographic landscape** with a growing number of elderly people as well as due to changing care structures with a shift of patient care to the outpatient domain, a **patient group that is at increased risk for infection** is being treated in the hospital.

There is thus considerable scope for action to prevent and control nosocomial infections. Of particular concern is the rise in antibiotic resistant microorganisms, which will be addressed below (see ECDC 2007, *Chapter 2.1.2.*).

Demographic changes are also associated with an increase in the number of persons at risk for infection; their proportion in the total population in the various European countries is given in → **Table 2.4.**

Early discharge of patients from hospital means that **infection risks are being shifted to other areas,** such as the home (outpatient care) and homes for the elderly.

Prospective studies by Engelhart et al. (2005) on the incidence of infections in German homes for the elderly revealed the incidence of nosocomial infections in such establishments was thought to be on a par with that of hospitals. For that reason the high standards upheld in hospitals must be applied in such homes too. The RKI Commission for Hospital Hygiene and Infection Prevention tried to address this issue by publishing in 2006 a **Recommendation for Prevention of Infection in Homes for the Elderly.**

2.1.2 Epidemiological implications of infectious diseases worldwide

2.1.2.1 General epidemiological overview

Despite the fact that the annual number of deaths and the loss of healthy years of life attributable to infectious diseases have markedly declined further over the past 10 years, the epidemiological significance of infectious diseases worldwide is considerable. In the USA infectious diseases continue to rank third as the cause of death each year and in global terms they rank second.

For → **Europe** the ECDC report is now available (2007). According to this, the infections with **an overall rising trend** in Europe include infections caused by HIV, chlamydia, hepatitis C, avian influenza, legionellae, campylobacter, verotoxin-producing *Escherichia coli* and *Listeria*.

→
Trends in infectious diseases in Europe (examples):
Declining trend:
– Hepatitis B, tuberculosis, invasive meningitis infections, diphtheria, typhoid fever, plague, measles, mumps, rubella, salmonellosis, cholera
Unchanging trend:
– Gonorrhoea, syphilis, influenza, invasive pneumococcal infections
Increasing trend:
– Campylobacter infections, new HIV infections, chlamydia infections, legionelloses, hepatitis C

The **declining diseases include**: hepatitis B, tuberculosis, invasive meningitis infections, invasive infections due to *Haemophilus influenzae* type B, pertussis, diphtheria, tetanus, measles, mumps, rubella, poliomyelitis, salmonellosis, typhoid/paratyphoid fever, shigellosis, brucellosis, cholera, hepatitis A, cryptosporidiosis, eschinococcosis, trichinellosis, toxoplasmosis, yellow fever and plague.

The diseases showing an **unchanging trend** include: gonorrhoea, syphilis, influenza, invasive pneumococcal infections, yersiniosis, botulism, giardiasis, tularaemia, Q fever, leptospirosis and anthrax.

On reviewing the trends observed in Europe and other factors such as their implications for the public health service, the following conclusions can be drawn, as pointed out in the ECDC report, as regards the most important risks for communicable diseases in Europe:

– Nosocomial infections with and without antibiotic resistant microorganisms. The → **most important infection risks in Europe** are thought to be posed by microorganisms that have developed **resistance to antibiotics.** Infections caused by such bacteria are of paramount importance, constituting a rapidly growing problem in European hospitals, as well as being seen increasingly outside the hospital. Each year some 3 million people in the European Union contract a nosocomial infection, resulting in some 50,000 deaths.

→
The most important infection risks in Europe are thought to be posed by microorganisms that have developed resistance to antibiotics.

- **HIV infections:** 28,044 new cases of HIV were observed in European countries in 2005. The total number of people living with HIV in Europe is estimated to be around 700,000. Of these, some 30 %, i. e. 200,000 persons are unaware of their HIV status.
- **Pneumococcal infections:** Pneumococci are the most important cause of respiratory tract infections and are associated with a high mortality rate (in particular in young children and elderly persons) if the infection embarks on an invasive course and results in bacteraemia or meningitis. There are now effective vaccines available in Europe against the invasive forms of this disease.
- **Influenza** (pandemic potential as well as yearly epidemics): each winter some 100,000 persons in the EU contract a severe influenza infection. Among these, thousands die unnecessarily in view of the fact that effective vaccines are available for those at highest risk for influenza.

As shown in → **Figure 2.1** (Fauci 2005), around 15 million (more than 25 % of the annually estimated 57 million deaths worldwide) are directly caused by infectious diseases. Millions of other deaths occur because of the secondary effects of infectious diseases.

Infectious diseases lead to compromised health and disease and account for around 30 % of all Disability Adjusted Life Years (DALYs) worldwide (1 Disability Adjusted Life Year is the loss of one healthy year of life). Infectious diseases accounting for almost 1.5 billion total DALYs each year are listed in → **Figure 2.2** (Fauci 2005).

Based on data from the World Health Organisation (Health and Millennium Development Goals), 57 million people died in 2002. Analysis of the causes of death and of the age at which death occurred shows that changes in health patterns are becoming more complex worldwide.

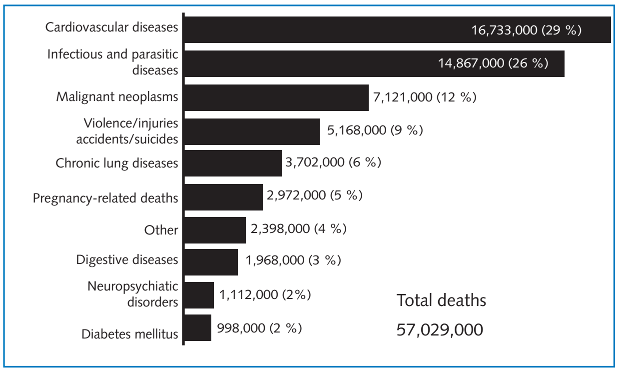


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Figure 2.1:
Break down of causes of death worldwide (2002) according to WHO data.
Source: Fauci et al. 2005.

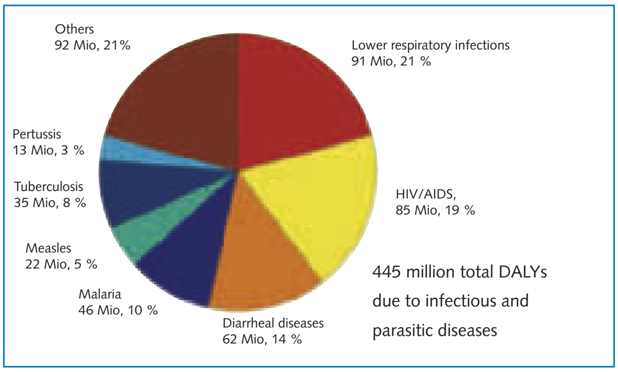

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Figure 2.2:
Leading causes of disability associated life years (DALYs) due to infections (estimates related to 2002) from WHO.
Source: Fauci et al. 2005.

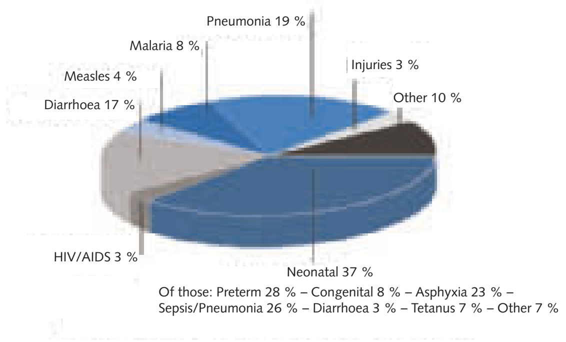

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Figure 2.3:
The most common causes of death worldwide among children below 5 years, calculated from the annual average for the years 2000–2003.
Source: Gordon (WHO) 2004.

HIV, malaria, tuberculosis and other communicable diseases (including maternal mortality) account for 32 % of deaths → **Figure 2.3.** Developing countries have an essentially higher mortality rate across all age groups. Of particular concern is childhood mortality (WHO Atlas of Children's Health and Environment 2004 by Bruce Gordon et al.). The proportion of communicable diseases among adults is conversely declining, despite the fact that HIV/AIDS has been one of the leading causes of death among adults between 15 and 59 years. In summary, the following observations have been made:

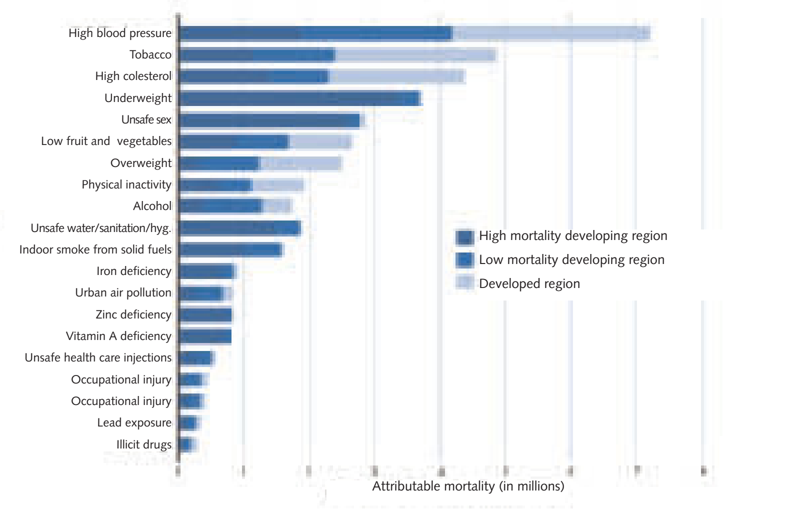
– Approximately → **20 % of all disease-related deaths worldwide involve children under the age of 5 years.**
– 98 % of all childhood deaths (around 10 million per year) occur in **developing countries.**
– Almost 90 % of all childhood deaths are attributable to **6 underlying diseases (→ Figure 2.3):**
  – Perinatal diseases
  – Pneumonia
  – Diarrhoea
  – Malaria
  – Measles
  – HIV/AIDS.

→
20 % of all disease-related deaths worldwide involve children under the age of 5 years. 98 % of these deaths occur in developing countries. The majority of these deaths could be prevented by using existing interventional measures which are readily available and effective.

The majority of these deaths could be prevented by using existing interventional measures which are readily available and effective.

Malnutrition or undernutrition is one of the main risk factors for the widespread susceptibility to infection among children in developing countries. Often, the children are suffering concurrently from several infectious diseases. Based on data from the World Health Organisation, the high infection rates are attributable, in particular, to the lack of access to safe drinking water, poor general environmental conditions, lack of a sanitary infrastructure, pollution of indoor room air, the existence of vectors for communicable diseases as well as increased risks of accidents and injuries → **Figure 2.4** and Chapter 2.3ff.

→
Figure 2.4:
Total mortality (figures in millions) and the 20 leading risk factors in 2000.
Source: WHO 2002.



Poverty and infectious diseases
The global distribution of infectious diseases concords with the distribution of poverty worldwide. Around 30 % of the population of the countries of the underdeveloped regions are compelled to live on an income of less than 1 US dollar per day. The relationships between infectious diseases, poverty and undernutrition are multifactorial. This means that specific challenges must be surmounted for effective control of communicable diseases in developing countries. These countries shoulder concurrently the burden of both communicable and non-communicable diseases. This presents a dual challenge to the already stretched healthcare systems. In such countries there is a high risk of resurgence of infectious diseases that have already been brought under control. This derives from the complex natural behavioural patterns of microorganisms, which are constantly evolving and adapting. Microorganisms avail of every opportunity to proliferate, mutate, adapt and acquire resistance to the commonly used drugs and insecticides. The increase in microbial resistance presents a further challenge for these countries.

→
The additional burden caused by the increase in microbial resistance means that, in particular, the poorer countries are becoming epicentres for antibiotic resistance.

They become → **epicentres for antibiotic resistance,** as borne out e. g. by the resistance to malaria drugs in regions in which more than 30 % of the population are at higher risk for infectious diseases.

→
Apart from infections of the lower respiratory tract and diarrhoea, HIV/AIDS, malaria and tuberculosis have the greatest epidemiological significance worldwide.

Apart from → **lower respiratory tract infections and diarrhoea** analysis of the manifold data has revealed that, in particular, the following three specific infectious diseases are of the greatest epidemiological significance in terms of single cause:

– HIV/AIDS
– Malaria
– Tuberculosis.

Therefore the clinical manifestations associated with these three diseases will now be discussed in detail. In terms of their implications for DALYs, measles and pertussis must also be mentioned.

2.1.2.2 HIV/AIDS

HIV/AIDS accounts for more than 20 million deaths each year worldwide and, with a proportion of 14 %, is the leading cause of death among persons between 15–59 years. Approximately 40 million persons are estimated to be infected with HIV worldwide. The following data have been obtained from the guide “Infectious Diseases – Instructions for Physicians”, HIV/Aids (RKI 2006).

The global figures as well as the estimated figures in Africa, Eastern Europe and Germany are compared in → **Table 2.5.** In 2004 alone, some 5 million persons contracted a new HIV infection.

Worldwide, around half of adults living with HIV or AIDS are women. **More than 95 % of all HIV-infected persons are living in developing countries.** By the end of 2005, 27 million people had already died from the sequelae of HIV infection. This figure was three million for 2005 alone.

The → **high prevalence regions,** in which more than 1 % of the adult population is currently infected, include all countries in sub-Saharan Africa, large parts of the Caribbean and a number of countries in Southeast Asia; prevalence rates of up to 40 % are seen in the adult population in those regions of southern Africa most affected.

→
The high prevalence regions for HIV/AIDS are the countries in sub-Saharan Africa, large parts of the Caribbean and a number of countries in Southeast Asia.

In Germany around 26,000 persons have died of HIV infection since the beginning of the epidemic in the late 1970s up to the end of 2005. Based on estimates from the Robert Koch Institute, the number of people presently living with HIV in Germany is around 49,000, which reflects a low prevalence compared with other European countries. Germany is one of those countries in which hitherto HIV infections remain essentially confined to population groups at particularly high risk for infection. These groups comprise **men who have sex with men (MSMs)** (approx. 55 % of infections currently diagnosed), **persons originating from countries with a high prevalence of HIV** in the general population (approx. 20 %) and intravenous drug users (8 %). Around 15 % of HIV infections diagnosed in Germany are currently contracted through heterosexual contact, mainly from a partner belonging to one of the three main groups mentioned above. Reflecting an unchang-

	World-wide*	Sub-Saharan Africa*	Eastern Europe*	Germany+
Persons infected	40 Mio	26 Mio	1.6 Mio	49,000
New annual infections	5 Mio	3.2 Mio	270,000	2,000
– of which in children < 15 years	700,000	600,000	2,000	15
Annual deaths	3 Mio	2.4 Mio	62,000	750
AIDS orphans	15 Mio	12.1 Mio	–	–

→
Table 2.5:
Number of HIV infected persons and AIDS deaths by way of global comparison.
Source: RKI 2006.

* Estimates by WHO as at end of 2005
+ Estimates by Robert Koch Institute as at end of 2005

ing trend, HIV infections are predominantly confined to a few large cities. Around 40 % of HIV infections are diagnosed in the large cities such as Berlin, Frankfurt am Main, Munich, Cologne, Düsseldorf and Hamburg.

The most important **opportunistic infections** associated with HIV/AIDS are:

- *Pneumocystis jirovecii* infection
- Toxoplasmosis
- Candidiasis
- Atypical mycobacteriosis
- Infections by cytomegalovirus
- Infections by herpes simplex viruses and varicella-zoster virus
- Cryptococcosis
- Aspergillosis
- Cryptosporidiosis
- Microsporidiosis.

The earlier risk of HIV infection through **blood transfusion** is in the meantime <1 in three million transfusions, and as such negligible.

2.1.2.3 Malaria

Malaria is caused by a **protozoan** of the genus *Plasmodium* (Class Haematozoea, Order Haemosporida, Family Plasmodiidae). There are different *Plasmodium* species that are human pathogens: *Plasmodium (P.) falciparum* (causative agent of tropical malaria), *Plasmodium ovale* and *Plasmodium vivax* (causative agents of tertian malaria) and *Plasmodium malariae* (causative agent of quartan malaria). The morphology of the parasites is characteristic of each species and each developmental stage.

Plasmodia are intracellular parasites, with their life cycle unfolding in two parts: one cycle in the human host and another in the mosquito vector. It is important to be conversant with the details of this parasite's life cycle so as to understand the pathogenesis, clinical manifestations as well as diagnostic and treatment modalities.

Non-sexual reproduction takes place in the human host. The sporozoites of the *Anopheles* mosquito vector, which are injected (into the host) in the course of the "blood meal" rapidly exit the bloodstream to enter the liver parenchymal cells. There they grow, by division, into a tissue schizont that fills the entire hepatocyte (pre-erythrocytic phase). The duration of this cycle varies depending on the Plasmodium species; it lasts between 5 and 7 days in *P. falciparum* and 6 to 18 days in the other species. The number of merozoites produced by each tissue schizont, again, varies in accordance with the *Plasmodium* species. *P. falciparum* produces the greatest number of merozoites. In *P. vivax* and *P. ovale* only some of the schizonts develop into mature forms with merozoites, which are then periodically released into the blood. Another proportion of the schizonts persists in a unicellular form for months or years in a kind of dormant phase. Due to an hitherto unidentified stimulus (stress, infections) these hypnozoites mature into merozoite-producing schizonts, giving rise to the relapses characteristic of tertian malaria. Once schizogony is complete, the liver parenchymal cell ruptures, releasing the merozoites into the bloodstream where they attach themselves to the (outer) membrane of the erythrocytes, going on to develop into a 'ring stage' and then to mature erythrocytic schizonts inside a vacuole (erythrocytic phase). Merozoites are released once again when the erythrocytes rupture, and they go on to invade other erythrocytes. In the course of time some merozoites differentiate within the erythrocytes into the sexual forms (gamogony), giving rise to macro-and microgametocytes.

Once they are taken up by (competent) mosquitoes, the macro- and microgametes engage in sexual reproduction, leading to the formation of an oocyst within which sporozoites are formed (sporogony), which via saliva are able to infect a new (human) host.

Malaria is **typically a tropical** disease and is one of the most important infectious diseases worldwide. It is found in tropical and subtropical regions on all continents – apart from Australia – and is endemic in some 100 countries. Around **→ 40 % of the world population live in areas endemic for malaria.** Here it is estimated that between 300 and 500 million people contract malaria each year. **Worldwide between 1.5 and 2.7 million people die from malaria,** around the half of whom are children younger than five years. Malaria is found predominantly in the countries of Africa, Asia and South America, with **Africa with around 90 % of cases** being most affected.

→
Around 40 % of the world population live in areas endemic for malaria. It is estimated that between 300 and 500 million people contract malaria each year. Worldwide between 1.5 and 2.7 million people die from malaria.

Rare cases of infection, some of which are important in practical terms, occurring outside an endemic area are known as "airport malaria" and are caused by infectious mosquitoes imported in an airplane; these are seen in or around airports. There is also "baggage malaria" where the infective mosquitoes are imported in the baggage of airplane passengers.

In Germany 707 cases of malaria infections were reported in 2004 pursuant to mandatory notification stipulated by the Protection against Infection Act. This was lower than in the previous years. In 2003, 820 cases were reported, 859 cases in 2002 and 1,045 in 2001. In 2004 the country in which infection was contracted was specified for 576 cases (81.5 %). The majority (87 %) of malaria infections, as in the previous years, **→ were imported from African countries.** A particularly high number of cases occurred in travellers to West African countries and Kenya. Papua New Guinea and India, accounting for 11 and 8 cases, respectively, were the most important countries for infection outside Africa. **No case of malaria was contracted in Europe.**

→
The majority of malaria infections imported to Germany are from African countries. No cases of malaria have been contracted in Europe.

In 666 of the cases reported in 2004 (94 %), data were available on the *Plasmodium* species implicated. Analysis of these revealed that *P. falciparum,* accounting for 77 % of cases, was the most commonly diagnosed species. This finding is consistent with the observation that the majority of cases were contracted in Africa. *P. vivax,* accounting for 12 %, of cases, ranked second, followed by *P. ovale* (3 %) and *P. malariae* (2 %). Tertian malaria (*P. vivax* or *P. ovale*), not further differentiated, accounted for 2 % of infections. Mixed infections were implicated in 4 % of cases.

Humans are the only host for those *Plasmodium* species that are human pathogens. But there are many other *Plasmodium* species that cannot be transmitted to humans under natural conditions.

In general, plasmodia are transmitted via the bite of a blood-feeding female mosquito of the genus *Anopheles*, which injects sporozoites into the human bloodstream in saliva. Possible, but rare transmission pathways – mainly of theoretical interest as far as a country like Germany is concerned – include the transmission of plasmodia via blood transfusions, shared use of inadequately sterilised syringes and cannulas (intravenous drug users), needlestick injuries or reuse of infusion systems as well as diaplacental transmission from mother to foetus.

Malaria begins with atypical complaints such as fever, headache or joint pains as well as a general feeling of malaise. Often such signs are thus misinterpreted as flu or a gastrointestinal infection. The clinical picture of malaria is determined by the processes unfolding during schizogony.

The intensity of the clinical manifestations of *Plasmodium* infection will depend on the level of immunity of the patient. Repeated infection in an endemic area gives rise to temporally limited semi-immunity, which prevents severe disease. Non-immune persons are thus at greatest risk, in particular young children and the elderly.

Persisting hypnozoites can lead to relapses. Misdiagnoses are common because of the long latency period between a visit to the tropics and the subsequent onset of malaria.

Tropical malaria: this is the most dangerous form of malaria and is associated with a 20 % mortality in non-immune persons if untreated. The clinical picture is very varied. Often the first sign is a feeling of malaise, headache, joint pains as well as irregular high temperatures. The fever type is not a diagnostic criterion of tropical malaria since only rarely is periodic intermittent fever seen. Thrombocytopaenia is seen in around 60 % of patients. Other manifestations may include splenomegaly (in around 26 % of cases), hepatomegaly (around 14 % of cases) or diarrhoea. Any central nervous signs, e. g. convulsions and clouding of consciousness, resulting even in coma, are indicative of cerebral malaria. Other complications are acute kidney failure, pulmonary involvement, circulatory collapse, haemolytic anaemia and disseminated intravasal coagulopathies.

Tertian malaria: this is caused by *P. vivax* or *P. ovale* and begins with sudden fever and atypical complaints. Within a few days regular feverish attacks are often seen, going on to appear every 48 hours. Typically, shaking chills occur in the late afternoon, during which the body temperature rises quickly to around 40°C. After a feverish period lasting 3 to 4 hours the temperature falls abruptly to normal values with profuse sweating. Tertian malaria only rarely results in death.

Quartan malaria: this is caused by *P. malariae* and is less common than the other forms of malaria. The clinical picture is determined by regular 72-hour patterns of fever. There are no hypnozoites involved but recrudescences can generally occur up to 40 years after the initial infection.

Treatment depends in principle on the Plasmodium species involved, on the resistance level, any chemoprophylaxis already administered and on the clinical symptoms (uncomplicated or complicated course of tropical malaria).

→ **Malaria control measures** are aimed at reduction of the parasite reservoir in the population (selective treatment), are targeted against the vector (elimination of breeding sites, use of larvicides, insecticides) and aimed at reducing contact with the vector (constructional measures, mosquito nets, repellents). Effective **surveillance** is a prerequisite here.

→
Malaria control measures are aimed at reduction of the parasite reservoir in the population, are targeted against the vectors and aimed at reducing contact with the vector. Effective surveillance is a prerequisite.

Current preventive measures against malaria
The overall aim must be to ensure that visitors to tropical and subtropical countries are made thoroughly aware of the general and specific risks they face as well as of requisite hygiene practices and prophylactic measures.

To date → **there is no vaccination available** against malaria. Hence the possible ways to prevent infection entails **exposure prophylaxis** and **chemoprophylaxis:**

→
To date, there is no vaccination available against malaria. Due to a lack of resources effective means of exposure prophylaxis and chemoprophylaxis are not being sufficiently exploited.

Exposure prophylaxis: the *Anopheles* mosquitoes are active during the night (from twilight). Exposure prophylaxis can markedly reduce the risk of contracting malaria. The following measures could be considered:

– remain within mosquito-proof rooms (air conditioning, insect window grids),
– sleep under a mosquito net, which is preferably impregnated with an insecticide,
– wear appropriate clothing (long-sleeved blouses and shirts, long trousers, socks),
– use a repellent.

Malaria can occur in clusters in endemic regions. Worldwide surveillance by WHO means that such areas are well-known and hence preventive measures in the form of exposure prophylaxis and chemoprophylaxis can be taken. **If such measures are observed the risk when travelling to endemic areas is low and can be calculated.**

The prevention and control measures are currently inadequate in many countries due to limited resources. To assist those countries that have special problems, WHO has devised the **Roll Back Malaria Programme.** The aim is to use effectively, and with international help, a number of tried and tested antimalarial measures (e. g. mosquito nets, insecticides, antimalarial drugs).

2.1.2.4 Tuberculosis

Each year **8–9 million persons contract a new tuberculosis (TB) infection,** with almost 4 million of whom becoming infected with the highly infectious, microscopy-positive type. Around two million people die each year from the sequelae of disease. Despite the fact that tuberculosis can be cured, more people die from it than from any other treatable infectious disease. Hence tuberculosis is rightly the focus of **world politics,** as was borne out at the G8 Summit in 2006 which addressed this infectious disease in a political context.

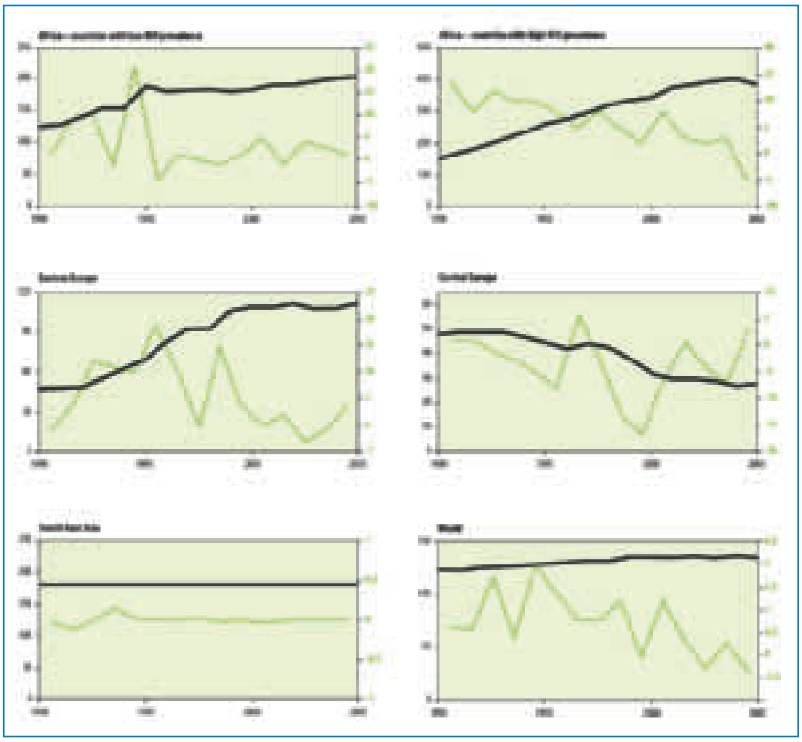
In 2005, 6,057 cases of tuberculosis were reported to the Robert Koch Institute for Germany, compared with 6,549 cases in 2004. To mark World Tuberculosis Day in 2005 and in commemoration of the award of the Nobel Prize to Robert Koch for discovery of the causative agent of tuberculosis, the Robert Koch-Institute published a detailed overview of the tuberculosis situation in Germany and worldwide; attention is drawn to that publication (RKI 2005). Important data needed to assess the epidemiological situation and the successes and failures are cited from that publication:

- A declining trend has been observed in the tuberculosis incidence in Germany for many years. In 2003 this figure was 8.7 per 100,000 inhabitants, representing, nonetheless, a number of 7,184 new cases of disease.
- For 2005 a total of 6,057 cases of tuberculosis were reported to the RKI, corresponding to an incidence of 7.3 cases per 100,000 inhabitants. Compared with the previous year's figure of 7.9 (6,549 reported cases), this represented a 7.6 % decline in the incidence. As such, this **declining trend seen in recent years continued** in 2005 too.
- The number of tuberculosis–related deaths reported to the RKI was 164. This corresponds to an average mortality rate of 0.2 per 100,000 inhabitants.
- Species differentiation within the *Mycobacterium* tuberculosis complex was conducted for 57 % of cases of disease. Accounting for 98 % of cases, *Mycobacterium tuberculosis* was the prime species implicated, whereas other species played only a minor role.
- In 2005, 91 clusters with a total of 220 cases of disease were reported to the RKI. Bigger clusters, involving five or more cases in each cluster, were reported on four occasions.
- For 2004, data on the treatment results were provided in 85 % of cases. The proportion of successfully treated cases, i. e. with cure or completion of treatment over the entire period was 77 %.

→
The WHO goal aimed at 85 % treatment success rate has not been achieved in Germany.

The → **WHO goal** aimed at 85 % treatment success has not been achieved in Germany.

More data were analysed for 2003, showing that 44 % of persons infected with tuberculosis as reported to the RKI were born outside Germany. The latter came mainly from Eastern European countries. Accounting for a proportion of **2.1 % of multiresistant tuberculosis diseases,** this figure for resistant bacteria remained



→ Figure 2.5: Trends in the estimated TB incidence (per 100,000/year, all types, black lines) and the estimated annual incidence (green line) for certain subregions and the world. Source: WHO Report 2007, Global TB Control.

mainly constant in 2003. But a continually rising trend was discerned among mycobacteria that were resistant to at least one of the five drugs of choice. This also increases the potential risk of emergence of secondary resistance during treatment. For Germany the proportion of multiresistant isolates has risen sharply among patients from countries of the former Soviet Union.

The Robert Koch Institute believes that over the coming years there will not be any significant reduction in the number of TB cases in the current problem regions of Eastern Europe. On the contrary it is assumed that due to the already high rates of resistant strains and rising HIV figures the situation is likely to deteriorate. To what extent the enlargement of the EU towards the east and **increasing touristic and economic ramifications** will pose a greater threat of TB in Germany remains to be seen.

For that reason continual epidemiological analysis and intensive research in the various fields of tuberculosis, in particular for development of new tuberculostatics, are deemed necessary.

The → **worldwide growing trend** in tuberculosis is reflected in the **rise in the incidence** of tuberculosis to around 1.1 % each year. In **Western and Central Europe as well as in the Middle East, a decline** in the incidence has been observed in recent years but, conversely, this has sharply increased in **Eastern Europe and Africa.** Furthermore, in Africa the increased rate varies from one country to the next depending on whether there is a high or low HIV prevalence. In the West Pacific Region and in Southeast Asia the incidence is relatively stable → **Figure 2.5.**

→ **Whereas the incidence of tuberculosis has continually declined in Western and Central Europe, it has sharply increased in Eastern Europe and Africa.**

Whereas treatment has proved successful in an average of 82 % of cases worldwide, the success rate in Africa (71 %) and in Eastern Europe (70 %) was markedly lower. This is due to HIV, multidrug-resistant (MDR) TB and to inadequate control mechanisms.

→

Risk factors for the spread of tuberculosis include:
– poverty, undernutrition, war, expulsion and flight
– co-infection with HIV
– increased occurrence of resistance and multiresistant strains
– poor infrastructure and inadequately qualified personnel in high-risk regions.

→ **Factors underpinning the spread of TB** include:

- **Poverty, undernutrition, war, expulsion and flight** as well as a collapse of existing social systems and hence of associated tuberculosis control programmes (e. g. in countries of the former Soviet Union)
- High **co-infection rates of TB with HIV**, since HIV infection reinforces the risk of reactivation of latent TB as well as of rapid progression of new infection to active disease. In Africa alone 30 % of all TB cases are attributable to co-infection with HIV.
- Increased occurrence of **resistant or multiresistant strains** (MDR, resistance to at least isoniazid and rifampicin).

Positive developments in the fight against, and control of, tuberculosis include:

- The sharp increase in the spread of DOTS (directly observed treatment, short-course) programmes, in particular in countries with a high TB incidence.
- Improved funding of DOTS programmes.

Negative aspects in the fight against, and control of, tuberculosis include:

- The fact that many sections of the population, in particular in the high risk countries, do not have access to TB services
- Inadequately qualified personnel, poor documentation and evaluation standards
- Poor infrastructure, underdeveloped laboratory services as well as inefficient decentralisation
- Unfavourable trends in the HIV pandemic
- Endangerment of TB control mechanisms worldwide due to rising drug resistance.

The following aspects are of relevance in the fight against, and control of, tuberculosis:

- Eliminating the weak links already identified in the DOTS programmes in high risk countries
- Education and training of staff and complete implementation of DOTS strategies
- Enhancement and motivation of political commitment and technical support
- Promotion of theoretical and practical competences in laboratories at national level in order to bridge significant lacunae in the information available on drug resistance and thus surmount the unfavourable consequences of co-infection with HIV
- Increase the proportion of HIV-infected persons who are treated with antiretrovirals
- Funding of programmes

Various successful programmes carried out, e. g. in Peru, demonstrate that **containment of the tuberculosis epidemic is possible in principle.**

2.2 Infections and chronic diseases

Link between infections and chronic disease or malignant tumours

Over the past ten years great strides have been made in identifying the infectious agents and their role in chronic diseases and malignant diseases (O'Connor et al. 2006, American Academy of Microbiology 2006). This is mainly thanks to the innovative diagnostic and epidemiological methods used in microbiology.

It has in the meantime been accepted that **non-communicable chronic diseases can be triggered by microorganisms.** At least 13 of the 39 microbial agents recently described can trigger chronic syndromes.

Elucidation of the reciprocal relationship between microorganisms and chronic diseases can have an impact on large sections of the population and open up new prospects for reducing the burden of chronic diseases through prevention or treatment of infections. The more widespread is the scientific acceptance of such a mutual relationship, the more rapidly will the progress seen in laboratory technology and epidemiology drive the discovery of non-culturable, new or only now identified aetiological agents of chronic diseases. A spectrum of various pathogens and chronic syndromes has been identified with a number of transmission pathways ranging from exposure to onset of chronic disease.

In → **Table 2.6** are listed the microorgansims that **can trigger more than one chronic disease.** On the other hand, **different pathogens can also trigger the same chronic disease.** One such example is HBV or HCV, both of which can trigger, in terms of histopathology a similar form of, chronic hepatitis.

Important examples attesting to this link between viruses and cancer is borne out by hepatitis viruses and papillomaviruses:

- Of the two billion people estimated by WHO to be infected with HBV, 350 million suffer from chronic infection. A further 170 million have chronic HCV infection, and between 500,000 and 750,000 people die each year from hepatocellular carcinoma. The disease is particularly common in sub-Saharan Africa and in Southeast Asia. Men are more often affected. Only 5 % of patients in whom hepatocellular carcinoma is diagnosed survive the next five years.
- Of considerable epidemiological significance is also the association between human papillomaviruses and → **cancer of the cervix** in women. In Germany around 6,500 women develop cervical cancer each year. Based on data from the Robert Koch Institute, 1,660 women died in Germany in 2007 from this disease. Cervical cancer is caused by certain genotypes of human papillomaviruses (Standing Committee on Vaccination – STIKO 2007). Different studies have identified HPV DNA in more than 90 % of malignant cervical cancer tumours. Epidemiological and molecular biology investigations corroborate the causal role of these viruses in the development of cervical cancer in women. The numerous genotypes of the human papillomavirus differ in terms of human pathogenicity. The prevalence of HPV infections with detection of (HPV) DNA in swab specimens is estimated to be 8–15 % for Europe.

→

Cervical cancer is the 2nd most common type of cancer in women and the 5th most common of all cancer types. At least 95 % of invasive cancers of the cervix are associated with human papillomavirus.

Aetiological Agent	Chronic Disease
Borrelia burgdorferi	Lyme disease
Chlamydia trachomatis	Reiter's syndrome and reactive arthritis Sterility in women
Cytomegalovirus	Post-transplantation arteroslerosis
Echerichia coli O 157:H7	Haemolytic uraemic syndrome
Epstein-Barr virus (EBV)	Burkitt's lymphoma Nasopharyngeal carcinoma Hodgkin's disease Post-transplantation lymphoproliferative diseases B cell lymphoma in AIDS patients
Hepatitis B virus (HBV) Hepatitis C virus HBV and deltavirus	Hepatocellular carcinoma Chronic hepatitis
HBV	Polyarthritis nodosa
HCV	Cryoglobulinaemia
Helicobacter pylori	Gastric lymphoma MALT lymphoma, Peptic ulcers
Kaposi's herpesvirus sarcoma-associated	Lymphoma, Kaposi's sarcoma
Histoplasma	Chronic pericarditis
Human T cell lymphotrophic virus (type 1)	Adult T cell leukaemia, tropical spastic paraparesis
Human papillomavirus (HPV)	Cancer of the cervix, laryngeal papilloma, Cancer of the penis and of the anus Intraepithelial neoplasms of the vulva and vagina Warts Head and neck cancer
Measles virus	Subacute sclerosing panencephalitis (SSPE)
Mycobacterium leprae	Leprosy
Mycobacterium tuberculosis	Tuberculosis
Parvovirus B 19	Anaemia, arthritis
Prions	Jakob-Creutzfeldt disease, kuru, Fatal familial insomnia
Rubella virus	Post-rubella arthritis syndrome, congenital rubella syndrome
Group A streptococci	Poststreptococcal glomerulonephritis
Syphilis bacterium (Treponema pallidum)	Tertiary and neurosyphilis

→
Table 2.6:
Aetiological agents and chronic diseases associated with them.
Source: American Academy of Microbiology 2005.

The prevalence is highest among young women and declines in line with advancing age. 74 % of infections are seen in women between the ages 15–24 years. Estimates for the USA suggest an 80 % lifetime prevalence amongst 50-year-old women.

To reduce the burden of cervical cancer disease, STIKO recommends the introduction of a general vaccination against human papillomavirus (types HPV 16, 18) for all girls aged 12–17 years.

In → **Table 2.7** are listed the chronic diseases for which an aetiological agent has been identified.

Further research calls for the use of innovative epidemiological and diagnostic techniques such as PCR, in situ PCR, PCR detection and characterisation of conserved sequences, microbiological culture techniques, microarray assays, such as Virochip, serological tests, marked viruses, immunohistochemistry, histology and animal transmission studies (American Academy of Microbiology 2006).

Research into these relationships also calls for **multidisciplinary cooperation** between clinicians, microbiologists, and bioinformatics specialists, infection control experts, imaging specialists, geneticists, epidemiologists, statisticians, immunologists and pathologists. Such cooperation will in future ensure that much progress can be made in this field. New treatment modalities and prevention strategies as well as public health programmes can be developed to reduce or prevent to a large extent chronic diseases, worldwide.

If only 5 % of chronic diseases are triggered by infectious agents, this would mean that in the USA alone 4.5 million out of 90 million living with chronic diseases could benefit from such strategies. The implications of such efforts worldwide would be far greater. This → **prevention potential** could be realised by avoidance of exposure, prevention of transmission, use of immunoprophylactic strategies and early treatment, leading to a dramatic reduction in the worldwide burden of chronic diseases, as measured by the Disability Adjusted Life Years (DALYs). Such strategies have to be based on well-corroborated evidence. Through the combination of proteomics, genomics, microarray, nanotechnology and mass spectometry with tradi-

→
Interdisciplinary research into the aetiological agents of chronic diseases can drive novel treatment and prevention strategies. Millions of people could benefit from the potential residing in such efforts.

Diseases	Suspected Agent(s), If Any
ALS	Prions, HTLV-1; Ebola virus
Alzheimer's disease	*Chlamydia pneumoniae*
Atherosclerosis	*C. pneumoniae,* cytomegalovirus
Crohn's disease	*Mycobacterium paratuberculosis* and others*
Diabetes	Enteroviruses
Mesothelioma	Simian virus 40
Multiple sclerosis	Epstein-Barr virus
Primary biliary cirrhosis	*Helicobacter pylori,* retrovirus
Prostate cancer	BK virus
Sjogren's disease	*H. pylori*
Sarcoidosis	*Mycobacterium spp.*
Schizophrenia	Intrauterine exposure to influenza

** Clostridium, Campylobacter jejuni, Campylobacter faecalis, Listeria monocytogenes, Brucella abortus, Yersinia pseudotuberculosis, Yersinia enterocolitica, Klebsiella spp., Chlamydia spp., Eubacterium spp., Peptostreptococcus spp., Bacteroides fragilis, Enterococcus faecalis, and Escherichia coli*

→
Table 2.7: Chronic diseases and associated aetiological agents. Source: American Academy of Microbiology 2006.

tional techniques such as histopathology, these hypotheses regarding the causal role could be confirmed or discounted. However, such endeavours would have to be backed up by well-substantiated epidemiological studies in the corresponding populations.

At present, cancer diseases, autoimmune diseases, immunomodulatory and neurological diseases are prime candidates attesting to microbial provenance. But, in principle, other chronic diseases have to be taken into consideration too.

Altogether, the infectious determinants of chronic diseases open up potential sources of research and prevention that must not be allowed to remain unexploited. Of course, not all chronic diseases are attributable to infectious causes. Nonetheless, the prevention potential inherent in such efforts can have enormous implications for clinical and preventive medicine.

Selected sources and transmission pathways of pathogens 2.3

2.3.1 Water for human consumption
2.3.2 Foodstuffs

2.3 Selected sources and transmission pathways of pathogens

2.3.1 Water for human consumption

Epidemiology

Water has always played a pivotal role in the transmission of pathogens. Water is indispensable for life. Water of a safe hygienic quality is one of the most fundamental needs for life. In the event of contamination of the water supply systems serving large regions, up to 1 million people can be confronted or infected from the same source. Consequently, in its **"Guidelines for Drinking Water Quality"** (2006) the World Health Organisation deems water essential for sustaining life, and adequate safe water must be available for everyone. The potential health implications of microbial contamination are so serious that controlling them is of paramount importance and efforts in that direction must never be curtailed.

Despite these insights, the situation as regards an assured water supply is a catastrophe in many parts of the world. More than one billion people have no access to safe drinking water. Based on WHO data, 2.4 billion people live under unsafe general sanitary conditions **→ Figures 2.6 and 2.7.**

In 1883/1884 Robert Koch was able to identify *Vibrio cholerae* in the water tank of the water supply system in Calcutta, linking it to cholera outbreaks. Since then, it has been possible to make great strides in the purification and disinfection of drinking water. Hence for a long time the developed countries had felt assured that the risks presented by waterborne microorganisms had in the meantime been brought under control.

This belief was, to begin with, undermined in 1976 with the first outbreak of **Legionella**, and was fundamentally challenged in 1993 by the USA's greatest waterborne epidemic caused by **Cryptosporidium**. During the Milwaukee epidemic triggered in 1993 by cryptosporidia, over 400,000 people contracted cryptosporidiosis, a cholera-like infection, leading to hospitalisation of more than 4,000 persons and to the death of over 100 people, primarily immunosuppressed persons, such as persons infected with HIV.

Microbial agents and reservoirs

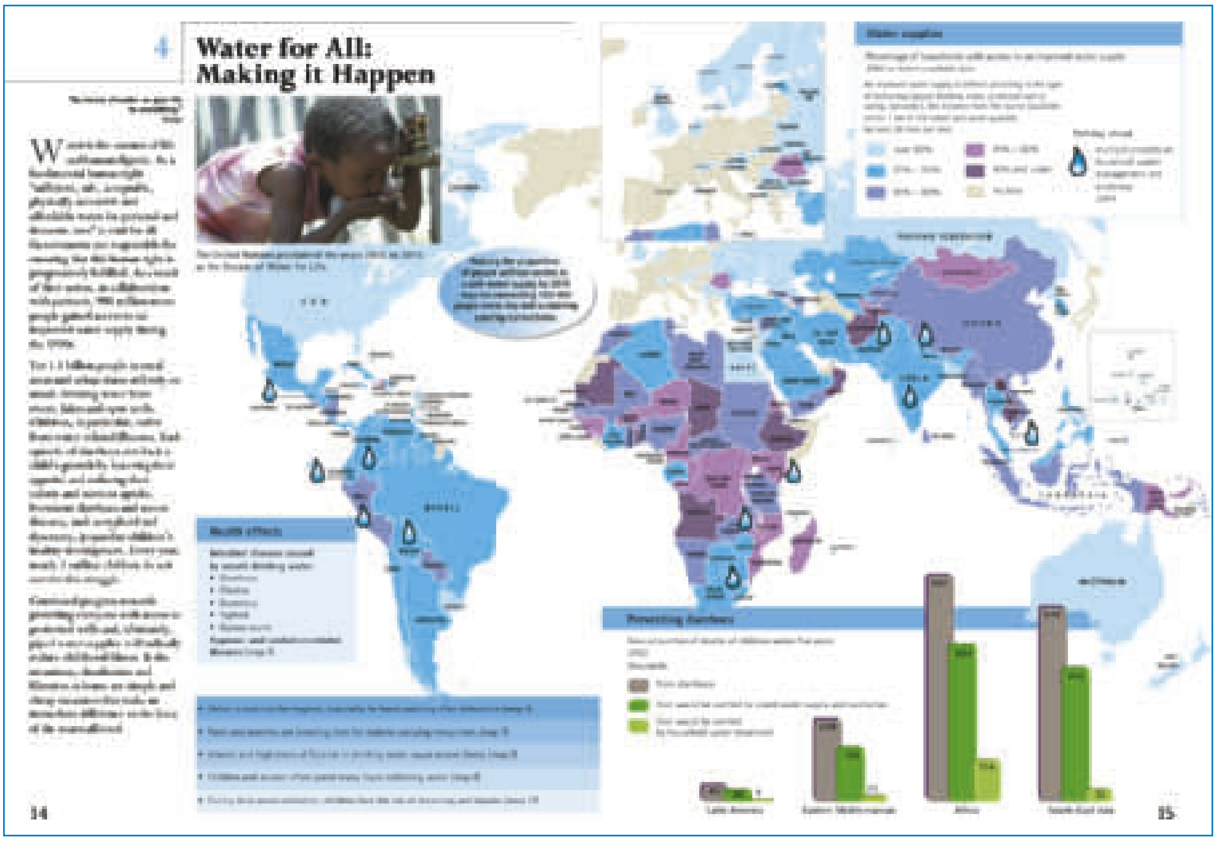
The most important waterborne pathogens and their implications for water supply and transmission channels (ingestion, inhalation and contact) are listed in → Table 2.8 (p. 51). It must be borne in mind that in most countries systematic surveillance of such infections is not carried out.

The most important pathogens that can give rise to waterborne outbreaks by **entering from the catch basin** or through **leaks in the network** of **water pipes** are **Campylobacter, noroviruses as well Cryptosporidium and Giardia** (see also → Table 2.9, p. 51).

While for a long time control of waterborne pathogens was based on water filtration as well as chlorination, today it must be acknowledged that, in particular certain non-enveloped viruses, and protozoa to a greater extent, are well known for their **extremely high resistance** to chlorine.

In Germany, too, there have been waterborne outbreaks of Giardia and noroviruses, evidencing a high level of chlorine resistance. For example, in the Rengsdorf district of the Rhineland-Palatinate a cluster of diarrhoeal diseases was observed at one

→
Figure 2.6 and 2.7:
The implications of inadequate water supplies and overall unsafe hygiene conditions.
Source: Gordon (WHO) 2004.



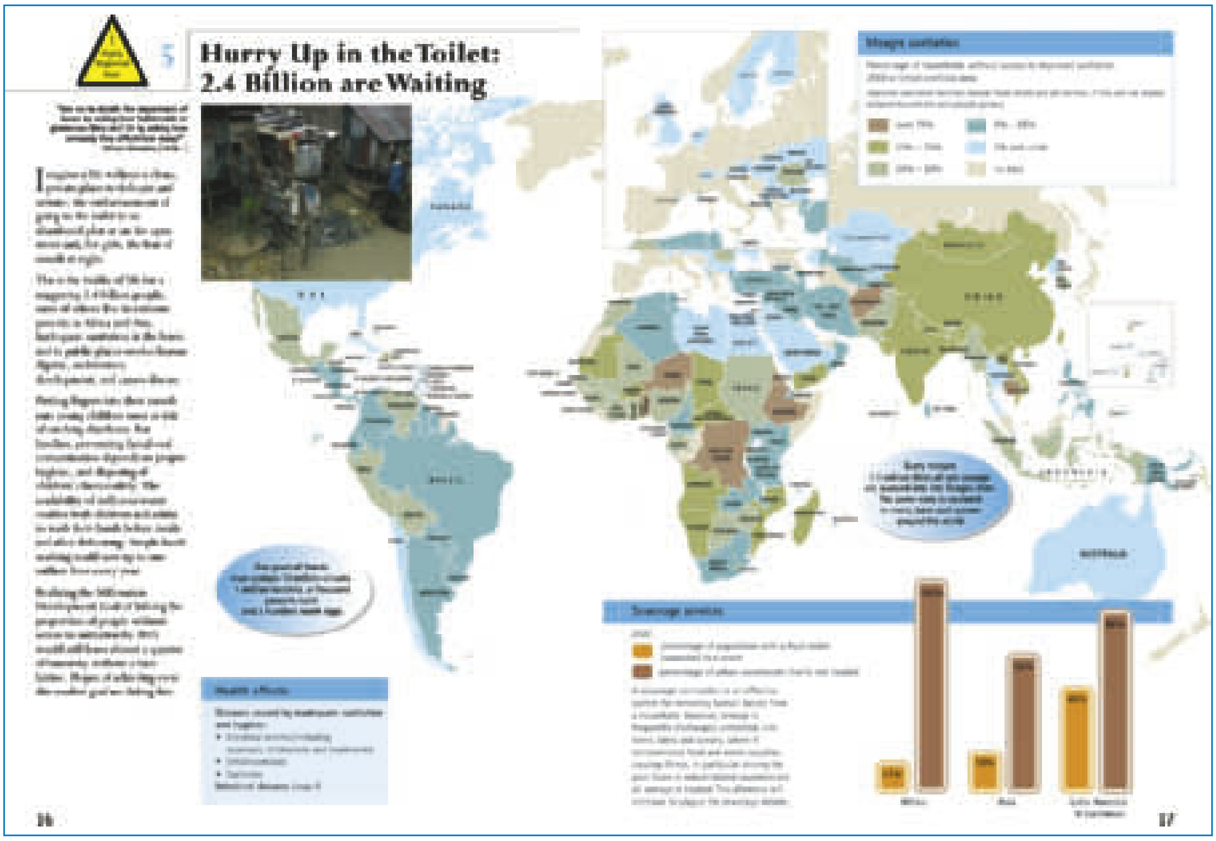
general practitioner's surgery in 2000. Systematic investigations identified the origin as contamination of the drinking water because of an unsafe well, situated in the middle of a field. This apparently caused a Giardia epidemic in Germany. This epidemic was not picked up by the classic drinking water testing methods and could not be brought under control through chlorination (Kistemann et al. 2003).

Noteworthy is equally the norovirus outbreak that occurred in Germany following contamination of the water supply network, with over 90 % of the population using this water developing a classic norovirus infection (RKI 2004).

Hence in Germany, too, it must be assumed that in view of the high levels of chlorine resistance, high prevalence and the inability to detect waterborne pathogens using the classic bacteriological indicator principles, unidentified waterborne infections can occur.

→ **In the developed countries, too, the microbial risks posed by the water supply destined for human consumption must be re-evaluated in the light of resistance development and the danger of spread via the water distribution system.**

Apart from contamination by those pathogens entering from the catch basin or the central water supply, in recent years there is a much greater understanding of the waterborne microbes that can proliferate in **water distribution systems** and pose a risk to the population using this water. In the developed countries, too, the water supply destined for human consumption must be re-evaluated in the light of these observations and → **resistance development.**



Ingestion (Drinking)			Inhalation and Aspiration (Aerosol)	Contact (Bathing)
Infection channels (sepsis and systemic infections can be manifested)				
Gastrointestinal infections			Respiratory tract infections	Infections of the skin (in particular in the presence of abrasions), mucosa, wounds, eyes
Bacteria *Campylo-bacter* *E. coli* *Salmonella* *Shigella* *Vibrio cholera* *Yersinia*	**Viruses** Adenoviruses Astroviruses Enteroviruses HAV HEV Noroviruses Rotaviruses Sapoviruses	**Protozoa and Worms** *Cryptospori-dium parvum* *Dracunculus medienensis* *Entamoebia histolytica* *Giardia intestinalis* *Toxoplasma gondii*	*Legionella pneumophila* Mycobacteria (non-tuberculoid) *Naegleria fowleri* Diverse viruses Many other microbes in high-exposure settings	Acantamoeba spp. Aeromonas *Burkholderia pseudomanei* Mycobacteria (non-tuberculoid) *Leptospirus spp.** *Pseudomonas aeruginosa* *Schistosoma mansoni*

*Primarily through contact with heavily contaminated surface water

→
Table 2.8:
Transmission channels of common waterborne pathogens.
Source: WHO 2006.

The most important pathogens that can proliferate in the water distribution systems are:
– *Legionella* spp.
– Atypical mycobacteria
– *Pseudomonas aeruginosa.*

In particular in the temperature range 20–50°C legionellae can grow to reach concentrations that pose a risk of infection. Differences in virulence vary according to the legionellae species, and this is something that must be paid greater attention when devising prevention strategies in the future. Depending on the status of the exposed persons' immune system, legionellae can pose infection risks that hitherto have been underestimated.

The RKI and CAPNET believe that in Germany between 6 and 8 % of all cases of community-acquired pneumonia cases are caused by legionellae. Of the some 500,000 annual cases of community-acquired pneumonia, around 30,000 to 40,000 cases are thus likely to be cases of legionnaires' disease *(see also 2.1.1.3).*

→
Table 2.9:
Waterborne gastrointestinal diseases in Europe. Number of outbreaks in countries, maximum number of cases based on pathogen.
Source: modified as per Medema 2006.

Pathogens Isolated									
		Bacteria		Protozoa		Viruses			
	Number of outbreaks	*Campylo-bacter*	*Shigella*	*Cryptospori-dium*	*Giardia*	Norovirus	Viruses (not further identified)	Mixed	Gastroen-teritis
Outbreaks	86	9	3	46	2	8	1	5	12
Cases	72,546	16,222	531	7,772	232	11,408	2,500	2,511	31,370*

*no number of cases is available for one outbreak

In addition to the hitherto underestimated role of legionellae in community-acquired pneumonia, the considerable risk posed by nosocomial legionellosis must be taken into account. Time and again there are cases of nosocomial legionellae outbreaks, linked mainly to the new construction or conversion of water distribution systems. Apparently, the stagnation problems associated with such interventions further drive proliferation of legionellae such that very high legionellae concentrations are suddenly found once the system is placed back in operation again. This scenario is mainly seen in hospitals, hotels, nursing homes and other large institutions. Current investigations reveal high concentrations of legionellae above the safety threshold can also be seen in some cases in private households.

In view of the epidemiological implications of waterborne legionellosis, preventive efforts and diagnosis must be greatly improved.

While legionellae have been identified as waterborne pathogens since 1976, it is only in recent years that, thanks to the use of molecular typing, it has been demonstrated that up to 40 % of the *Pseudomonas aeruginosa* infections occurring in hospitals, and in particular in intensive care units, originate from the water supply. Studies by Trautmann et al. provided convincing insights, which have in the meantime been corroborated by other studies. It has also been demonstrated that after the introduction of sterile filtration by means of terminal filters, the rate of *Pseudomonas* infection dramatically fell in intensive care units and on a haemato-oncological ward.

→ **The water distribution system in hospitals is probably one of the most important sources of nosocomial pseudomonas and legionellae infections.**

Set against that background, there is considerable scope for preventive measures in the future. Anaissie postulates that the → **water distribution system in the hospital, and possibly also in private households,** is the nosocomial infection source most commonly overlooked but easiest to control, especially as far as Pseudomonas aeruginosa and *Legionella* infections are concerned (Exner et al. 2007).

Helicobacter must be pointed out as one of the newly identified drinking water-associated pathogens. It is also featured in the WHO Guidelines for Drinking Water Quality. New studies on the survival of *Helicobacter pylori* in fresh water have revealed that this bacterium can survive in a "viable but not culturable status" in coccoid form, thus posing a risk to public health.

Studies carried out by the working group led by Rolle-Kampczyck et al. (2004) in Germany showed that *Helicobacter pylori* could be detected in well water and that positive detection in drinking water was consistent with a positive colonisation status among well users. The authors concluded that *Helicobacter pylor* infection was associated with usage or drinking of well water contaminated with *Helicobacter pylori.*

In the meantime these study findings have been corroborated by other epidemiology studies, in other countries too.

If this turns out to be the case, these findings could be of enormous importance in terms of prevention of this pathogen, the second most common of all infectious agents worldwide, and which can cause stomach cancer. These insights could attain a level of importance similar to that accorded to the discovery of the aetiological agent of cholera and cholera transmission by John Snow and Robert Koch. In particular, the steady decline in *Helicobacter pylori* infections seen in the developing countries in line with hygiene improvements, including of drinking water, would appear to lend credence to this belief.

In summary it can be noted that even in developed countries, but more so in developing countries, water plays → **an absolutely underestimated role as a transmission channel for infectious agents** not only for diarrhoea but also for other diseases such as pneumonia and nosocomial infections.

→
Water has been greatly underestimated as a transmission channel for pathogens, not only for diarrhoea but also for other diseases (such as community-acquired) pneumonia and a number of nosocomial infections.

These insights must urgently be studied in greater depth by stepping up research and deploying new techniques for detection of microorganisms in drinking water, based on molecular biology methods, epidemiological methods as well as new indicator systems. Furthermore, a new strategy is needed for prevention of waterborne infections through **improvement of the microbiological surveillance systems used hitherto** and modification of investigation techniques, while expanding the spectrum of microorganisms to include parasites and viruses.

2.3.2 Foodstuffs

Epidemiology

Apart from drinking water, normal **foodstuffs** are also an important source of infectious diseases. The US Centre for Disease Control (CDD) estimates that each year 76 million persons contract a foodborne infection, over 300,000 of whom are hospitalised and over 5,000 die because of food-related diseases. Young children and adult immunosuppressed persons are at highest risk. The costs incurred for foodborne infections are estimated to be → **in the region of 5 billion euros for the USA** (CDC 2006). Changes in demographic trends and food practices, changes to food production and distribution systems, microbial adaptation and inadequate resources for control and for the public health infrastructure have led to the emergence of new as well as of long-established foodborne diseases. With the constant rise in tourism it is not surprising that there is a growing danger of contracting a foodborne infection locally, regionally or even globally.

→
Around 76 million foodborne infections are thought to occur each year in the USA, of which more than 300,000 require hospital treatment.

At present it is not possible to estimate exactly how many foodborne infections occur in Germany each year. In 2006, 5,921 potential foodborne outbreaks were reported to the Robert Koch Institute, involving a total of 70,530 persons (RKI 2006, 2007 *see also Chapter* 2.1.1.3).

The term “foodborne diseases” denotes all diseases resulting from the ingestion of foodstuffs; gastrointestinal symptoms are the most common clinical manifestation of foodborne diseases.

→
Camplyobacter infections in Germany (example) (RKI 2006):
- **Total incidence: 63.1/100,000 inhabitants (52,035 cases)**
- **Highest incidence: children under 5 or under 1 year of age,**
  Second peak: adults between 20 and 29 years
- **596 clusters with 1,499 cases of disease**

Pathogens

Foodborne diseases can be caused by both **microorganisms** as well as by their toxins, and also by **fungi** and their toxins and by **chemical contaminants** (which will not be addressed here). During the past 20 years several foodstuffs were implicated as the cause of outbreaks of foodborne diseases, including milk (*Campylobacter*), crustaceans (noroviruses) and pasteurised *Apfelschorle* (an apple juice drink mixed with sparkling water) (*E. coli O157:H7*), raw and inadequately cooked eggs (*Salmonella*), raspberries (*Cyclospora*), strawberries (hepatitis A) and various finished products (*Listeria*).

Doctors and other public health personnel play a decisive role in monitoring and preventing potential disease outbreaks; nonetheless, only a small proportion of these infections are recorded since only some of the people suffering from a gastrointestinal infection consult a doctor. In the case of those who do seek medical treatment, there is a high probability of detecting **bacteria** as the causative agent rather than any other pathogen.

The most important bacterial pathogens causing foodborne infections in Western countries are:

- *Campylobacter*
- *Salmonella*
- *Shigella*.

Only rarely are examinations conducted to investigate the viral aetiology of diarrhoeal diseases, despite the fact that **viruses** are thought to be the most common cause of foodborne infections.

In recent years a number of other foodborne pathogens have been identified or have newly emerged → **Table 2.10.**

The most important aetiological agents associated with the various manifestations of foodborne diseases are listed in → **Table 2.11.** To devise further improved prevention strategies it is of paramount importance that more information be available on the conditions under which, and in which areas, foodborne infections can be transmitted.

The large variety of **ready-to-eat-foods, importation of foodstuffs** from other countries, where different hygiene conditions prevail, point in principle to the increased risks of foodborne infections during the production, distribution and processing of foodstuffs. The hazards undoubtedly faced here are borne out to an extent by reports of foodborne outbreaks in Germany too. Nonetheless, it is thought that the majority of foodborne infections result from inadequate hygiene standards **within private households.**

Clinical manifestations

Whereas the majority of foodborne infections in immunocompetent persons give rise to gastrointestinal complaints, which may only be mild and last for a short time, prolonged symptoms and a more severe course of disease must be expected in immunocompromised persons, in the elderly or in children.

Typical long-term sequelae are seen in the case of some pathogens, such as

– *Salmonella*/yersiniae	Reactive arthritis
– *Campylobacter*	Guillain-Barré syndrome
– EHEC	Haemolytic uraemic syndrome (HUS)
– *Listeria*	Miscarriage, meningitis, etc.

The proportions of foodborne infections attributable to various pathogens were estimated as follows for the USA:

– EHEC	85 %
– *Salmonella*	95 %
– *Campylobacter*	80 %
– Noroviruses	40 %.

Prevention strategies

The following is needed to devise further prevention strategies:

- the requirements for production, distribution and processing of foodstuffs must be met
- the handling of foodstuffs in restaurants must be assured by government inspections and quality assurance measures, such as the tried and tested **HACCP (Hazard Analysis Critical Control Points) concept**, and
- more information must be provided on handling foodstuffs in the household, and the necessary hygiene measures must be greatly tightened.

To monitor and verify compliance with **hygiene regulations** governing **production and distribution of foodstuffs,** appropriate supervision of foodstuffs must be carried out by the competent authorities.

There must not be any doubt that such **government-regulated supervision of foodstuffs** is of paramount importance, just as in the case of drinking water, and this cannot be compensated for alone by any measures taken by the producer at his own initiative. In addition to in situ inspections conducted by experienced personnel, provision must be made for appropriate supervision of foodstuffs in line with the latest scientific knowledge and diagnostic techniques.

In view of the pivotal role played by foodborne infections in the household setting, consumers must be properly informed about the risks and instructed better on how to observe personal hygiene as well as good hygiene practices throughout the household.

Pathogens Causing Foodborne Infections
Brucella spp.
Campylobacter spp.
Clostridium spp.
Cryptosporidium parvum
Enterohaemorrhagic E. coli (EHEC)
Escherichia coli
Giardia lamblia
Hepatitis A virus
Listeria monocytogenes
Norovirus
Salmonella enterica
Salmonella spp.
Shigella spp.
Trichinella spiralis
Vibrio cholerae
Yersinia enterocolitica

→ **Table 2.10:**
Pathogens causing foodborne infections based on data from the RKI 2006, 2007.

Clinical Picture	Potential Foodborne Pathogens
Gastroenteritis (vomiting as the most important symptom; fever and/or diarrhoea may also occur)	Viral gastroenteritis, mainly rotavirus in infants or noroviruses or other caliciviruses in older children or adults; or food poisoning due to toxins (e.g. vomitoxin, *S. aureus* toxin, *B. cereus* toxin and heavy metals
Non-inflammatory diarrhoea (acute watery diarrhoea without fever / dysentery, some patients may have fever	May be caused by almost all microorganisms of the gastrointestinal tract (bacterial, viral, parasitic), but is a classic symptom of – Enterotoxic *E. coli* – *Giardia* – *Vibrio cholerae* – Gastrointestinal viruses (astroviruses, noroviruses and other caliciviruses, adenoviruses, rotaviruses) – *Cryptosporidium* – *Cyclospora cayetanensis*
Inflammatory diarrhoea (invasive gastroenteritis, pronounced bloody stools and fever may be seen)	*Shigella* spp. *Campylobacter* spp. *Salmonella* spp. Enteroinvasive *E. coli* Enterohaemorrhagic *E. coli* *E. coli O157…H7* *Vibrio parahaemolyticus* *Yersinia enterocolitica* *Entamoeba histolytica*
Persistent diarrhoea (longer than 14 days)	In cases of persistent diarrhoea, investigations should be conducted for parasites, especially in the case of persons travelling to mountainous regions or other regions where raw water is drunk. Furthermore the following should be considered; *Cyclospora cayetanensis, Cryptosporidium, Entamoeba histolytica* and *Giardia lamblia.*
Neurological manifestations (e.g. paralysis, respiratory insufficiency, bronchospasms, paralysis of the cranial nerve)	Botulism (*Clostridium botulinum toxin*) Organic-phosphate-based pesticides Thallium poisoning, fishborne poison (histamine, saurine, ciguatoxin, tetradotoxin) Neurotoxic, paralytic, amnesic shellfish poisoning (brevitoxin, saxitoxin, domoic acid) Fungal poisoning Guillain-Barré syndrome (*Campylobacter jejuni*-associated infectious diarrhoea)
Systemic disease (e.g. fever, weakness, arthritis, jaundice)	*Listeria monocytogenes* *Brucella spp.* *Trichinella spiralis* *Toxoplasma gondii* *Vibrio vulnificus* Hepatitis A and E *Salmonella typhi* and *Salmonella paratyphi* Amoeba-associated liver abscess

→

Table 2.11:

Clinical picture and potential pathogens causing foodborne infections.

Source: CDC 2004.

Much needs to be done to achieve this because over the past years **misguided risk perceptions** had been fostered **among consumers** because of the → **hygiene hypothesis** and, from a present-day perspective, incorrect interpretation of hygiene practices (downplaying of the role of cleaning and disinfection).

→
The "hygiene hypothesis" and the ensuing downplaying of the general role of hygiene has fostered a misguided risk perception and inappropriate risk behaviour in large sections of the population.

In Germany the **surveillance** of foodborne infections is now of a high standard thanks to the **Protection against Infection Act.** In the event of any clusters (outbreaks), the responsible authorities must conduct systematic investigation of foodborne infections.

The **rapid warning systems** in force in Europe have proved to be very beneficial for the food supervisory authorities.

However, there is a continued need for regular reporting of foodborne infections to assure a high level of up-to-date epidemiological data, and thus use these as a basis for prevention and control.

2.4 Infectious diseases and crisis situations

Infectious diseases in crisis situations 2.4

- **Epidemiology**
- **Infectious diseases**
- **Current prevention strategies**

Epidemiology
Crisis situations include complex crises and natural catastrophes (flooding, earthquakes). The term **"complex crisis situation"** was chosen by the World Health Organisation to denote crisis situations such as war or civil catastrophes involving large sections of the population and resulting in flight and expulsion, and in turn in food shortages and poor hygiene conditions.

Globally, there are more than **200 million people** who are living in countries where not only refugees but also the entire population are affected by complex crisis situations. → **Communicable diseases are one of the leading causes of mortality and morbidity in such scenarios**. The highest morbidity rate and excess mortality are often seen during the first acute phase of crisis situations. During this phase the mortality rate can be up to 60-fold higher than the normal rate seen among refugees, with up to one-third of these deaths being caused by communicable diseases. **Children are at particular risk.** Of the 10 countries with the highest mortality rate for children below the age of 5 years, 7 countries are facing an imminent threat of complex crisis situations.

→
Communicable diseases are one of the leading causes of mortality and morbidity in crisis situations.

Refugees and expellees from crisis areas are mainly placed in crowded refugee camps and distributed among the local population. Various factors propitious to the spread of infectious diseases **interact to produce a synergistic effect** in complex crisis situations.

These factors include:

– Mass movements of peoples

– Placement in refugee camps

– Overcrowding
– Economic problems and disruption of the environment
– Poverty
– Lack of safe water
– Inadequate sanitary conditions and inadequate disposal of waste and effluent
– Lack of protection against personal attacks
– Poor nutritional status
– Inadequate access to health services
– Collapse of the public health infrastructure and of prevention and control programmes (vaccinations).

Malnutrition and **traumatisation**, in particular, play a role in the occurrence and ensuing course of infectious diseases. The death rate among refugees or other population groups in complex crisis situations shows a tenfold rise compared with that seen in the normal population. More than two-thirds of these deaths are attributable to infectious diseases, which either alone or in combination with malnutrition and traumatisation are the most common cause of death.

Infectious diseases
The most important infectious diseases that can be transmitted in complex crisis situations are:
(see also → **Table 2.12**):
– Diarrhoeal diseases
– Acute respiratory infections
– Measles
– Malaria
– Meningitis
– Tuberculosis
– HIV/AIDS.

Diarrhoeal diseases are the most important cause of morbidity and mortality in complex crisis situations. These diseases are caused by poor quality and quantity of water, inadequate sanitary conditions, overcrowding, poor hygiene and lack of soap.

In refugee camps **diarrhoeal diseases** account for more than **40 %** of these deaths in the acute phase, with more than 80 % of deaths occurring in children below the age of 2 years.

A study of outbreaks reveals that the factors most commonly implicated in infections are contaminated water (due to faecal contamination of the surface water in wells), contamination of water during transportation and storage (due to faecally contaminated fingers), shared water containers, lack of soap and contaminated foodstuffs.

→
Table 2.12:
Communicable diseases classified as relevant or highly relevant during the armed conflict in Lebanon.
Source: Mbabazi (WHO) 2006.
(Note: Lebanon is a country that has a relatively high standard of public services)

Diseases Occurring During the Armed Conflict in Lebanon
Acute lower respiratory tract infection (***)
Brucellosis (**)
Typhoid fever (**)
Shigellosis (**)
Hepatitis A + E (**)
Measles (***)
Meningitis (**)
Mumps (**)
Pertussis (**)
Rubella (**)
** = moderate risk *** = high risk

Acute respiratory infections are also responsible for a large proportion of the morbidity and mortality seen in complex crisis situations. Unfavourable conditions such as overcrowding, indoor fires in the absence of adequate ventilation, inadequate protection and warmth, especially in cold climates promote development of respiratory infections caused, inter alia by droplet transmission. Acute respiratory diseases augment the risk of transmission of meningococcal infections, too, through aerosol transmission of respiratory secretions when coughing and sneezing.

In some refugee camps **measles epidemics** were the main cause of death: measles accounted for up to 53 % and 42 % of deaths in refugee camps in eastern Sudan and Somalia, respectively, in 1985. Overcrowding is associated with transmission of high infective doses of the measles virus, giving rise to severe clinical cases of disease. The incidence of severe measles disease courses is also higher among undernourished children.

At least 90 % of the 1 million cases of **malaria** with a mortal outcome occur in sub-Saharan Africa and over 30 % of malaria deaths occur in countries affected by complex crisis situations. Refugees fleeing from regions of low malaria endemicity (including non-immune persons) into endemic zones are exposed to a high risk of malaria. Conversely, refugee movements from hyperendemic areas into regions of lower endemicity can pose an increased risk of infection to the local population, in particular if conditions propitious to the survival of the mosquito are assured, such as stagnant water, flooding and environmental changes and favourable weather conditions.

Major outbreaks of **meningococcal meningitis** have also been reported in complex crisis situations. Serogroup A and C meningococci are the main causes of epidemic meningocccal meningitis in most countries although serogroup W 135 is becoming increasingly more prevalent in sub-Saharan Africa. Epidemics also occur south of the traditional meningitis belt, including in eastern, southern and central Africa. Drought, sand storms, overcrowding and high rates of acute respiratory infections augment the risk of contracting epidemic meningococcal disease.

Tuberculosis continues to be a major problem in complex crisis situations. The risk of contracting TB is increased due to the overall prevailing conditions (inadequate access to healthcare) and increased transmission as seen in overcrowding situations. In complex crisis situations the risk of chronic disease courses and of development of multiresistance is also greatly increased in a situation of a lower case-detection rate and lower cure rates.

Tuberculosis is the leading cause of death among **HIV**-infected persons. **Co-infection with HIV** increases the risk of latent infection progressing to active tuberculosis from 10 % to 60–80 %. HIV-infected persons are also at increased risk for severe side effects of tuberculostatics.

There is extensive overlapping of countries affected by complex crisis situations and by a high HIV prevalence, in particular in sub-Saharan Africa. Conflicts and refugee movements can increase the risk of a new HIV infection resulting from unsafe blood transfusion, poor hygiene conditions in hospitals, collapse of services to treat sexually transmitted diseases, which promote HIV transmission, changes in behavioural practices, lack of condoms and sexual violence.

Current prevention strategies

The most important prevention and control measures include:

- Planning of refugee camp facilities, whereby the rate of diarrhoeal diseases, acute respiratory infections, measles, meningitis, tuberculosis and vector-borne diseases can be greatly reduced.
- Provision of hygienic water supplies and safe sanitary conditions
- Immunisation
- Vector control
- Epidemic preparedness and reaction
- Surveillance.

→ **Worldwide, more than 200 million people live in countries affected by complex crisis situations. The morbidity and excess mortality attributable to communicable diseases during complex crisis situations are largely avoidable since the necessary interventional measures are available in principle.**

The morbidity and excess mortality attributable to communicable diseases during complex crisis situations are → **largely avoidable** since the necessary interventional measures are available in principle. Experience has shown that **timely and coordinated implementation** of suitable interventional measures can greatly reduce the mortality and morbidity rates.

What is most tragic is the destruction of the infrastructure needed to prevent infectious diseases during war. The selective destruction of electricity power stations, water supply systems, effluent and waste disposal facilities dramatically augment the risks posed by communicable diseases, especially to children below the age of 5 years. This has been shown to be associated with increased mortality. In particular the disruption of water supplies leads to, apart from the waterborne infections directly transmitted in drinking water, diseases resulting from poor hygiene and lack of washing facilities.

The collapse of the healthcare system gives rise to a reduction in vaccination uptake rates, which in turn drives the rates of measles, mumps, rubella, pertussis, tetanus, meningitis and hepatitis B. Accordingly, e.g. following the armed conflict in Lebanon in 2006 an increase in the measles rate was observed (see also → **Table 2.12**).

In view of the far-reaching consequences of the destruction of sanitary infrastructures and their implications for upholding the most important infection-prevention measures by assuring an intact healthcare system, it is necessary to ensure that in the event of war, electricity, water supplies and effluent disposal services are placed under special protection, so as to avoid a situation whereby large sections of the population, in particular young children and elderly persons, bear the brunt of the aftermath of military conflict.

2.5 Antibiotic resistance

Since the discovery of penicillin in 1928, antibiotics have become the most important instruments in the treatment of infectious diseases. However, in view of the **increase in antibiotic resistance,** the effectiveness of antibiotics is something that can no longer be relied upon. There are ample data suggesting that antibiotic resistance is a growing problem in Germany too.

Hence the rise in antibiotic resistance over the past decades is one of the biggest problems when it comes to controlling communicable bacterial diseases. According to the first Epidemiological Report on Communicable Diseases in Europe, published in June 2007, → **the increase in antibiotic resistant microorganisms is the most serious threat posed by communicable diseases** in Europe. Whereas for a long time the development of new antibiotics was able to keep abreast of antibiotic resistance, the financial risks faced by the pharmaceutical industry have in the meantime become so enormous that only very tentative steps are taken towards the development of new antibiotics.

In particular, the following two aspects of the spread of resistance must be continually monitored:

– the ongoing trends in the development of antibiotic resistance

– the restricted usage of antibiotics aimed at reducing antibiotic resistance to a minimum.

Resistance development

Whereas in recent years it was mainly **Gram-positive** bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and glycopeptide-resistant enterococci that elicited interest, there is now a growing trend towards emergence of **Gram-negative** bacteria that are resistant to all betalactam antibiotics as well as to other antibiotic groups.

Hence much importance is being ascribed to the **surveillance** of antibiotic resistance. Two different assessment systems have been devised over the past decade:

1. GENARS (German Network for Antimicrobial Resistance Surveillance) and
2. EARSS (European Antimicrobial Resistance Surveillance System).

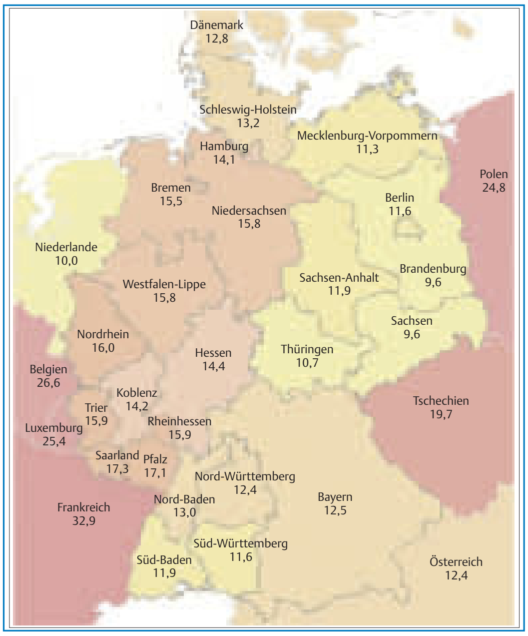
GENARS was founded in 1999 as a network of microbiology laboratories based at university hospitals with the support of the following specialist societies: German Society for Hygiene and Microbiology (DGHM), Paul Ehrlich Society for Chemotherapy (PEG) and the German Society of Infectiology (DGI); this endeavour was sponsored between 2002 and 2005 by the German Federal Ministry of Health. Since the middle of 2005 its coordination has been assumed by the Robert Koch Institute (RKI). The aim is continual acquisition of **resistance data based on routine diagnosis** for the entire spectrum of clinically relevant microbes. Comparison of the data provided by the various laboratories is assured thanks to standardisation of the microbiological methodology used for microbial identification and sensitivity testing.

Antibiotic resistance **2.5**

- **General trend in resistance development**
- **Resistance situation of selected microorganisms**
- **Administration of antibiotics to animals**

→

The increase in antibiotic resistant microorganisms is seen as the most serious threat posed by communicable diseases in Europe.



→ **Figure 2.8:**
Regional antibiotic consumption (expressed as Defined Daily Dose - DDD) per 1,000 inhabitants and day) in Germany and neighbouring countries. The data are based on the year 2001.
(Data source: Rapid Risk Information on Drugs for the Statutory Health Insurance Companies (Arzneimittel-Schnellinformation der Gesetzlichen Krankenversicherung (GKV) GAmSi "European Surveillance of Antibiotic Consumption").
Source: de With 2004. Reprint with kind permission of Georg Thieme Verlags KG, Stuttgart.

EARSS, the European Antimicrobial Resistance Surveillance System, was founded in 1998. This international initiative is sponsored by the General Director for Health and Consumer Protection (DG SANCO) of the European Commission and of the Dutch Ministry of Health, Welfare and Sport. In 2004, 800 laboratories from 30 countries participated in the surveillance system. The aim of the surveillance initiative is to present the trends in resistance development for seven indicator bacteria: *Staphylococcus aureus, Streptococcus pneumoniae, Enterococcus faecium/faecalis, Escherichia coli, Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (Grundmann (EARSS) 2004–2005).

Unregulated, excessive antibiotic usage promotes resistance development, whereas regulated, reduced antibiotic usage can attenuate resistance development, but the relationship between the two is of a complex nature. Set against a background of a critical rise in resistance problems in many European countries, the Council of the European Union in November 2001 called upon the Member States, as part of a recommendation for circumspection in the use of antimicrobial substances in human medicine, to collect, and evaluate data on antibiotic prescription practices at different levels. The format offering optimal comparability at present is the usage density, expressed as the Defined Daily Dose (DDD), in accordance with the WHO recommendations per inhabitant (or insured person) or per hospital nursing day and year. Antibiotic consumption for the different German federal states and the countries bordering Germany is presented in → **Figure 2.8** (de With et al. 2004). Antibiotic usage in the community in Germany is in the lower third compared with other European countries (25 countries). High-consumption European countries prescribe more broad-spectrum betalactams as well as more of the new macrolides and fluoroquinolones. Based on a study by Goosens et al. (2007) conducted within the framework of the European Surveillance of Antimicrobial Consumption (ESAC), it was noted that antibiotic usage outside hospitals in the USA was being increasingly exceeded only by three European countries (Italy, France and Greece). This was the first study that compared antibiotic usage outside hospitals in Europe and in the USA using the same methodology. The study revealed that in the USA antibiotic usage is higher than in most other European countries, showing a trend towards the use of new antibiotics in the USA.

Resistance profiles of selected microorganisms
Over the past six years the resistance profiles of these microorganisms show a clear **north-south gradient for penicillin** insensitive *Streptococcus pneumoniae*, with a high degree of macrolide co-resistance in various southern countries as well as in northern countries. Trend analysis shows that in those countries with the highest rate of penicillin insensitivity, a declining trend was noted in 2004 whereas in countries with traditionally low rates, higher rates of penicillin insensitive *Streptococcus pneumoniae* were observed.

Of paramount importance is the development of **methicillin-resistant staphylococci.** These are the most common causative agents of nosocomial infections, but in addition to the classic hospital-selected MRSA strains, community-acquired MRSA strains are also being increasingly observed. These strains are designated as **community MRSA (cMRSA),** because they infect and colonise non-hospitalised persons. cMRSA is isolated primarily from deep-seated, necrotising skin or soft-tissue infections, in particular furunculosis. Only rarely is cMRSA implicated as the cause of necrotising pneumonia. These clinical manifestations are apparently attributable to the fact that cMRSA is able to produce Panton-Valentine leukocidin toxin. Compared with the hospital-associated MRSA epidemic strains, cMRSA often exhibits a narrow resistance phenotype (RKI 2007).

Based on data collected for 1999–2003, EARRS calculated an average MRSA rate of 21 % for Europe. Noteworthy in this respect are the considerable disparities between the various European countries (→ **Table 2.13**). Low rates of MRSA (<1 %) are observed in northern Europe, higher rates in central Europe (5–20 %) and the highest proportions in southern Europe as well as in the United Kingdom and Ireland (30–40 %). In 2004 the MRSA proportion in Europe rose to 24 %, but with the same inter-country disparities mentioned above being still evidenced. A rise in the MRSA rate is seen in virtually all countries, with Romania with up to 61 % (2005) showing the highest rate; conversely, a declining trend is observed in France and Slovakia.

Vancomycin-resistant enterococci (VRE) rates in most countries are less than 10 %. However, increasing rates of vancomycin-resistant *Enterococcus faecium* were seen in Germany, France, Italy and Ireland, linked to the spread of hospital-adapted clonal complexes comprising 17 strains.

E. coli resistance to aminopenicillins is widespread in European regions, with only Sweden reporting resistance rates of less than 30 %. The trend towards rising *E. coli* resistance appears to be the result of further spread of extended-spectrum betalactamases (ESBLs) among this species, too, and the frequent use of fluoroquinolones.

→
Table 2.13:
MRSA rates in % in various European countries.
Source: EARSS Report 2005.

Country	MRSA Rate in %
Austria	13
Belgium	31
Bulgaria	31
Czech Republic	13
Denmark	2
Estonia	2
Finland	3
France	27
Germany	21
Greece	42
Hungary	19
Iceland	0
Ireland	42
Italy	37
Netherlands	1
Norway	1
Romania	61
Slovakia	19
Spain	27
Sweden	1
United Kingdom	44

Nosocomial and community-acquired *E. coli* infections will pose an increasing challenge for the European healthcare system in the coming years.

The development of antibiotic resistance highlights the urgent need for alternative measures, control measures and preventive measures. In particular, efforts must be stepped up to elucidate why there are these major differences between the various European countries. This could provide the key to enhanced prevention and control of antibiotic resistant microorganisms.

The highest risk for the emergence and development of antibiotic resistant microorganisms is posed by the **hospital**. For that reason, appropriate hygiene (infection control) measures must be accorded top priority in that setting. The spread and emergence of **multiresistant Gram-negative bacteria** such as ESBL-producing Enterobacteria and metallobetalactamase-producing *Pseudomonas* are also being driven largely by antibiotic treatment regimens. Apart from hospital-based measures, other effective approaches include the formulation of hospital-related guidelines based on in-house resistance data as well as the organisation of continuing professional development courses on antimicrobial treatment for clinicians.

Antibiotic usage in animals

No doubt, one of the most important goals is to ensure very **restrictive usage of antibiotics** to counter the emergence of antibiotic resistance. On the other hand, antibiotics must continue to be available to treat infections.

Apart from the selection of antibiotic-resistant microorganisms in persons treated with antibiotics, the administration of antibiotics to **animals** represents a further considerable potential risk for selection of antibiotic-resistant microorganisms. One problem is that pathogens that can be transmitted from animals to humans, i. e. **zoonotic pathogens,** such as salmonellae, campylobacter and *E. coli*, have become in the meantime resistant to various antibiotics and can pass on their resistance genes to other bacteria. This in the long term can lead to failure of antibiotic treatment in sick persons.

Despite the significant decrease from 85 % in 2000 to 63 % in 2003, a high average rate of 70 % was recorded for salmonellae from food-producing animals (cattle, pigs, poultry), based on data from the National Reference Laboratory for **Salmonellae** at the Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung –BfR). 42 % of *E. coli* isolates are resistant to antimicrobials. 52 % of salmonellae isolated from domestic animals and 42 % of salmonellae from foodstuffs as well as 37 % of all *E. coli*-isolates are → **multiresistant.** A rising trend in resistance to quinolones is being observed, especially in poultry. Many multiresistant isolates harbour integron structures which can be transmitted en block horizontally and vertically.

→ **52 % of salmonellae isolated from domestic animals and 42 % of salmonellae from foodstuffs as well as 37 % of all *E. coli* isolates are multiresistant.**

In the light of the above findings, the Federal Institute for Risk Assessment has proposed the following options and recommendations:

- Antimicrobial substances should be used only selectively as per the licensing regulations. In general, the aim is to reduce antimicrobial usage. Fluoroquinolones should not be administered through a general medication, e.g. in drinking water.
- Apart from monitoring resistance, the quantities of antimicrobials consumed in veterinary medicine should also be recorded.

Factors contributing to the **selection and spread of resistant bacteria in animals** include:

- Mass medication of entire herds
- Subtherapeutic dosage of antibiotics
- Long-term use of antibiotic treatment
- Use of broad-spectrum antibiotics in animal husbandry as well as their prophylactic and methaphylactic deployment.

It is not possible to identify exactly to what extent antibiotic usage in animal husbandry has contributed to the development of resistant microorganisms in humans. However, there is no disputing that **→ resistant microorganisms can be spread to humans via animal foodstuffs and products.** Apart from infections with a mortal outcome, this can lead to a prolonged hospital stay for patients, to the need for hospital treatment and, in particular in the case of immunosuppressed patients, to increased risk for supervention of co-infections.

→
There is no disputing that resistant microorganisms can be spread to humans via animal foodstuffs and products.

Based on data from the Federal Institute for Risk Assessment, around 250 salmonella cases are thought to occur each year in Germany which no longer respond to antibiotic treatment. Around 10 % of these infections have a mortal outcome.

In summary, Federal Institute for Risk Assessment states that the following measures must be taken to prevent and control multiresistant bacterial strains linked to animal husbandry:

- Measures that contribute to restricting overall usage of antibiotics
- Improved animal husbandry conditions, especially where many animals are kept in confined spaces, such as in chicken, turkey and pig production
- Improvement of animal health by resorting to appropriate infection control and immunisation measures
- Selective use of antimicrobials in animal production
- Replacement of broad-spectrum antibiotics with antibiotics endowed with a specific action
- Use of antibiotics also used in human medicine, such as fluoroquinolones and 3rd and 4th generation cephalosporines only for treatment of individual animals
- Strict indications
- Restriction of the licensing of new antibiotics for use in veterinary medicine.

Bioterrorism 2.6

- Baseline situation
- Infectious agents
- Transmission channels

2.6 Bioterrorism

Baseline situation

In the Memorandum published in 1996 by the Rudolf Schülke Foundation it was originally planned to devote a special chapter to bioterrorism. But this was not done since at that time the risk of bioterrorism did not seem so relevant as to warrant an analysis of this topic as posing an important risk of infection.

However, in recent years the possible deployment of pathogens by bioterrorists has become a highly relevant scenario. In 2001 there was an **anthrax outbreak** with a bioterrorist background in the United States. While only 22 persons became infected and 5 regions were affected, this event demonstrated that bioterrorism presents a real danger (CDC 2001). In particular in the aftermath of 9/11 (11 September 2001) there was much fear as to when or whether such bioterrorist attacks would be carried out, engendering in some cases a widespread sense of helplessness and anxiety among broad sections of society. Furthermore, there were extensive speculative and fictional reports about the development of pathogens for bioterrorist purposes.

→ **Independently of the, to some degree unfounded, risk scenarios, there is a broad consensus among experts that it is not a question of "whether" one or several biological agents will be released, but rather of "when" this is going to happen.**

Independently of the, to some degree unfounded, → **risk scenarios** there is, nonetheless, a broad consensus among experts that it is not a question of "whether" one or several biological agents will be released, but rather of "when" this is going to happen.

The release and spread of highly contagious agents, such as e.g. smallpox, could have catastrophic effects if effective measures are not immediately taken to control them. The use of **genetically modified, highly virulent agents** with concomitant high environmental resistance and persistence (tenacity) would herald a scenario of frightening proportions.

The possible spread of **SARS (coronavirus)** or the scenario arising in the event of pandemic influenza following natural mutations in the virus conjures up images of the ensuing situation if highly virulent pathogens are spread from person to person or through other channels (the air, foodstuffs, water).

→ **To date it is believed that the developed countries are not, or not adequately, prepared to cope with the serious microbiological risks posed by bioterrorist attacks.**

The developed countries are **not prepared or not adequately prepared** to cope with the serious microbiological risks posed by bioterrorist attacks. As such, failure to address these risks → **is no longer acceptable today in a political context.**

It is extremely difficult to prevent the deployment of biological weapons. By now the recipes for production of biological weapons are available on the internet, enabling even poorly resourced groups to produce some very effective biological weapons.

Infectious agents

In the meantime various international institutions, such as WHO, CDC as well as European institutions, have compiled a list of the most important pathogens that could lend themselves as candidates for a bioterrorist attack. In doing so they took account of epidemic aspects, morbidity, mortality, contagiousness, the number and concentration of agents needed, availability of treatment and preventive measures, diagnostic facilities, production aspects in respect of quantity, stability of the pathogen in the environment and the immune status of the population. Five agents and diagnostic groups are ascribed → **special importance.** The diseases they cause are as follows:

- Smallpox
- Anthrax
- Plague
- Botulism toxin poisoning
- Tularaemia
- Viral haemorrhagic fever (Ebola, Marburg, Lassa).

→
Five agents and diagnostic groups are ascribed special importance. The diseases they cause are: smallpox, anthrax, plague, botulism toxin poisoning, tularaemia and viral haemorrhagic fever (Ebola, Marburg, Lassa).

Only a few medical specialists or working groups are conversant with differential diagnosis of practically any of these diseases.

In the United States a strategic plan was drawn up in preparation of, and to respond to, biological and chemical terrorist attacks and published in 2000 by CDC.

The critical biological agents were classified into three groups → **Table 2.14** (p. 68).

The aim targeted in a bioterrorist attack is to release a bioterrorist agent so efficiently that as many people as possible will be affected. This can be achieved in principle through contamination of

- Foodstuffs
- Water supply systems
- Airborne or aerosol dispersal.

Transmission channels

Airborne transmission

So far it has been believed that transmission as → **aerosols** presents the greatest hazard to the population.

→
Airborne transmission presents the greatest bioterrorism hazard to the population.

All Category A agents can be spread as fine aerosol particles measuring 1–5 µm. Inhalation of aerosols small enough to reach the lungs can cause infection. An aerosol of this size is invisible to the naked eye and behaves like smoke, and is also able to penetrate indoor environments. Such agents can survive for several hours or days. The anthrax outbreak in Sverdlowsk caused infection in people located more than 4 km away from the point of release; animals more than 50 km away also contracted anthrax. Release of anthrax spores can have dramatic effects. According to a report by the *US Office of Technology Assessment* (OTA), if 100 kg of anthrax spores were to be released in the direction of the wind from Washington DC between 130,000 and 3 million deaths could be expected.

Category A	Category B	Category C
Characterisation High-priority agents posing a risk to national security because they – can be easily disseminated or transmitted from person to person; – result in high mortality rates and have the potential for major public health impact; – might cause public panic and social disruption; and – require special action for public health preparedness.	*Characterisation* Agents that are – moderately easy to disseminate; – result in moderate morbidity rates and low mortality rates; and – require specific enhancements of diagnostic capacity and enhanced disease surveillance.	*Characterisation* Emerging pathogens that could be engineered for mass dissemination in the future because of – availability; – ease of production and dissemination; and – potentially high morbidity and mortality rates and major public health impact.
Agents – *Variola major* (smallpox) – *Bacillus anthracis* (anthrax) – *Yersinia pestis* (plague) – *Clostridium botulinum toxin* (botulism) – *Franciscella tularensis* (tularaemia) – Filoviruses: - Ebola haemorrhagic fever - Marburg haemorrhagic fever – Arenaviruses: - Lassa (Lassa fever) - Junin (Argentine haemorrhagic fever) and related viruses	*Agents* – *Coxiella burnettii* (Q fever) – *Brucella* species (brucellosis) – *Burkholderia mallei* – Alphaviruses - Venezuelan encephalomyelitis - Intoxication through *Clostridium perfringens* toxin and – Staphylococcal enterotoxin B. A subgroup of List B agents include food- and waterborne pathogens. Without claiming to be complete, the following are listed: *Salmonella species, Shigella dysenteriae, Escherichia coli O157:H7, Vibrio cholerae* and *Cryptosporidium parvum.*	*Agents* – Nipah viruses – Hanta viruses – Haemorrhagic fever viruses – Yellow fever – Multiresistant *Mycobacterium tuberculosis.*

→

Table 2.14:

Classification of critical biological agents.

Source: CDC Emergency Preparedness & Response.

Transmission in drinking water

A further potential risk is release in → **drinking water.** In the case of large water supply companies, drinking water is supplied to as many as one million people. In large cities such as Paris more than eight million people are supplied with drinking water. Only certain microorganisms can be spread in drinking water, such as *Bacillus anthracis*, salmonellae, shigellae, *E. coli O157:H7, Vibrio cholerae, Cryptosporidium parvum* or noroviruses.

→

The spread of pathogens as aerosols presents the most serious hazard for the population. A further potential risk is their transmission via drinking water.

Natural outbreaks have highlighted the considerable scope for spread in drinking water. Attention has already been drawn to the biggest drinking-water-associated outbreak of infectious diseases in Milwaukee, USA, in 1993. This gave rise to over 400,000 cases of severe diarrhoeal infections in the population of Milwaukee (*see Chapter 2.3*).

A number of waterborne pathogens can only be controlled to an extent by the classic disinfection procedures such as chlorine or chlorine dioxide. Cryptosporidia are highly resistant to chlorine and can survive chlorine concentrations of more than 80 mg for a long period of time. Noroviruses are also endowed with high chlorine resistance. It must also be borne in mind that over 50 % of the German water supply companies no longer use chlorine for disinfection purposes. This means that selective release of pathogens, including after decontamination measures in the water network, can pose major risks which can no longer be controlled by classic disinfection procedures.

Therefore the possibility of transmission in drinking water must be taken more seriously when contemplating risk scenarios than has been the case hitherto. The reality is that the spread of suitable pathogens within the water supply system **cannot be controlled.**

Transmission in foodstuffs

To what extent the spread of pathogens, e.g. in the form of botulism toxin, could be achieved in **foodstuffs** is a matter of speculation.

This means that the spread as aerosols or in drinking water must be viewed as presenting the most serious hazard to public health.

Prevention

In terms of prevention and control, CDC identified in 2000 the following main areas (*see also Chapter 3.3.3*):

- Preparedness and prevention
- Detection systems and surveillance
- Diagnosis and characterisation of biological agents
- Establishment of efficient control systems and communication systems.

The most important detection systems (Bravata et al. 2004) include:

- Anthrax Sensor
- BioCapture
- Digital Smell/Electronic Nose
- Fluorescence-based array immunosensor
- LightCycler; Ruggedized Advanced Pathogen Identification Device (RAPID)
- MiniFlo
- Model 3312A Ultraviolet Aerodynamic Particle Sizer (UV-APS) and Fluorescence Aerodynamic Particle Sizer-2 (FLAPS-2)
- Sensitive Membrane Antigen Rapid Test (SMART) and the Antibody-based Lateral Flow Economical Recognition Ticket (ALERT).

2.7 Pandemic infections

Epidemiology

Pandemic outbreaks of infectious diseases encompassing many countries or, indeed, the entire globe, can pose a threat to the entire world population. Certain infections such as **smallpox, plague, typhoid fever** and **cholera,** which had formerly often triggered pandemics, have now largely forfeited their pandemic potential. For a long time it was thus believed that it was possible to keep the risk of pandemics under control. But even cholera can present an imminent hazard, as borne out in 1991, when cholera was introduced into South America, which for decades had been free of this disease, going on to be transmitted in the water as far as the frontiers to the USA.

AIDS, too, must be viewed as a pandemic even though in this case large sections of the population have not suddenly become infected. The year 2003 witnessed the advent of **SARS (Severe Acute Respiratory Syndrome)** a new respiratory infectious disease whose aetiological agent was initially unknown. Unlike AIDS, thanks to excellent cooperation coordinated by **WHO** it was possible to identify this agent as a **coronavirus**. By taking appropriate measures, in the light of the ecological properties of the coronavirus, and restricting travel, further spread of this infection was controlled within a short time.

Influenza

From a present-day perspective, **pandemic influenza** poses the greatest threat. Each year there are more or less severe cases of seasonal influenza epidemics, generally originating in Southeast Asia where new strains of virus, infectious to humans, emerge because of genetic mutations in the virus.

The close **contact** between **humans and animals** in Southeast Asia and poor hygiene conditions are driving the continual adaptation of new viruses to humans too, thus presenting a risk of potential spread to humans.

Since 1918 three strains have triggered major pandemics, causing millions of deaths in each case. The implicated strains were:

- H1N1 (1918) accounting for some 40 million deaths worldwide;
- H2N2 (1957) and
- H3N2 (1968), both causing an estimated 1–4 million deaths worldwide.

The pandemic H1N1 virus that emerged in 1918 is deemed exceptional in terms of its high pathogenicity and its ability to infect also young adults.

A smaller-scale pandemic occurred in 1977 when an H1N1 strain emerged that did not cause a high number of deaths and only partially replaced the H3N2 strain, hence H1N1 and H3N2 strains are circulating worldwide together with the far less pathogenic influenza B strains.

The natural reservoir of influenza A strains is diverse pools of viruses harboured by aquatic wild bird populations, known as **avian influenza** (AI) viruses. These viruses are well adapted to various aquatic species of birds, less so to other bird species and only rarely to humans or other mammals.

The main risks associated with the avian influenza virus reside in its potential to give rise to new pandemic strains. This is caused either directly by the virus or through → **recombination** of its genetic material (RNA) with the RNA of other viruses infecting humans or animals.

→
The main risks associated with the avian influenza virus reside in its potential to give rise to new pandemic strains. This is caused either directly by the avian virus or through recombination of its genetic material (RNA) with that of other viruses infecting humans or animals.

In 1997 there were a number of outbreaks among poultry caused by the highly pathogenic avian influenza virus strain that first emerged in Hong Kong. On that occasion A/H5N1 strains were isolated from both poultry and humans (with 8 cases of human infections and 6 deaths). This was also the first time that human-to-human transmission was seen as well as the first cases of occupational infections in medical personnel. This outbreak was contained by extensive control measures (slaughter, biosafety measures). It is thought that the virus strain had been circulating in China already prior to 1997. The virus belongs to a group of newly emerged viruses characterised by a pronounced genetic stability. They are able to infect a surprisingly large number of birds, and in some cases also certain mammals. The fact that they can be spread from one mammal to another poses major risks to public health. Towards the end of 2005 there was a markedly more extensive spread, accounting to date for over 140 cases of infection and a mortality rate of more than 50 %. Against the background of that spread, the World Health Organisation drew up Phase 3 measures.

Up till the present day, only in a few cases has transmission of the H5N1 avian influenza virus from poultry to humans been reported. In view of the fact that million-fold exposure of humans to this ubiquitous avian influenza virus will have taken place, it is thought that so far the risk of transmission to humans has remained low because of an inadequate level of **virulence** where transmission to humans is concerned. On the other hand, those human cases that did occur embarked on a fulminant course and are characterised by a **high mortality rate.**

However, there continues to be a very high **risk of recombination of an H5N1 virus with a "normal" human influenza virus** and of the emergence of a new H5N1 variant. This is especially true for southern and eastern Asia as well as for other countries where there is very close contact with poultry. In view of the fact that there is far less close contact between infected poultry and humans in European countries, Europe is unlikely to serve as the cradle of an H5N1 pandemic.

The major pandemics seen in the 20th century were attributable mainly to **antigenic shift in human influenza viruses.** The following factors are responsible for that happening:

- direct jumping of the species barrier;
- reassortment of entire gene segments; in that respect, birds and pigs too (because

the latter have binding receptors for both human and avian influenza viruses), serve as particulary efficient "mixing vessels ("commingling vessels") in "generating" newly combined viruses.

- a serious mutation; this too can give rise to greatly altered influenza viruses; as such, close contact with pigs, or with birds, can play a pivotal role in the emergence of such pandemics.

The preconditions needed for the emergence of a pandemic are assured if influenza A viruses emerge in which antigenic shift has taken place and if these viruses

- are pathogenic and virulent,
- can be spread from person to person,
- encounter a human population where at least broad sections of it have no, or inadequate, immunity to viruses harbouring these greatly modified surface antigens.

How great is the probability of adaptation, recombination or mutation to a pandemic strain that is highly virulent to humans is something that at present cannot be reliably predicted. But this should not mean failure to take appropriate countermeasures.

The epidemiological implications of even "normal" influenza are considerable.

Based on data from the German Pandemic Influenza Plan II, the number of medical consultations because of influenza infections in an average season are in the range of 3 to 5 million, while the number of hospital admissions because of influenza are between 10,000 and 20,000 and the number of influenza-related deaths between 5,000 and 8,000. Here it was revealed that while this infection equally affects all age groups, but with a slightly declining trend compared with the elderly population, it is **young children** and the **elderly population** that are at highest risk for **hospital admission** because of influenza, and influenza-related **deaths are seen almost exclusively in the elderly population.**

Just as suggested by the data showing the effects of pneumococcal and meningococcal immunisations, so it must be assumed that children play a pivotal role in the further spread of influenza, and as such in the dynamics underlying the influenza waves. Accordingly, in the past it has been observed in Germany time and again that the winter school holidays taking place during the 6^{th} to 8^{th} calendar week had delayed onset of the influenza wave in the new federal states, which by that time had already begun in the old federal states. The findings gleaned from pneumococcal vaccinations and the incidence of invasive pneumococcal infections also attest to the role of children as the **transmission vehicles of infections**. Based on data from the Robert Koch Institute, surveillance of invasive pneumococcal infections in just below 19 million US inhabitants before and after the introduction of general immunisation with the 7-valent pneumococcal conjugate vaccine for children up to the age of 2 years showed its beneficial effects also for the adult population, in terms of **herd immunity**. These data revealed that the incidence of invasive pneumococcal disease declined among adults as from age 50 years from 40.8 to 29.4 infections/ 100,000 of the age group (minus 28 %). The incidence of invasive pneumococcal disease caused by serotypes covered by the 7-valent pneumococcal conjugate vaccine declined from a total of 22.4 cases to 10.2 cases of infection/100.000 of the age group (minus 55 %). These insights are of paramount significance for **prevention strategies**.

Of **epidemiological** significance is the fact that the three major pandemics that occurred during the 20th century were heralded by an initial, weaker wave, preceding the main wave by about 4–6 months. For that reason it is believed that viruses of the pandemic strain had circulated already for a few months before the epidemic really took off. As regards the 1918 pandemic, Pandemic Plan data would seem to indicate that up to 50 % of the world population had been infected and 25 % of the world population became ill. Observations in respect of the other pandemics, too, put the estimated → **number of cases of disease at between 30 and 50 %.**

→
Observations in respect of the major pandemics of the 20th century put the estimated number of cases of disease at between 30 and 50 %.

Estimates of effects based on model calculations are only of limited value. For a pandemic scenario with a 15% infection rate and without treatment or prophylactic measures it has been estimated that in an 8-week period there would be more than 6 million medical consultations, approx. 180,000 hospital admissions and 48,000 influenza-related deaths. With a 30 % infection rate, there would be 13 million additional medical consultations, 360,000 hospital admissions and 96,000 deaths. With an infection rate of 50 %, these figures rise to above 21 million extra medical consultations, almost 600,000 hospital admissions and up to 160,273 deaths. These figures highlight the importance of **proactive formulation** of a Pandemic Plan.

In terms of **clinical manifestations,** the 1918 pandemic was characterised by a severe, but typical clinical picture. There were reports of bluish skin changes, beginning around the mouth. Bleedings from the mouth and nose were also frequently reported. In the case of patients with a fulminant course of disease, the interval between admission to hospital and death ranged from a few hours up to 2–3 days. Post-mortems showed no signs of secondary bacterial inflammation. The bloody, foamy fluid in the lungs was more suggestive of pneumonia caused directly by the influenza virus.

When drafting a → **Pandemic Plan,** the criteria underlying **onset, transmission, clinical picture and immunisation possibilities** must be taken into consideration in the overall concept.

→
When formulating prevention strategies, the criteria governing the onset, transmission, clinical picture and immunisation possibilities must be taken into consideration.

There is a consensus between WHO and the originators of the various national guidance plans and of the German Pandemic Plan that the following constitute the most important criteria for prevention and control:

- Phase classification of the epidemic phases
- Surveillance
- Vaccination
- Antiviral drugs

- Communication and cooperation
- Infection control and hygiene management
- In-house hospital management, communication and information
- Implementation.

3 RISK MANAGEMENT

General aspects 3.1

General aspects of risk management,
Multi-barrier strategy

3.1 General aspects

Effective strategies aimed at prevention and control consist of myriad individual strategies which together create a **multi-barrier strategy.** Multi-barrier strategies complement each other and ensure that despite the failure of a single barrier other barriers incorporated into the system will prevent or control health risks and infections. The aim here is to reduce to a minimum the demands made on the individual as well as on the general public.

Prevention measures are *proactive* measures that serve not only to prevent an infection from progressing to a stage where it is clinically manifested but to eliminate and control existing infection reservoirs, prevent transmission of infection to people (*pathogen-specific prevention*) or to boost the immune system through e.g. vaccinations, so that despite infection there is no ensuing infectious disease (*host-specific prevention*).

Control measures are measures taken *after* onset or manifestation of a clinical infection. These include rapid clinical diagnosis, microbiological diagnosis, choice of appropriate treatment and the prevention or curtailment of further spread. Diagnosis, acquisition of epidemiological data as well as surveillance and analysis belong to the remit of control measures.

Prevention and control are embedded in an **infrastructure** of institutions for hygiene and medical microbiology, public health structures and scientific institutions providing for vigorous **research**. Furthermore, **communication** as well as **implementation** of appropriate strategies are decisive pillars in the overall system of prevention and control measures → **Figure 3.1**.

The system aimed at prevention and control begins with controlling the infection reservoir, the release of the infectious agent and its ecological characteristics in the environment, the transmission channels, host invasion, the host's immune response to the pathogen, development and manifestation of disease. In terms of control, it begins with medical ascertainment and diagnosis, going on to epidemiological surveillance, treatment and, in the event of any unusual cluster formation, efficient outbreak management structures. These approaches are embedded in a system of research, communication and structures aimed at implementation and assurance of suitable, effective prevention and control measures.

Since the publication of the first "Memorandum on the Threat Posed by Infectious Diseases" (1996) a number of key, **very positive developments** have taken place in Germany **for prevention and control of infectious diseases**.

This includes:

– A modern, well-structured → **Protection against Infection Act** that grants broad scope to prevention and has extended the obligation to report a number of important pathogens

→
In terms of health policy, positive developments include, inter alia:
- **Introduction of a modern Protection against Infection Act**
- **New structuring of the Robert Koch Institute**
- **Award of legal powers to important infection epidemiological commissions (STIKO, KRINKIO)**
- **Reinforcement of surveillance.**

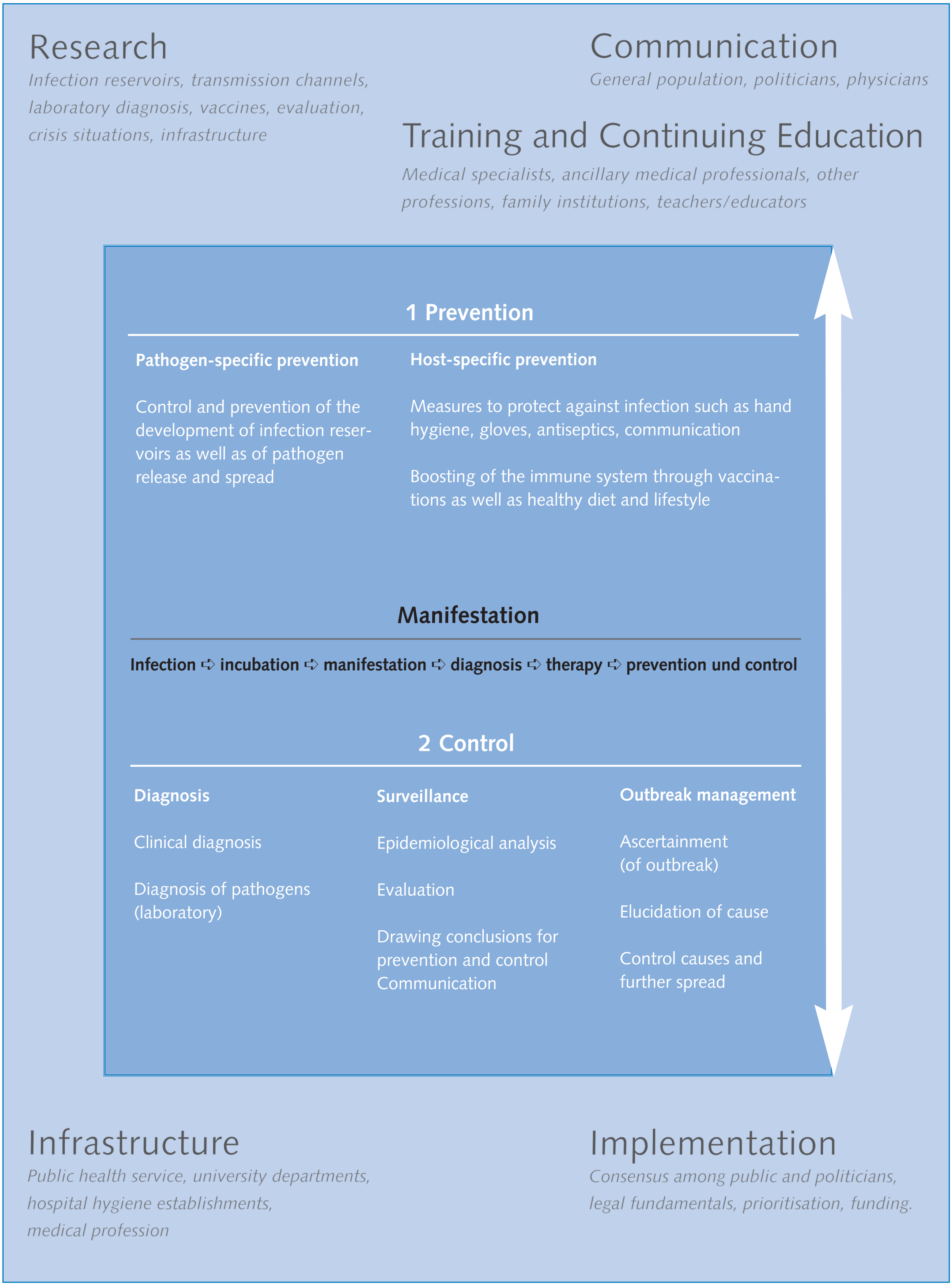


Figure 3.1: Risk management through prevention and control of infectious diseases

– New structuring of the Robert Koch Institute with clear assignment of tasks aimed at formulation of prevention concepts for communicable and non-communicable diseases, backed up by an infrastructure of good scientific personnel which has received much recognition
– Publication of the *Epidemiologisches Bulletin* (in German) with the latest information for the public health service and for all institutions involved in prevention and control of infectious diseases:
– Award of legal powers to important commissions at the Robert Koch Institute (RKI) such as the
  • the Standing Committee on Vaccination (STIKO) at the Robert Koch Institute
  • the Commission for Hospital Hygiene and Infection Prevention (KRINKO). The recommendations issued by both commissions have achieved considerable importance for prevention and control of infections;
– Improvement of surveillance and epidemiology in Germany, constituting the scientific database for evaluation of the significance of infectious diseases and of the requisite measures.

However, leaving aside these very positive aspects, there are still **deficits**, such as
– An infrastructural → **dismantling of state institutions** which had been entrusted with duties aimed at prevention and control of infectious diseases, and which dispose of laboratory-analytical competence in several federal states
– Diversification of federal institutes, leading to, in some cases, competing competences and loss of corporate identity
– Cutting back on the public health service and, in particular,
– Weakening of the structure on which hygiene (infection control) institutes and microbiology institutes are based, which had previously been assured by, for example, the fact that they were entrusted with the duties of a Medical Test Centre (*Medizinaluntersuchungsstelle*). In situ monitoring of disease with the latest molecular technologies and required level of efficiency is greatly endangered
– Weakening of the universities with the abolition of chairs for hygiene and in the meantime also for microbiology, which means that education, training and continuing professional development are no longer adequately assured in the field of modern-day hygiene;

→
Shortcomings include, inter alia:
– diversification of federal institutes
– weakening of the structure on which infection control institutes and microbiology institutes are based
– abolition of chairs for hygiene and medical microbiology.

With regard to the measures required in future for prevention and control of infectious diseases, attention is drawn to the document compiled by the European Academies Science Advisory Council (**EASAC: "Infectious Diseases – Importance of Coordinated Activity in Europe"**). The issues elaborated on therein will be addressed below.

It has been demonstrated that the lack of suitable prevention and control strategies for infectious diseases has vast health and economic implications, as clearly demonstrated by the World Health Organisation not only in the case of influenza, but also of SARS, cholera epidemics or HIV, nosocomial, water- and foodborne infections.

Below are given suggestions for improving strategies relating to prevention, control and the infrastructure.

3.2 Measures for infection prevention

3.2.1 Prevention through control of infection reservoirs

The main infection reservoirs for important infectious diseases include

- The human host
- Animals
- The environment such as water, soil, air
- Foodstuffs
- Instruments and surfaces.

→ **The main reservoir for infectious organisms that are pathogenic to humans is the human being. In addition, animals, the animate and inanimate environment as well as foodstuffs play a key role.**

The → **human being** is the most important infection reservoir for infectious organisms that are pathogenic to humans. The role of children as infection reservoirs for pneumococci and meningococci has been impressively demonstrated through the effects of immunisation against pneumococci and meningococci. By availing of such vaccinations the rates of pneumococcal infections can be reduced among adults too (STIKO 2006). There are ample data to attest to the role of healthcare workers and patients in the transmission of nosocomial infections.

There can be no disputing the importance of sexually transmitted diseases such as AIDS, syphilis, gonorrhoea, and infections with *Chlamydia trachomatis* etc.

Measures aimed at prevention and control of the human infection reservoir include:

- Education
- Appropriate personal hygiene practices
- Training
- Disinfection measures such as hand disinfection
- Protective measures (gloves, orofacial masks) and in particular immunisation measures.

Animals are important infection reservoirs, in particular in relation to avian influenza, but also to a number of other bacterial and viral infectious diseases (Cotruvo et al. 2004). Here, too, strategies to prevent transmission are of paramount importance.

The role of the **environment** as an infection reservoir for pathogens is equally of importance for certain microorganisms.

Several waterborne pathogens have been identified, such as legionellae and pseudomonas, which have their own independent infection reservoir here as well as other pathogens, especially those shed in faeces via effluent leading to contamination of the water. There are established measures aimed at control of effluent- and water-associated pathogens.

Foodstuffs, especially those that may be contaminated because of their animal origin or in which pathogens can grow due to improper handling, are also important infection reservoirs that, in principle, are amenable to prevention and control strategies.

3.2.2 Prevention through curtailment of transmission

3.2.2.1 Good hygiene practices

Human pathogen shedding can be effectively controlled through **good hygienic practices** when coughing, sneezing, speaking, etc, thus preventing transmission. However, this calls for commensurate education and training. Pneumonia and diarrhoeal rates can be markedly reduced by improved hygiene practices such as better observance of hand hygiene (IFH 2007). As regards sexually transmitted infections, **education and condom usage** are of paramount importance. In the light of these findings, it is vital to provide ongoing, unrelenting instruction, already during childhood, in particular in respect of AIDS.

3.2.2.2 Hand hygiene

Much progress has been made where hand hygiene is concerned. The widespread introduction of **alcoholic hand disinfection** in the healthcare sector is a very effective instrument for interruption of the infection chain, assuring a microbial count reduction that is essentially greater than that achieved by handwashing (IFH 2007).

3.2.2.3 Hospital hygiene

When it comes to hospital hygiene there are myriad important operational / organisational and structural / functional measures, as described in the guidelines governing hospital hygiene and infection control (RKI 2004).

3.2.2.4 Animal and stable hygiene

For animal hygiene, measures aimed at optimising stable conditions are decisive.

The global hazard presented by influenza, and not just by avian influenza, is ultimately a problem emanating from cohabitation of humans and animals (pigs, poultry), mainly in Southeast Asia, where under such conditions of close contact between people and animals new variants of pathogens and influenza viruses are being selected time and again.

The risk of **zoonoses** could be greatly reduced by improving stable hygiene and ensuring that there is no close contact with high-risk animals. To that effect, **legal regulations**, in particular, are needed to launch education campaigns and ensure that the appropriate structural and functions requirements are met.

3.2.2.5 Water and food hygiene

By now, there are ample data available to attest to the key role of water as an infection reservoir and pathogen transmission channel. This risk can be controlled by amending the regulations in place for water decontamination. **New decontamination technologies such as UV disinfection as well as above all membrane filtration techniques** based on ultra- and nanofiltration have in recent years brought about a quantum leap in the field of decontamination technology. These technologies reduce bacterial, viral and parasitic counts by >6 log levels and, as such, assure the best reduction performance noted for any decontamination method, whereby for example a reduction of only <2 log levels is achieved using the classic flocculation filtration method. Using membrane filtration systems, effluent can be treated such that the decontaminated effluent is of bathing water quality. Such membrane technologies have in the meantime become the gold standard for effluent treatment in large cities.

However, these methods have to be adapted to permit detection of other, potentially waterborne, pathogens. This includes detection of *Cryptosporidium, Giardia, Campylobacter* and viruses already in the untreated water. At present, there is no such policy in place as regards German drinking water hygiene. This is something that is urgently needed. This section of the → **Drinking Water Regulation** must be amended in the light of this present-day knowledge.

→ **Detection of pathogens such as** ***Cryptosporidium, Giardia, Campylobacter*** **and viruses should be conducted already in the untreated water. The Drinking Water Regulation must be amended in the light of this present-day knowledge.**

Apart from **overhauling the detection technologies and the indicator concept for microorganisms in drinking water**, the risks posed by the water distribution system must be systematically eliminated, while testing and monitoring the water for legionellae and other pathogens, e.g. especially pseudomonas. The recommendations issued in this respect by the Federal Environmental Office after consultation with the Drinking Water Commission are useful.

But a shortcoming encountered here is the supervisory structure in place in Germany. By now the number of government institutions with expertise in this field has been reduced.

Furthermore, in Germany increasingly more private, commercial laboratories and water supply companies have been entrusted with analytical tasks, thus supplanting or limiting the scope of independent, university-based scientific laboratories, which in the past had assumed the role of a Medical Test Centre. In particular in the case of the smaller or medium-sized water supply companies there is considerable need in Germany to optimise supervision of the incidence and management of outbreaks.

→ **Supervision of water supply companies should be entrusted to independent scientific laboratories. In Germany much needs to be done to supervise the incidence and management of outbreaks.**

It is necessary that → **independent hygiene institutes, in particular those based at the universities,** become more involved in routine monitoring or as appointed bodies in line with the provisions of the Drinking Water Regulation. Only in this way can provision be made for a new generation of scientists who can be trained to meet the demands of everyday practice.

Furthermore, **new molecular microbiology diagnostic techniques** going beyond the spectrum of the classic bacteriology must be established.

In global terms, optimisation of drinking water supplies must be given top priority. This situation has major shortcomings right up to the present day in many parts of the world, even in developed countries. The situation in developing countries is a catastrophe, where there is no political awareness of this problem and the general legal framework as well as the expertise needed to supply safe water are lacking.

The World Health Organisation has recognised the significance of this critical situation, going on to usher in the **"Water Decade from 2005 to 2015"** aimed at bringing about major improvements in water supplies worldwide. But much effort is needed to accomplish this, and the expertise available in Germany must be exploited much more so as to provide a sustained system of support.

Of all the hygiene measures that could be put in place to date to prevent foodborne infections, only a few have been availed of in Germany. While in the current reports of the rising figures of *Campylobacter jejuni* infections (RKI 2007), on the risk posed by EHEC infections through game meat (Federal Institute of Risk Assessment) as well as many other reports of foodborne disease outbreaks, it is pointed out by the authorities that specific hygiene recommendations are of paramount importance for manufacturers, food inspectors and the consumer, the majority of foodborne infections could be avoided by observing good hygiene practices in the kitchen as well as hand hygiene. But the knowledge needed to assure good hygiene practices during transportation, storage and processing of foodstuffs is not systematically imparted in a standardised fashion to the consumer in Germany.

3.2.2.6 Disinfection

Disinfection procedures play a key role in prevention of pathogen invasion and spread. However, the role of disinfection has in the past been generally called into question time and again in Germany. To an extent, this was due to worries about environmental pollution or to the lack of evidence of its role in reducing infection rates or to a desire to cut costs. This **negative view has led to a general rejection of disinfection practices instead of fostering a well-differentiated approach**. It cannot be ruled out that the current dramatic increase in the MRSA prevalence in Germany and Austria is not linked to, inter alia, the declining use of disinfectants.

It was only the Recommendation by the Commission for Hospital Hygiene and Infection Prevention at the Robert Koch Institute "Hygiene requirements for cleaning and disinfection of surfaces", recommending **→ disinfection of surfaces coming into contact with hands,** both on general wards as well as in high-risk units, which managed to uphold a hygiene standard that had previously been jeopardised because of widespread confusion among users (RKI 2004).

→
In medical institutions disinfection, with tested disinfectants, of surfaces coming into contact with hands is an indispensable precondition for upholding a good standard of hygiene.

This example demonstrates how important it is to assure a uniform communication structure regarding infection prevention measures.

The **independent testing and evaluation of disinfection procedures** as practised in Germany in both human and veterinary settings serve as a role model. These accomplishments have been brought about in particular thanks to the Disinfectants Commission in the **Association of Applied Hygiene (formerly the German Society of Hygiene and Microbiology).**

With the exception of Austria and France, no other European country maintains such an official list of approved disinfectants. Furthermore, there is much variation in the extent to which disinfection procedures are established, and also as regards the disinfectants and concentrations used. The use of effective disinfection procedures rather than cleaning methods should be better promoted globally. **Research** in this area must be optimised, in particular in order to reduce the infection rate by using selected disinfection procedures.

Whereas Germany, for example, has been using alcohol-based hand disinfection for the past 50 years, this practice was introduced into the United States only in 2002 with the publication of the "Guideline for hand hygiene in health care settings" (CDC 2002). Since then the use of alcohol preparations for hygienic hand disinfection is being promoted increasingly and used on a global scale. This confers additional benefits over handwashing and contact-mediated infections can be controlled also in situations where there is no water available.

→
There is an urgent need for differential communication of the potential risks but also of the advantages conferred by disinfection.

It has, however, been revealed that in terms of the **risk perception** there are concerns about potential skin irritations, damage from inhalation as well as worries about adverse environmental effects. In addition to more research into these aspects, there is an urgent need for improved **→ risk communication** regarding the potential risks but also the advantages conferred by disinfection procedures.

In Phases 3–6 of its **Pandemic Plan for Preventing the Spread of Influenza**, the World Health Organisation recommends the following:

- Hand hygiene as a basic measure (handwashing)
- Disinfection of potentially contaminated surfaces in the household
- Good general hygiene practices.

Non-selective disinfection or disinfection of the air are not recommended in these phases.

3.2.2.7 Sterilisation

The German Medical Devices Act (*Medizinproduktgesetz* – MPG) and the German Medical Devices Operator Ordinance (*Medizinproduktebetreiberverordnung* – MPBetreibV) regulate the placement on the market and use of medical devices in terms of patient safety, including infectious risks. The Medical Devices Operator Ordinance serves as the basis for supervision, by the statutory authorities, of medical device decontamination in all areas of the healthcare sector, including the premises of commercial reprocessors.

In the German hospital hygiene sector, vast improvements have been seen in the field of decontamination and sterilisation thanks to the recommendation jointly drawn up by the Robert Koch Institute and the Federal Institute for Drugs and Medical Devices **"Hygiene requirements for decontamination of medical devices"** (RKI 2001). But this guideline has still to be implemented by doctors' surgeries.

In certain risk areas, such as in dentistry where, while the dental instruments e.g. hand and angled pieces, are properly decontaminated, this is not done after each patient. There is vast room for improvement here since, especially in cases where there is direct blood contact between different patients via instruments, **→ the risk of transmission of HIV, hepatitis B and hepatitis C** cannot be ruled out. The same holds true for decontamination of the instruments used for piercings and tattooing.

→
In certain risk areas instruments must be properly decontaminated after each patient. There is vast room for improvement here.

3.2.2.8 Social distancing measures

Social distancing measures mean the **spatial distancing of potentially infected persons** to protect other persons or voluntary avoidance of public contact in the event of pandemics. The World Health Organisation recommends, for example in pandemic situations, that symptomatic persons infected with influenza, voluntarily remain at home. One example in this respect is the avoidance of mass public gatherings.

3.2.2.9 Personal protective measures

Personal protective measures such as the wearing of gloves, orofacial masks and condoms play a key role in pathogen invasion and spread.

Proof has been furnished of the benefits of **protective gloves** when carrying out contaminated tasks or duties involving the handling of potentially contaminated blood. But there is a risk of further spread through contaminated gloves. For example if gloves worn in risk areas such as in dialysis units are not replaced between patients, healthcare workers can serve as a vehicle for transmission of HBV, HCV and HIV. In such cases, gloves merely protect the wearer.

Orofacial masks can be important both in terms of pathogen release in the case of clinically manifested infections but also for protection against pathogen invasion.

Hence, in its pandemic influenza plan, the World Health Organisation recommends the use of orofacial masks for symptomatic persons and their possible use by exposed persons, depending on the proximity to potentially infected persons and the frequency of exposure.

Today, the use of **condoms** is one of the most important measures for protection against sexually transmitted infections, including HIV. Their widespread use in developed countries has made a large contribution to controlling the spread of HIV, and if consistently used could achieve a preventive effect on a par with that assured by immunisation.

The measures outlined for controlling the infection reservoir, pathogen release, curtailment of transmission and pathogen invasion call for good communication, education and training. On their own they constitute effective measures, something that is often underestimated, especially in the case of those infectious diseases that are hardly amenable to other forms of control, for which there is no treatment, are highly infectious and which cannot be controlled, or controlled on time, by vaccination. In any case, they will complement any other specific measures.

→
In Germany the effectiveness of measures for controlling the infection reservoir, pathogen release and curtailment of pathogen transmission are often underestimated. There is also need to improve communication and implementation of personal protective measures.

→ Communication and implementation have not been adequately practised in Germany to date. As a result of this, public acceptance is low despite the fact that such measures, for example in the case of an influenza pandemic, can play a key role. Practices in Germany are diametrically the opposite of those recommended by the **World Health Organisation** and also by the USA's **Centres for Disease Control and Prevention**, which recommends intensive training measures, e.g. handwashing and hand disinfection even in the workplace and in schools.

3.2.3 Immunisations

3.2.3.1 Availability of vaccines, efficacy, cost-benefit relation

Immunisations confer specific immunity to specific pathogens. **They protect both the vaccinee and the general public** against specific infectious diseases, since the vaccinee can no longer shed or transmit the respective pathogen and, as such, can no longer act as an infection reservoir. Hence immunisations are among the **→ most effective and affordable preventive measures** of modern medicine. In addition, immunisations prevent the occurrence of epidemics.

→
Immunisations are among the most effective and affordable preventive measures of modern medicine.

→ Table 3.1 lists vaccine-preventable diseases in accordance with the year when a vaccine was developed or licensed in the United States between 1798–1998. **→ Table 3.2** compares the average morbidity baseline values during the 20th century with the provisional morbidity data for new diseases that could be prevented by vaccines recommended for general use for children in the USA before 1990.

Virtually no other medical intervention has such a favourable **cost-benefit relation as** immunisation. With high vaccination uptake rates pathogens can be eliminated regionally, and then globally eradicated as seen in the case of smallpox which, as per the official World Health Organisation declaration has been eradicated since 1980.

A comparison of the cost effectiveness of 500 lifesaving measures in the USA revealed that the childhood vaccinations recommended cost less than 1 US dollar per life year saved. The cost-benefit index for measles vaccinations is given as 1:32. Thanks to immunisation with the acellular pertussis vaccine some 225 million euros are saved in Germany each year alone in terms of direct disease-related costs (Reiter and Rasch 2004).

Standing Vaccination Commission at the Robert Koch Institute
The recommendations issued by the **Standing Commission on Vaccination (STIKO)** at the Robert Koch Institute play a pivotal role in assuring a uniform strategy in Germany where immunisations are not mandatory. The recommendations and vaccination schedule, used by the majority of the German federal states, are contin-

ually updated. The vaccinations generally recommended by the *STIKO* for children, adolescents and adults are paid for by most statutory medical insurance companies. Pursuant to Section 15 of the Biological Substances Regulation (*Biostoff-Verordnung*), the employer must offer employees the opportunity to have vaccinations if they face a considerably higher occupational risk.

However, the costs of travel vaccinations, or of any related passive immunisations, are no longer borne by the German statutory medical insurance companies.

The **general practitioner** plays a key role in carrying out and assuring a high vaccination uptake rate. It is estimated that 85–90 % of vaccinations are administered by the general practitioner and 10–15 % by occupational medical services.

The standard immunisations recommended in Germany by STIKO as of July 2006 for infants, adolescents and adults are those to protect against the following:
- Diphtheria
- Pertussis
- Tetanus
- Haemophilus influenza type b
- Hepatitis B
- Poliomyelitis
- Pneumococci (for children under 2 years)
- Meningococci (for children under 2 years)
- Measles
- Mumps
- Rubella
- Chicken pox
- Adult influenza.

Based on *STIKO*, the following immunisations are indicated:
- Spring / summer meningoencephalitis
- Yellow fever
- Hepatitis A
- Pneumococci (see Standard Vaccination List)
- Typhoid fever
- Chicken pox.

At present, vaccination with the currently available BCG vaccine (TBC vaccine) is not recommended.

3.2.3.2 Implementation of vaccination recommendations in Germany and globally

High vaccination uptake rates are essential to assure a high level of health protection for the general population. The percentage of the population that must be vac-

Disease	Year
Smallpox	1798 +
Rabies	1885 +
Typhoid fever	1896 +
Cholera	1896 +
Plague	1897 +
Diphtheria	1923 +
Whooping cough (pertussis)	1926 +
Tetanus	1927 +
Tuberculosis	1927 +
Influenza	1945 *
Yellow fever	1953 *
Poliomyelitis	1955 *
Measles	1963 *
Mumps	1967 *
Bordetella	1969 *
Anthrax	1970 *
Meningitis	1974 *
Pneumococcal pneumonia	1977 *
Adenovirus	1980 *
Hepatitis B	1981 *
Haemophilus influenza type B	1985 *
Japanese encephalitis	1992 *
Hepatitis A	1995 *
Chicken pox	1995 *
Lyme disease	1998 *
Rotavirus	1998 *
Human papillomavirus	2006

+ vaccine development (first published results of vaccine use)
* vaccines licensed for use in the United States

→
Table 3.1:
Vaccine development and availability of vaccines in the USA.
Source: CDC 1999.

Disease	Baseline 20th Century Annual Morbidity	1998 Provisional Morbidity	% Decrease
Smallpox	48,164 a)	0	100.0
Diphtheria	175,885 b)	1	100.0 m)
Pertussis	147,271 c)	6,279	95.7
Tetanus	1,314 d)	34	97.4
Poliomyelitis (paralytic)	16,316 e)	0 k)	100.0
Measles	503,282 f)	89	100.0 m)
Mumps	152,209 g)	606	99.6
Rubella	47,745 h)	345	99.3
– congenital rubella syndrome	823 i)	5	99.4
Haemophilus influenza B	20,000 j)	54 l)	99.7

a) Average annual number of cases between 1900–1904.
b) Average annual number of reported cases during 1900–1922, 3 years before vaccine development.
c) Average annual number of reported cases during 1922–1925, 4 years before vaccine development.
d) Estimated number of cases based on reported number of deaths during 1922–1926, assuming a case-fatality rate of 90 %.
e) Average annual number of reported cases during 1951–1954, 4 years before vaccine licensure.
f) Average annual number of reported cases during 1958–1962, 5 years before vaccine licensure.
g) Number of cases reported in 1968, the first year reporting began and the first year after vaccine licensure.
h) Average annual number of reported cases during 1966–1968, 3 years before vaccine licensure.
i) Estimated number of cases based on seroprevalance data in the population and on the risk that women infected during childbearing year would have a foetus with congenital rubella syndrome.
j) Estimated number of cases from population-based surveillance studies before vaccine licensure in 1985.
k) Excludes one case of vaccine-associated polio reported in 1998 .
l) Excludes 71 cases of *H. influenza* disease of unknown sertoype.
m) Rounded to the nearest tenth.

→
Table 3.2:
Annual average morbidity (baseline value) for 9 vaccine-preventable diseases compared with the provisional morbidity figures after introduction of the corresponding immunisations in the USA.
Source: Modified as per CDC 1999.

cinated against specific infectious diseases to assure herd immunity varies in line with the respective infectious diseases.

Vaccination uptake rates in the general population of approx. 80 % assure herd immunity in the case of diphtheria, of 90 % for mumps and between 92–95 % for measles.

Despite the favourable preconditions and rising trend, vaccination protection against **measles, mumps and rubella is not still adequately assured in Germany,** in particular is not of a level to assure elimination of measles since only 30 % of children have received the prescribed second measles vaccination before entry into school, and in quite a few circles even the first vaccination has been given in far less than 80 % of cases. For that reason there are time and again measles outbreaks, e.g. as seen in the states of Hesse and North-Rhine Westphalia in 2005 and 2006.

Already in 2004 it was pointed out that considerable efforts were still needed to eliminate measles in Germany. Apart from the national situation, inadequate vaccination coverage in Germany could jeopardise the immunisation successes already scored in other countries such as the USA or Sweden since, just like other infectious diseases, measles is often exported to such countries by German tourists. Moreover, serological tests have revealed that there are still major vaccination gaps among German children and, often, they are vaccinated too late.

In a resolution adopted at the first meeting, held in Berlin on 18–19 May 2006, by the German-speaking countries and regions focusing on the elimination of measles and rubella, it was agreed that the most important single measure to boost vaccination uptake rates was → **the need for greater political support at all levels.**

→
To boost vaccination uptake rates, there is a need for greater political support at all levels.

In each of the German-speaking countries and regions the existing immunisation rates should be stepped up by:

1. Promoting public awareness
2. Formulating an action plan in line with the local regional circumstances
3. Implementing suitable measures at local and national level
4. Verifying the outcome of hitherto achievements (e.g. as regards monitoring of vaccination uptake rates and infection rates).

The activities needed here should comprise the following, in strict compliance with, and implementation of existing legislation on infection protection:

- Formulation of national strategies aimed at giving children greater rights where routine immunisations are concerned
- Strengthening surveillance of infection epidemiology, early detection, investigation and containment of outbreaks, provision of the requisite laboratory capacities
- Improvement of the data situation regarding vaccination coverage, in particular for children up to 24 months
- Intensification of epidemiological research and information exchange on successful immunisation strategies
- Extensive and well-directed communication strategies and public relations' campaigns to create greater public awareness of the benefits of vaccination and of the risks of failure to vaccinate
- Regular continuing professional development of medical personnel on the topic of immunisation
- Devise additional vaccination strategies targeted at non-vaccinees.

Among **adults** the greatest vaccination gaps are seen in the case of those who fail to have the recommended booster vaccinations against **tetanus and diphtheria**. Based on data from the Robert Koch Institute studies of the vaccination status of different population groups show considerable shortcomings. The reasons for poor vaccination uptake rates in Germany is not reflected mainly in the number of those who absolutely oppose immunisation, their number being estimated at less than 2 % of the population, rather based on the RKI data the main reason for poor vaccination acceptance resides in the **lack of experience or concern, regarding infectious diseases.**

The following factors were also identified by the RKI as other reasons for inadequate vaccination uptake rates:

- Lack of awareness of the hazards presented by infectious diseases
- Inadequate knowledge of the benefits and safety of, and need for, vaccination in broad sections of the general population and among some doctors

- The low status accorded to preventive medicine
- Failure to address this topic in the schools
- Confusion among parents caused by those opposed to vaccination
- Forgetfulness where booster vaccinations are concerned
- Inadequate use of doctor-patient consultations to verify immunisation status
- Fear of side effects
- Lack of standardised approaches to bearing costs by the medical insurance companies
- Uncertainty among doctors because of liability issues
- Poor remuneration for administration of immunisations
- Lack of cooperation among those participants coordinating immunisation efforts.
- Deficits in the knowledge base and training of some general practitioners.

→
In particular the advice given by a physician can largely determine willingness in the general population to accept a vaccination.

Studies have revealed that → **in particular the advice given by a physician can largely determine the willingness to accept a vaccination.** If advised by their doctor, 85 % of those surveyed would comply (Reiter and Rasch 2004).

The following measures are deemed necessary to boost vaccination willingness in the **German population**:

- Definition and consistent implementation of national immunisation targets
- Improvement of the data situation regarding vaccination and immune status
- Improvement in recording vaccination complications
- Ongoing updating of information for the medical profession
- Education campaigns tailored to specific groups in the general population, highlighting the benefits of, and need for, vaccinations
- Elimination of existing infrastructural impediments to immunisation.

The following messages must be spread to achieve high vaccination uptake rates for the **world population** and reduce the risk emanating from vaccine-preventable diseases:

- Immunisation has been proven to be an effective health-related interventional measure.
- Immunisation prevents suffering, disease and death on a large scale.
- Immunisation is one of the most cost-effective and efficient health-related interventional measure.
- Immunisation can strengthen the healthcare system.
- Immunisation confers economic advantages. It underpins the Millennium Development Goals through eradication of extreme poverty and achievement of universal primary education because immunisation protects the children's health so that they can complete primary schooling.
- Immunisation strategies are evidence-based and are of proven effectiveness.

The goals reached hitherto at global level thanks to immunisation are outlined below in relation to the respective infectious disease (WHO 2006).

Immunisation successes

Smallpox: smallpox was eradicated in 1977 following a 10-year campaign by WHO. At the outset of the eradication programme, 60 % of the world population was at risk for smallpox. One out of every four persons infected with smallpox died.

Polio: since the launch of the campaign by WHO and its partners in the Global Polio Eradication Initiative in 1988, the polio infection rates have declined by more than 99 % and some 5 million people have been rescued from polio-mediated paralysis.

Measles: measles has been largely eliminated from the American continent. Between 1999 and 2003 measles mortality dropped worldwide by around 40 %, from 873,000 deaths to 530,000 in 2003.

Neonatal tetanus: tetanus mortality has been reduced by three-quarters. The estimated number of deaths fell from 800,000 during the 1980s to less than 200,000 in recent years.

Hepatitis: in the future more than 600,000 hepatitis B-related deaths (due to liver cirrhosis and cancer) will be prevented each year through childhood vaccination. Thanks to coordinated efforts by WHO, Unicef and non-governmental organisations within the framework of the *Expanded Program on Immunisation*, it has been possible since 1974 to increase the vaccination uptake rate in children from around 5 to 80 %. It is believed that this has contributed to saving the lives of 3-4 million children yearly worldwide and protecting 2–3 million children against the sequelae of chronic hepatitis.

Pneumcocci: a randomised-controlled, double-blind clinical trial from the Gambia has demonstrated that in the group that received a pneumococcal conjugate vaccine there were 37 % fewer cases of pneumonia, 15 % fewer hospital admissions and a 16 % reduction in all-cause mortality as well as 50 % fewer laboratory-confirmed cases of pneumococcal pneumonia, meningitis and septicaemia. As such, it is thought that this pneumococcal vaccine is highly effective against pneumonia and invasive pneumococcal diseases and can greatly reduce hospital admissions.

→
1 billion US dollars per year will protect up to 2015 almost 70 million children each year against the 14 most important childhood diseases.

35 billion US dollars is the total figure needed to achieve a 90 % vaccination uptake rate in the 72 poorest countries between 2006 and 2015.
- **One-third of this is needed to purchase vaccines.**
- **Two-thirds will be spent on delivery systems, including improvement of the healthcare systems.**

3.2.3.3 Immunisation programmes

In 1974 the World Health Organisation launched the *Expanded Programme on Immunisation (EPI),* aiming at the following:

– Global eradication of polio
– Elimination of neonatal tetanus
– Reduction of measles deaths by 95 %
– Reduction of measles cases by 90 %.

Other target diseases are

– Hepatitis B
– Yellow fever.

Based on WHO data, 2.1 million people died in 2002 from vaccine-preventable diseases despite immunisation recommendations, of whom 1.4 million were children under the age of 5 years. Of the deaths among children, more than 500,000 were caused by measles, more than 400,000 by *Haemophilus influenza* type b (Hib), more than 300,000 by pertussis and 180,000 by neonatal tetanus. The estimated number of deaths due to rotavirus, meningococci, and pneumococci in 2002 was 2.1 million, of which 1.1 million involved children.

In 2005 the **WHO Department of Immunisation, Vaccines and Biologicals** was restructured in Geneva. This reststructuring measure brought together three principle functions discharged by this WHO department:

1. Innovation
2. Quality and safety of vaccines
3. Access to immunisation.

Global Immunisation Vision and Strategy (GIVS)
At the World Health Assembly in 2005 an ambitious new strategy (Global Immunisation Vision and Strategy (GIVS)) was developed by WHO and Unicef, and the aim is to achieve this between 2006 and 2015. The World Health Organisation believes that up to the year 2015, 4–5 million childhood deaths can be prevented each year through immunisation. GIVS has four main goals:

1. To immunise more people against more diseases,
2. To introduce a number of available new vaccines and technologies,
3. To provide for new interventions and surveillance systems with immunisation,
4. To manage immunisation programmes and activities in the context of global interdependence.

The principle single targets are:

– To reduce morbidity and mortality: by 2015, or earlier, the aim is to reduce global childhood morbidity and mortality rates related to vaccine-preventable diseases by up to two-thirds, using 2000 as a point of reference.
– By 2010, or earlier, the aim is to achieve an immunisation uptake rate of up to 90 % in the various countries.
– To reduce measles mortality: by 2010, or earlier, the aim is to reduce global mortality due to measles by 90 %, using 2000 as a point of reference.

With the support of the Bill and Melinda Gates Foundation, the World Health Organisation has expedited the development and introduction of the human papillomavirus (HPV) vaccine for protection against cervical cancer in women. Cervical cancer is the leading cause of cancer deaths among women in developing countries, accounting each year for up to 250,000 deaths in women. The vaccine against HPV infections was licensed in Europe in September 2006.

3.2.3.4 Vaccine development

It is believed that in the future the figure of 20 currently available vaccines will double.

The following vaccines have been newly developed:

- two rotavirus vaccines
- two meningitis vaccines
- a 9-valent pneumococcal conjugate vaccine which will reduce overall mortality by 16 %
- two human papillomavirus vaccines against cervical cancer
- one malaria vaccine showing 58 % efficacy against malaria in Phase II clinical trials
- one oral cholera vaccine showing almost 80 % efficacy in developing countries
- one vaccine against Japanese encephalitis.

Despite the numerous successes scored in terms of the availability and development of new vaccines, to date there is → **no vaccine against protozoal parasites** (malaria, giardiasis, cryptosporidiasis), **HIV** and only vaccines that confer inadequate protection against **tuberculosis**, and as such against the most important infectious diseases presenting a threat to mankind.

→ **Despite the numerous successes scored, to date there is no vaccine against protozoal parasites or HIV and only vaccines that confer inadequate protection against tuberculosis, and as such against the most important infectious diseases presenting a threat to mankind.**

The main impediments to the development of new life-saving vaccines are of a scientific, financial, technical and regulatory nature. The lack of an effective supply chain for vaccines and the shortcomings in the healthcare systems of many developing countries are additional challenges to be surmounted here.

One of the most important and urgent priorities in vaccine development is rapid development and production of a safe and effective vaccine against pandemic influenza. It is thought development of a safe and immunologically effective vaccine is possible against pandemic influenza but this must be done in the spirit of international coordination to avoid unnecessary duplication of effort.

Below are listed the factors deemed important, according to WHO data, for stepping up immunisation rates and for development of new vaccines in the future:

- Long-term sustained financial support for vaccine development and administration of vaccinations
- Political commitment
- Improved infrastructure for immunisation and the healthcare system in high-risk countries
- Access to population groups that are difficult to reach

- Make provision for trained healthcare workers
- Investment in the development of new vaccines and technology
- Increase participation by developing countries in vaccine research and development
- Effective surveillance of vaccine-preventable diseases
- Efficient distribution of WHO guidelines to all countries to underpin evidence-based decision-making processes
- Vaccine quality and safety, including the safety of injections
- Highly effective national regulatory authorities
- Communication of scientifically based information on the safety of vaccines
- Adequate supply of vaccines to cope with the growing demand for immunisation
- Surmount the challenges posed by internal and inter-country conflicts
- Preparedness for potentially imminent pandemics, such as influenza.

Germany bears considerable responsibility for implementation of a global immunisation vision and strategy, and must also show financial, political and scientific commitment to that effect.

Dr. Marie Paule Kieny, Director of the WHO Initiative for Vaccine Research summed the situation as follows (WHO 2006):

→ „These are exciting times in vaccine development. Several new products will soon be available that together could protect millions of lives from disease. However, experience has shown that the uptake of new vaccines is extremely slow. We urgently must find solutions to deliver these powerful and proven health tools to all people at risk.“

3.3 Control

Control measures are taken once an infection is already being incubated or is clinically manifested; these include all measures aimed at rapid diagnosis, treatment, epidemiological analysis, surveillance and control of further spread.

3.3.1 Clinical diagnosis

Microbiological diagnosis is based on either detection of the causative agent in a relevant clinical specimen or on detection of a reaction by the host to the pathogen (Relman 2003). In both cases, there is a broad range of techniques available **→ Table 3.3.**

New technologies have been introduced for microbiological diagnosis, which provide for an essentially more rapid diagnosis using molecular biology. While culture methods are of key importance, in particular in bacteriological diagnosis, they can be very time consuming and in life-threatening situations, e.g. especially in intensive care units, they cannot always guarantee suitable and timely treatment (Reimann 2003).

Direct Pathogen Detection	Indirect Pathogen Detection
Microscopy Culture Antigen detection Molecular biology methods: – Gene probes – PCR: real time PCR, quantitative, qualitative – Chip technology Chemical /physical techniques (e.g. MALDI-TOF)	Serology methods (e.g. complement fixation test (CFT) immunofluorescence test (IFT), ELISA, immunoblot) Acuity markers (IgM, IgA, avidity tests, intrathecal synthesis) Allergisation (RAST, Prick) Emission of IFN- IFN-y from sensitised T cells

→ **Table 3.3: Techniques used for clinical diagnosis of pathogens.**

Antigen detection using serology methods have made it considerably easier to identify various pathogens, such as *S. pneumoniae* antigen detection in urine (Sewell 2003), *Legionella pneumophila* antigen detection in urine (Lück and Helhig 2006, Stout 1997) or detection of viral or parasitic aetiological agents of gastroenteritis in stools (Sewell 2003).

However, these techniques soon reach their sensitivity detection limit since they do not entail an enrichment step and, as such, only those pathogen proteins already present in the sample can be detected.

Non-culture microbial detection methods were first introduced in virological diagnostics because of the onerous cell culture techniques or because so many viruses will not grow in culture. There are some microorganisms, e.g. hepatitis C virus (HCV), *Tropheryma whippelii, Bartonella henselae*, human herpesvirus 8 (HHV 8) and the sin nombre virus, which were first identified as pathogens by means of molecular biology methods (Nolte 2003). By now, detection of RNA or DNA has become a standard procedure for HIV, HBV and HCV infections as well as for diagnosis of severe infections caused by herpesviruses such as in the case of meningoencephalitis. PCR too, is now well established and standardised for certain bacterial pathogens that either cannot be cultured or if so grow only slowly, such as *T. whippelii, Bordatella pertussis or Mycobacterium tuberculosis* complex (Nolte 2003). While PCR is used on a broad scale for other indications, the necessary standardisation is not assured as borne out by the findings of multicentre trials (Reischl et al. 2005) and the CAPNET Study (Wellinghausen et al. 2006, Bauer 2006). Hitherto, the only technologies that have been able to establish themselves are those that produced far superior results to those of the corresponding conventional methods, which are too slow, lack sensitivity, are too expensive or are not available (Nolte 2003).

→ **Molecular biology detection methods confer several advantages especially for diagnosis of sepsis and meningitis. Microarrays are very promising, but pathogen diagnosis could be further speeded up using the MALDI-TOF technique.**

Molecular biology detection methods appear to lend themselves, in particular, to → **diagnosis of sepsis and meningitis** because of the limited number of microbes implicated in this condition and the potential relevance of any pathogens isolated from the blood or cerebrospinal fluid (CSF); such methods reduce the detection time by up to 6 hours. Real-time-PCR protocols and Chip technologies are being currently tested in studies but are not yet widely available (Klaschik 2004, Corless et al. 2001, Paule et al. 2005, Brozanski et al. 2006). Furthermore, there are still unresolved issues in respect of DNA detection since it is not only viable microorganisms that are picked up by this method. There are also constraints regarding other primarily sterile clinical specimens such as when it comes to diagnosing endophthalmitis from vitreous humor specimens (Carroll et al 2000).

Microarrays are very promising for species detection, resistance detection and pathogen characterisation. These are based on synthesis of oligonucleotides (probes) which are immobilised on a chip surface; bacterial DNA is then isolated and DNA fragments are amplified and concomitantly marked with fluorescent dyes or biotin. The DNA fragments hybridise to the probes, following which evaluation is carried out using a laser, or an SCC camera following binding of streptavidin; data processing is conducted after both these procedures (Shang et al. 2005, Witte und Curry 2005). Examples of such techniques include:

– Identification of polymorphisms in the betalactamase gene associated with the ESBL phenotype (Grimm et al. 2004).
– Identification and characterisation, including detection, of important resistance determinants from isolates from blood cultures (Shang et al. 2005), Cleven et al. 2006).
– *E. faecium* and *E. faecalis:* detection of antibiotic resistance genes and virulence genes (Witte und Curry 2005).

Detection of bacterial pathogens can be further speeded up using the **MALDI-TOF technique** (Schweickert et al. 2004). The term “Maldi” denotes matrix-assisted laser desorption ionisation mass spectrometry and “TOF” means *time of flight*. The sample is placed on a matrix, the molecules to be analysed are ionised through a “laser shot” and the ions are then quickly passed through an electrical field in the direction of a detector. The time of flight is measured as a parameter of the mass, and evaluation of mass peaks is carried out using a data processing program (Bonk 2001, Lay 2001). It is possible in principle to

– embed the amplified RNA/DNA in the matrix; after measuring the mass peaks the differences in sequences are identified by comparing them with sequences stored in databanks

or

– embed proteins in the matrix; after measurement, pathogens are identified by comparing characteristic peptide patterns in databanks (Bonk 2001, Lay 2001, Putsch 2005).

One particular advantage resides in the fact that measurements are completed in a fragment of seconds and, as such, several samples can be analysed within a short period of time. So far, it is available as an open diagnostic platform that is not restricted to any manufacturer. This technique can also be employed for postculture differentiation, and automated procedural steps have already been tested.

However, the large field of → **bacteriological diagnostics** continues to be dominated by **culture methods**. Following automation and miniaturisation of methods for differentiation and resistance testing, greater speed and enhanced standardisation are also seen here (Mohr 2003).

→
Culture methods continue to be the mainstay in bacteriological diagnostics.

But organisms must still be cultured from the original specimen, generally involving overnight culture. One advantage of culture techniques is the vast spectrum of microbes that can be detected, including unknown or unusual agents, provided that they will grow on the culture media used; they also provide for phenotype resistance testing and hence for identification of new resistance mechanisms. In the case of applications where molecular biology techniques have so far been able to replace culture, sensitivity can be predicted, thus obviating the need for testing (Nolte 2003). In addition, in many situations it is absolutely necessary to gain quantitative or semi-quantitative insights to distinguish between colonisation and infection of the cultured microorganisms or to evaluate the aetiological relevance.

A drawback is the time window associated with culture-based diagnosis because e.g. when treating severe pneumonia or bacteraemia delays of 24–48 hours in choosing the appropriate antibiotic regimen in line with diagnosis of the causative agent is associated with significantly higher mortality than when the correct treatment is given from the onset (Kollef 2006, Kang et al. 2005, Ibrahim et al. 2000, Chamot et al. 2003, Wheeler und Bernard 1999).

Furthermore, delayed diagnosis may also mean failure to take the necessary infection control measures in the hospital setting to prevent further spread. Everyday examples of this are delayed implementation of isolation measures if colonisation or infection of MRSA patients is diagnosed only at a later stage. Thanks to the development of 2nd generation culture techniques such as chromogenic MRSA selective media, detection has been reduced to 24 hours. The various MRSA PCR protocols are particularly suitable for screening risk patients. The sensitivity is not quite as high as that offered by culture (e.g. 325 cfus per swab, according to data from the firm BD /GeneOhm), hence a further specimen must be investigated in parallel in culture. However, the negative predictive value is so excellent (>95%) that in the event of a negative result the patient need not be isolated or any precautionary isolation measures already taken can be rescinded. Under optimal conditions, the detection time is 2–5 hours depending on the manufacturer.

A further example of how time can be saved is the introduction of hospital infection control measures following diagnosis of hepatitis C. Serology-based anti-HCV detection confers a diagnostic window of 80 days, whereas HCV infections can be picked up already after 14 days using PCR.

For that reason there is urgent need for more widespread use of techniques that provide for → **rapid diagnosis** in routine practice and to make physicians aware of this when they engage in continuing professional development.

→
There is urgent need to introduce into routine practice the currently available techniques for rapid diagnosis.

To a large extent infectious diseases are treated empirically with antibiotics without making a diagnosis. In many cases this approach suffices in the outpatient setting when carried out in accordance with the latest published guidelines, such as in the recommendations by the Paul Ehrlich Society for Chemotherapy. However, in cases of previous antibiotic treatment and in the presence of other risk factors such as immunosuppression, previous hospitalisation and chronic diseases, the initiated treatment regimes must be verified on the basis of a **specific diagnosis**. In the case of severe infectious diseases resulting in admission to hospital or of nosocomial infections, the diagnosis must also be backed up by microbiological investigations to assure optimal treatment and subsequent de-escalation (Kollef 2006, Kollef 1998).

→
The most important reasons for failure of empirical treatment are antibiotic resistance of the implicated pathogens. By using more rapid diagnostic methods it is not only patient mortality and hospital stay, but also antibiotic consumption, which can be reduced.

The most important reasons for failure of empirical treatment are → **antibiotic resistance** of the implicated pathogen, as evidenced by MRSA and, especially in patients in intensive care units, by multiresistant Gram-negative bacteria, e.g. with the ability to produce extended-spectrum betalactamases (ESBLs) (Kang et al. 2005, Ibrahim et al. 2000, Wheeler und Bernard 1999, Valles et al. 2003, Obritsch et al. 2004, Filius et al. 2005, Scarsi et al. 2006, Gold et al. 1996).

By using more rapid diagnostic methods it is not only patient mortality and hospital stay, but also antibiotic consumption, which can be reduced (Brozanski et al. 2006). In addition to the widespread use of new diagnostic techniques, it must be ascertained to what extent clinicians can be encouraged to aim at achieving specific diagnosis.

Numerous infectious diseases whose aetiology is known today from the use of diagnostic techniques and which could be satisfactorily treated **are no longer taken account of in medical diagnosis because of issues relating to specific diagnosis.**

The drawbacks inherent in the currently available microbiological examinations are the low yield and inadequate sensitivity and specificity as well as an unfavourable cost-benefit relation. To date, the guidelines, e.g. those governing diagnosis of pneumonia, advocate that the scope of diagnosis should be restricted to seriously ill patients or to patients at risk for rare and resistant pathogens. Hence, when it comes to → **research**, too, it is of paramount importance that the available microbiology diagnostic methods be tailored to the needs of specific diagnosis in terms of sensitivity, specificity and cost-benefit relation.

→
In respect of research, too, it is of paramount importance that the currently available microbiology diagnostic methods be adapted to the needs of specific diagnosis in terms of sensitivity, specificity and cost-benefit relation.

To protect against **bioterrorist attacks** new diagnostic techniques have been developed assuring very rapid microbiological diagnosis and differential diagnosis for various clinical manifestations. These insights should be introduced as quickly as possible into routine clinical practices (*see also Chapter 2.6*).

More extensive fine typing is needed for identification of potential infection reservoirs (Peterson 2001). This would mean that e.g. legionellae could be attributable to environmental reservoirs such as the water distribution systems, heat exchangers, hot whirl pools, etc., or for investigation of MRSA, outbreaks could be traced back to the original source of infection, e.g. among healthcare workers or other patients.

Phenotypic Methods	Genotypic Methods
Phage typing Serotyping Resistogram Biotyping Protein typing (immunoblotting) Multilocus enzyme electrophoresis	Pulsed field gel electrophoresis (PFGE) Arbitrarily Primed PCR (AP-PCR) Random amplification of polymorphic DNA-PCR (RAPD-PCR) Plasmid finger printing Restriction enzyme analysis (REA) Rep RCR PCR-RFLP Ribotyping Sequencing (e.g. Spa typing as sequence-based method)

→ **Table 3.4: Overview of pheno- and genotypic methods of fine typing.**

To that effect, **pheno- and genotypic methods** are available in principle → **Table 3.4.** Among the phenotypic methods, whose main drawback resides in the variability of the phenotypic expression of the characteristic of interest, phage typing is still used for characterisation of MRSA. But thanks to their enhanced reproducibility, preference is given to genotypic methods, such as pulsed field gel electrophoresis (PFGE), ribotyping, e.g. for mycobacteria and *Clostridium difficile*, PCR-based methods and sequence-based methods such as Spa typing of MRSA strains. At present there is no gold standard, i.e. a method endowed with adequate sensitivity and reproducibility to discriminate all strains and microorganism species but PFGE is the most widespread method currently used and comes closest to resembling an optimal typing method (Wichelhaus und Brade 2000, Tenover und Goering 1997, Oliv 1999, Soll 2003, Trautmann et al. 2005).

While reference centres have very good typing facilities for certain pathogens, in view of the sharp rise in certain potentially communicable or common microorganisms that require typing, consideration must once again be given to the establishment of reference centres for fine typing and surveillance at regional level. The emergence of a new, highly virulent strain of *Clostridium difficile* is one such example. Toxin detection in stools is not, on its own, enough to permit discrimination of this strain from other strains of this ubiquitous bacterium. This calls for, in addition to a rapid antigen test, culture followed by molecular typing (e.g. ribotyping or toxin analysis). But resistance to gyrase inhibitors is suggestive of this virulent strain (Bartlett und Perl 2005, McDonald et al. 2005).

Infection sources can be unambiguously identified and controlled by making better use of such typing methods for identification of infection sources. This, in turn, is a precondition for effective control of infection transmission (Peterson 2001, Becke and Martone 1997, Loo et al. 2005).

For clinical diagnosis more attention must be paid to the **specific characteristics of different age groups.** Elderly persons, in particular, exhibit a different pattern of bacterial colonisation and specific infectious diseases such as urinary tract infections or community-acquired respiratory infections, something that must be taken into account during differential diagnosis. The more often patients have been previously treated with antibiotics, the greater is the risk of acquisition and selection of resistant pathogens, whereas the number of antibiotics available fails to keep abreast of the growing resistance trends (Gold und Moellering 1996).

In view of the better understanding of the association between infectious diseases and chronic diseases, efforts must be stepped up to introduce microbiological tests not only **to diagnose acute infections, but also chronic infections**. Such links include the already-mentioned association between *H. pylori* and MALT lymphoma, HPV and cervical cancer, chronic HBV, HCV or HDV infection and liver cancer (Nolte 2003, Suerbaum and Michetti 2002). A number of tests are already available to evaluate the therapeutic options and response. Once again, molecular biology techniques play a pivotal role here, e.g. by measuring the viral load in HIV infection and identifying the genotype implicated in chronic HCV infections (Nolte 2003).

3.3.2 Surveillance

The term **"surveillance"** of infections denotes the **ongoing systematic registration, analysis and interpretation of the infection data** needed for planning, introduction and evaluation of medical measures. This includes passing on the latest data to those persons needing this information. Maintenance of such a database plays a key role in health-policy decision-making. In the case of nosocomial infections, **meticulous surveillance, as well established in the meantime, can help reduce infection rates, thus having a preventive effect.** This is attributable to the "Hawthorne Effect" that fosters awareness among those being observed, thus promoting correct hygiene practices.

The importance of using surveillance data was already stressed by Florence Nightingale in her **"Introductory Notes on Lying-in Institutions"** back in 1871 in, while referring to mortality data in various European hospitals (Vienna, Prague, Munich, Greifswald, Frankfurt, etc.). Already at that time she pointed out that these data could be used not only for an analysis of the prevailing situation, but also to elucidate under what conditions the best results could be achieved, and to use these insights to underpin preventive measures in the long term. Likewise back then she advocated that systematic surveillance of mortality data and infection data be introduced.

With the enforcement of the **Protection against Infection Act** in 2001, surveillance of infectious diseases was given a legal basis in Germany. This provided for single-case electronic reporting as per uniform case definitions as well as for rapid summarisation and analysis.

On the basis of the infectious diseases and pathogens listed in Sections 6 and 7, an exemplary mandatory reporting model was drawn up for various infectious organisms.

Mandatory reporting is complemented by sentinel surveillance systems that process the data recorded on a spot-check basis by voluntary healthcare establishments, such as doctors' surgeries, laboratories or hospitals, and provide data on diseases that are not covered by the Protection against Infection Act.

Apart from legal implementation, an excellent rapid reporting system was also devised at the same time and this will be available in all areas of the healthcare sector, also providing to an extent for geo-medical analysis.

In addition to its activities at national level, the Federal Republic of Germany has also supported **surveillance systems** at European and global level.

At **national level**, the following must be mentioned in particular: surveillance systems for recording nosocomial infections, CAPNET for recording community-acquired pneumonia – sponsored by the Federal Ministry of Health and Research, SepNet, the Sepsis Competence Network, the EHEC-Salmonellae infections recording systems, the active surveillance of Creutzfeld-Jakob diseases, active surveillance of rare paediatric diseases in Germany (ESPED) as well as the sentinel recording of the incidence of sexually transmitted infections in Germany.

Apart from the national networks mentioned, such surveillance system should also be used for other major entities such as → **gastrointestinal infections.**

→
Surveillance systems such as the national network for recording community-acquired pneumonia should also be used for other major entities such as gastrointestinal infections.

Among the information systems to be mentioned at **European level** are the following:

- The Early Warning on European Public Health Information Network – Health Surveillance and Communicable Diseases (EUPHIN-HSSCD)
- The European Network on Imported Infectious Diseases Surveillance (TropNetEurop)
- The International Surveillance Network for the Enteric Infections – Salmonella and VTECO 157 (EnterNet)
- The already mentioned European Antimicrobial Resistance Surveillance System (EARSS)
- The Surveillance Community Network for Vaccine Preventable Diseases within the EU (EUVAC)
- The European Working Group for Legionella Infections (EWGLI) introducing the European Surveillance Scheme for Travel Associated Legionnaire's Diseases
- The Surveillance of Tuberculosis in Europe (EuroTB)
- Hospitals in Europe Link for Infection Controls – Rules for Surveillance (HELICS III)
- The European Programme for Intervention Epidemiology Training (EPIET-Programme)
- The European Influenza Surveillance Scheme (EISS).

To be mentioned at **international level are:**

- The Global Influenza Surveillance Network (FluNet)

– The Global Salm-Sir (GSS; global network for surveillance of salmonellae)

– The Global Outbreak Alert and Response Network.

Provision should also be made to assure an appropriate infrastructure for the future, since the data generated is urgently needed not only for epidemiological purposes but also for outbreak management.

An important step in this direction is the adoption of **International Health Regulations** (IHR) agreed by the 193 WHO Member States (WHO 2007). The reporting system will in future feature not only certain diseases but all findings of relevance to international health protection, while also taking into account newly emerged pathogens, globalisation of trade and mobility among the population. The German Protection against Infection Act must be slightly amended to bring it into line with these requirements. Specialist personnel and appropriate institutions must be available to accomplish these tasks.

It must be advocated that data be used increasingly not only to describe the current situation, but also serve as the basis for critical analysis of the extent to which some countries, thanks to their comprehensive infection data, dispose of structures and prevention strategies that could also be implemented in other European countries.

→ **The existing networks in Europe should be used to identify, evaluate and incorporate into European prevention guidelines the best infection-prevention strategies.**

The currently available European networks coordinated by the **European Centre for Disease Prevention and Control** on the basis of agreed standardised data registration systems should be used to identify, evaluate and incorporate into → **Prevention Guidelines for Europe** the best infection-prevention strategies. By virtue of its manifold, sophisticated governmental infrastructures, this would mean that Europe would have an excellent opportunity to further refine such strategies.

Besides, different structures related to surveillance and mandatory reporting should still be gradually standardised in various European countries, so as to have robust data on infection-related issues in Europe as well as to enhance preparedness for outbreak investigation and outbreak management.

To provide for better characterisation of those infections associated with chronic infections, these infections must be better recorded in the future within the framework of sentinel investigations.

3.3.3 Outbreak and crisis management

Up till 1997 there was virtually no appreciation, not even among the experts, of the important role played by an effective outbreak and crisis management in public health protection. It has already been pointed out that in the first Memorandum on the Threat Posed by Infectious Diseases, published in 1996, the topic of bioterrorism was not addressed.

In an international context, the majority of infection control (hygiene) and public health institutions viewed biological and chemical deployment of microorganisms as being morally abominable. At that time there did not appear to be any major risks of infection outbreaks.

A publication in JAMA (6 August 1997), a special supplement devoted exclusively to the topic of biological weapons and associated risks (Zilinskas 1997), served as a milestone to focus interest on the topic of bioterrorism. Once again, the catalyst behind that publication was Prof. Josua Lederberg, Nobel prizewinner and former president of Rockefeller University who already back in 1992 had played a leading role in the publication of the positional paper by the Institute of Medicine on the topic of *"Emerging Infections – Microbial Threats to Health in the United States".*

In 2000 a strategic plan was published in the Morbidity and Mortality Weekly Report (MMWR) on preparedness and reaction to biological and chemical terrorism. The following were deemed by this publication to be the most important steps for preparing an efficient counterresponse to biological attacks:

- Expansion of the existing epidemiological capacity so as to identify and be able to react to biological attacks
- Provision of diagnostic reagents to public health institutions at government and local level
- Development of communication programmes to provide appropriate information to the public
- Improvement of training and continuing professional development courses for healthcare professionals in respect of bioterrorism
- Preparation of training materials to inform the public, too, and ensure that the requisite measures are taken by the public during and after biological attacks
- Stockpiling of appropriate vaccines and drugs
- Establishment of molecular surveillance for microorganisms, including unusual and drug-resistant strains
- Further development and availability of diagnostic tests
- More research into antivirals and vaccines.

Five key areas have been defined as regards prevention and control of not only biological attacks, but also in respect of natural catastrophes and crisis situations, e.g. wars.

1. Preparedness and prevention
2. Detection and surveillance
3. Diagnosis and characterisation of biological and chemical agents
4. Response
5. Communication.

→

The five key areas for prevention and control in outbreak and crisis management are:

1. Preparedness and prevention
2. Detection and surveillance
3. Diagnosis and characterisation of biological and chemical agents
4. Response
5. Communication.

The crisis situations that have in the meantime occurred such as

- Fears about a release of smallpox viruses during the second Iraq war
- The emergence of SARS as well as of avian influenza

led to the formulation of a National Pandemic Plan in Germany too; this was published in December 2004 by the Federal and State Governments. This Pandemic Plan must be continually updated. It addresses and regulates the following: epidemiological and technical issues, surveillance, vaccination, stockpiling of antiviral drugs, preparedness measures by the state governments, communes and hospitals and communication and information.

One of the **key requirements set out in the Pandemic Plan** is that the existing structures and human resources' capacities at federal and state level should be increased both to conduct epidemiological investigations, for rapid investigation of outbreaks, exploitation of laboratory capacities, administration of mass immunisation campaigns and for formation of crisis teams. However, Germany does not have a National Pandemic Commission.

→
Only some of the key requirements set out in the Pandemic Plan have been implemented so far.

Such fundamental structures call for investment. Despite the fact that the basic concepts are in place, and well set out in writing, **→ to date only some of the key requirements** for the relevant infrastructure have been met.

It must be greatly criticised that while smallpox vaccine was stockpiled to meet the demands of the smallpox alarm plan and provision made by influenza pandemic preparedness measures for antivirals drugs for around 20–30 % of the population, depending on the respective federal state, **investment in an infrastructure to improve epidemiology, surveillance, laboratory capacity and infection control management in the event of an epidemic has only been inadequately promoted.** This represents a major deficit which could have serious consequences in the event of a pandemic or a bioterrorist attack.

A further drawback is that **education and training campaigns on the necessary hygiene measures** have not been conducted **at population level** as vigorously as e.g. in the USA.

The situation in North-Rhine Westphalia, Germany's largest state, is particularly dismal. Here the responsible state authorities are left without any laboratory capacities and no plans have been made to provide the state universities (with their hygiene institutes and medical microbiology departments), with the requisite laboratory capacity and human resources' capacity to assist the healthcare authorities in epidemic management in the event of a crisis situation.

Up till now, the university-based institutes, and in some cases also private institutes, were involved in the management of suspected cases of anthrax attacks. However, funding issues have not been resolved so far.

→
The failure to invest in a clearly defined infrastructure for personnel and equipment capacities to deal with a crisis situation in Germany must be viewed in a critical light.

A clearly defined infrastructure must be assured for personnel and equipment capacities so that in the event of a crisis clearly defined alarm channels and clearly assigned competences as well as the requisite laboratory capacities are available for rapid diagnosis. Stockpiling of vaccines and drugs alone is not sufficient. The **→ failure to invest in the deficient infrastructure** must be viewed in a critical light.

In this regard, Germany differs from other important countries that have a functioning, central network of laboratories; if needed, such a network could back up the Robert Koch Institute at regional level. Without such a network it is not possible to assure preparedness or an effective reaction in crisis situations, and this could lead to a disaster. The availability of an appropriate infrastructure for surveillance, diagnostics and epidemic management must be viewed as the **Achilles heal** of a rapid and efficient reaction, which at present is by no means satisfactorily assured in Germany.

In times of war, natural catastrophes as well as refugee movements, safe water supplies and effluent and waste disposal services are interrupted and the healthcare facilities destroyed.

The risk assessment for the prevention and control of expected infectious diseases published in July 2006 by WHO in relation to the armed conflict in Lebanon exemplifies risk assessment and interventional measures with regard to communicable diseases (Mbabazi (WHO) 2006). Based on this publication, the following must be assured:

– Risk profile of the population
– Risk factors
– Priority communicable diseases
– Acute interventional measures for control of communicable diseases (water, sanitation, planning shelter, reliable food supplies, trauma and medical services, case management, surveillance, immunisation, vector control, risk communication and information for the population with messages for improved hygiene).

3.4 Research

Against the background of major global challenges, there is need for a **broad spectrum of research** into the prevention and control of infections. Research is needed in the following areas: pathogens, infection reservoirs, transmission and invasion channels, effectiveness of various prevention strategies, development of vaccines, diagnostics and therapeutics, role of chronic infections, infection management in complex situations, factors underlying the emergence of infectious diseases and the implications of infection diseases for the global health economy.

Based on the monograph drafted by the **European Academies of Science Advisory Council: Infectious Diseases – Importance of Coordinated Activity in Europe** (2005) the following research activities should be systematically analysed.

3.4.1 Pathogens

Pathogen-associated research areas include:

– Basic research on the genetic flexibility underpinning pathogenic properties
– Research on genetic information underlying a pathogen's ability to trigger disease

Research 3.4

- Evolution of genomes and pathogens leading to “reductive evolution”
- Acquisition of new gene clusters (virulence genes, pathogenicity islands, fitness genes) through horizontal transfer, enabling them to colonise or infect new hosts.
- Selection of new pathogens or pathotypes of bacteria and viruses due to changes in the environment and in food production as well as in animal husbandry.
- Investigation of the role of pathogens in oncology, and of molecular and evolutionary aspects.

3.4.2 Infection reservoirs

There is a need for more research on infection reservoirs that enable microorganisms to persist in human hosts or in the environment, e.g. in the form of biofilms, and to generate virulence factors and exchange information.

3.4.3 Infection channels

The effectiveness of cleaning, disinfection and sterilisation processes must be further researched, in particular to devise strategies for disinfection procedures since different pathogens respond differently to disinfection procedures. Recent studies have revealed **that pathogens can be disseminated through cleaning procedures.**

3.4.4 Diagnostics

More research is needed into diagnostics for detection of pathogens in the environment, in foodstuffs, water, in the air as well as in relevant areas of hospitals. At present, in particular for investigation of water or in the hospital setting, there are essentially only culture detection methods available, but these do not lend themselves to hygienic characterisation of these environments.

The greatest constraint imposed by the use of conventional diagnostic methods in microbiology is the amount of time needed for a single application. This means that the scope for rapid and timely information to make treatment decisions, for outbreak management and hygiene measures is severely limited. Further development of molecular diagnostic techniques such as PCR, fluorescence, in situ hybridisation, DNA sequencing, macro- and microchips, exploitation of the possibilities residing in conventional diagnostics through the use of homogenous and fluorogenic substrates, use of automated systems and of macro-arrays must be progressed. Further refinement of PCR techniques, e.g. Real-Time PCR, spectroscopy (mass spectrometric analysis of bacterial cells) as well as microarray technology for parallel investigation of several target genes must be further developed and its suitability for routine tasks verified.

The following procedures should be available on a large scale for further identification and subdifferentiation of strains of microorganisms:

- Macrorestriction patterns in pulse field gel
- Sequence typing of the polymorphic region of protein A (gene A typing).

3.4.5 Evaluation

In respect of the effectiveness of basic hygiene measures, such as hand hygiene, hand disinfection, surface disinfection, protective measures, orofacial masks in cases of epidemics, there are **no in-depth epidemiological studies** to furnish proof of their effectiveness. Furthermore, there is an urgent need for more epidemiological data on the effectiveness of education campaigns in bringing about changes in hygiene practices. Likewise, the effectiveness of training programmes using e-learning technologies needs to be reviewed.

3.4.6 Vaccines

The development of new vaccines must be continued; in particular, the development of vaccines against **HIV/AIDS, malaria and tuberculosis** is one of the most important challenges to be surmounted on the vaccine development research agenda. Vaccines must also be developed against, for example, noroviruses and other vaccine-preventable diseases. The pharmaceutical industry must be motivated through international, government-level support.

3.4.7 Prevention and control strategies in developing countries

Whereas in developed countries high investments have been continually made in the formulation of prevention and control strategies for infectious diseases, much needs to be done for prevention and control, in particular of **tropical diseases** in Third World countries, especially Africa. Framework conditions are also needed in the developed countries for investigation of the prevalence, incidence, transmission, diagnostics and treatment of tropical diseases. **Here the geographic, infrastructural and cultural circumstances of the respective country must be taken into account.** It is not enough to merely study the presence of specific pathogens.

3.4.8 Chronic diseases

Research into → **the role of infections in the genesis of chronic and malignant diseases** must be greatly reinforced. The following main research topics are of paramount importance:

– Studies into how microorganisms can trigger chronic diseases (direct carcinogenisis, indirect carcinogenisis, inhibition of cell division, induction of structural changes in host proteins, immunosuppression, direct impact on cell activities or viability)
– Detection of the causal role of infectious diseases in chronic diseases
– Methods for detection of pathogens implicated in chronic diseases
– Epidemiological studies, transmission studies, T models, definition of the role of genetic markers, microorganism characteristics that could trigger chronic diseases (triggering of apoptosis, triggering of immunity, inflammation, transformation of host cells, etc.).

→
As regards chronic diseases, there is a need for research into:
– The mechanism whereby microorganisms trigger chronic diseases
– Detection of the causal role of infectious diseases in chronic diseases
– Methods for detection of the pathogens implicated in chronic diseases.

3.4.9 Antibiotic resistance

There is an urgent need for research into the **association between prescription practices for antibiotics and the development of antibiotic resistance at**

individual and population level. Furthermore, the impact of any political measures to restrict antibiotic consumption on the development of antibiotic resistance should be investigated. Antibiotic usage in animal husbandry continues to be an eminently important research topic.

Targets must be defined for the development of alternative drugs. Genome studies are useful to that effect. New technologies for isolation and characterisation of natural products in combination with binding-chemical methods could lead to production of new, potentially antimicrobial agents. **The increase in vancomycin-resistant *Staphylococcus aureus* strains and multi-resistant Gram-negative bacteria is a warning signal** that should induce the scientific community to define new targets and drive the development of new classes of drugs. The pharmaceutical industry must be given new incentives to engage in effective research in this field.

3.4.10 Prevention and control of infectious diseases in complex crisis situations

There is need for the following research as regards complex crisis situations:

- Development of rapid diagnostic techniques that can be used in the field
- Use of artemisin derivatives for malaria, in particular during pregnancy and development of new antimalarials for intermittent preventive treatment
- New short-term treatment for acute infections of the lower respiratory tract as well as for tuberculosis and typhoid fever
- Heat-resistant pentavalent vaccines; rotavirus vaccine for children
- Administration of zinc via oral rehydration solutions
- Surveillance methods for complex crisis situations
- Geo-medical information systems for characterisation of infectious diseases in complex crisis situations.

3.4.11 Infrastructure

Essential preconditions for a functional infrastructure as well as its role in prevention and control of infectious diseases must be defined on the basis of thorough investigations. These include elements of the public health service, laboratory capacities and communication structures.

3.4.12 Economic implications

The economic implications of infectious diseases must be analysed in health policy studies that look at economic feasibility, while also taking account of acute, chronic and social aspects. The conclusions drawn from these as regards the cost-benefit relation must then be made available for political decision-making processes.

3.5 Communication, education, training and continuing professional development

Communication in **education and ongoing training** for the general public as well as for specialists plays a pivotal role in prevention and control of infectious diseases.

Today there are several channels in Germany and Europe to disseminate information on a wide scale. This is done mainly using the internet as well as – sometimes in parallel – the print media. Examples of the latter include the *Epidemiologisches Bulletin*, published (in German) by the Robert Koch Institute, and *Eurosurveillance*, the European bulletin on infection epidemiology published by the European Centres for Disease Control.

The standardised systems now available for evaluating the content of training courses in the field of hygiene, microbiology and infectiology, which have found widespread acceptance among students thanks to topics focusing on hospital hygiene and environmental hygiene, diagnostics and therapeutics in microbiology and treatment in infectiology, are a necessary enrichment for the exercise of professional duties at a later stage.

However, this means that the corresponding modules must be taught in a structured manner. A → **coordinated training catalogue in hygiene, microbiology and infectiology** must therefore be further developed by the specialist societies in Germany and streamlined in cooperation with the German Medical Faculty Association (*medizinische Fakultätentag*).

→
The specialist societies in Germany must further develop a coordinated training catalogue in hygiene, microbiology and infectiology and this must be streamlined in cooperation with the German Medical Faculty Association.

3.5.1 Communication with the general public

The key importance of communication with the public is still underestimated and its **prevention and control potential is not being exploited at present**. The relevance of infection risks is not appreciated by the public because of a failure to focus on the fact that threatening infectious diseases occur not only in developing countries. Nor is there sufficient public awareness of the risks arising from antibiotic resistance. The public's perception of the risks posed by other environmental factors is often overestimated compared with infection risks. The importance of infectious diseases must be communicated together with instructions on individual basic hygiene measures and vaccinations. The **general practitioner** also plays a vital role in providing information to the patient, as borne out in cases of mass outbreaks.

With regard to → **pandemic prevention** basic hygiene measures can make a contribution only if their importance is communicated to the public on time. Therefore there is urgent need for improved communication of the importance of infections and of appropriate prevention and control measures.

→
With regard to pandemic prevention basic hygiene measures can only make a contribution if their importance is communicated to the public on time and continually.

3.5.2 Training for physicians and medical specialists

If provision is not made to ensure that physicians are properly qualified in the field of hygiene and microbiology, effective prevention and control of infections will not be possible. In the past, the medical curriculum or medical licensure regulations did not ascribe much importance to these topics, possibly in view of the relatively low importance of infectious diseases in Germany. This is highlighted by the fact that in the new medical licensure regulations the subjects Hygiene, on the one hand, and Microbiology, Virology, on the other hand, are combined and no longer taught as separate disciplines. As such, infection prevention, subsumed under Hygiene, as well as infection diagnostics and treatment, subsumed under Microbiology and Virology, are neglected already in the medical curriculum.

Following the abolition of hygiene chairs, infection prevention is no longer taught in the depth urgently required. While hospital epidemiologists are present in many university hospitals, they no longer participate in teaching.

There is therefore an urgent need to treat

– Hygiene
– Microbiology and Virology
– Infectiology

as independent disciplines in the → **medical curriculum**, and present these topics separately as examination subjects.

→
Hygiene, microbiology and virology as well as infectiology must retain their independence as separate disciplines of medicine, also in the medical curriculum so as to ensure that physicians are properly trained in prevention and control of infectious diseases.

It is imperative to retain independent hygiene chairs and independent chairs for microbiology and virology as well as improved facilities with independent chairs for infectiology.

There has been a particularly dramatic trend towards continually reducing the number of independent hygiene chairs. This has also been deeply regretted in the press release issued by the Federal Environmental Office in 2002, which is reproduced below:

→ Hygiene and environmental medicine – threatened with extinction?

Research and training capacities for hygiene and environmental medicine are declining in Germany

The Federal Environmental Agency (Umweltbundesamt -UBA) views with concern the continual decline in the research and training capacities for hygiene and environmental medicine at German universities. Of the 20 institutes in which up to 10 years ago research was being carried out on a fulltime basis into issues relating to hygiene and environmental medicine and specialists trained, only 12 remain today. Retention of the institutes of hygiene, environmental medicine and public health is no longer guaranteed at such highly traditional universities as Tübingen, Frankfurt, Jena and Kiel. In Bavaria, Saxony and Saarland there are in the meantime no independent institutes for these disiciplines. Universities lend their support to the Federal Environmental Agency in many ways.
Many of the consultation and decision-making committees located at the Federal Environmental Agency often rely on the voluntary input from university experts, even when it comes to having German positions occupied at international level. The Federal Environ-

mental Agency, on its own, is able to conduct only a small part of the research needed in the field of environmental medicine. Therefore it is investing in research: research projects to the tune of millions are awarded each year to external bodies, in particular to universities. Any further reduction in the number of existing institutions will not only impede the activities of the Federal Environmental Agency but will also jeopardise Germany's contribution to environmental and health research at international level. Jobs and training placements in environmental hygiene are declining not because of a lack of problems that need to be solved. On the contrary, there are numerous new challenges at executive level, in teaching and research: noise, electromagnetic radiation and new chemicals. We are facing a resurgence of pathogens against a background of increasing globalisation and altered environmental conditions. It is furthermore imperative that regulations governing environmental and health protection be updated following European unification. Who is supposed to identify the links between pathogen spread and environmental conditions or to conduct research into the resistance evinced by changing and newly emerged pathogens to disinfection processes? Who will be able to recognise on time and eliminate the hazards to health emanating from water, soil and air pollution? And more importantly, where will those experts be trained, who tomorrow will fight for healthy environmental conditions in EU committees, in the public service at federal, state and local level? At the close of the 19th century Max von Pettenkofer and Robert Koch, among others, laid the foundation for hygiene as a scientific discipline in Germany. Many people owe their health and life to these achievements and to those of their successors. High standards of hygiene are not something to be taken for granted; rather they need unrelenting efforts in research and public health practices. Only with a sufficiently high number of well-equipped research and training centres will this continue to be assured in the future.

Berlin, 20 February 2002

Only if hygiene and environmental medicine coupled with public health are re-established as an independent discipline at German universities can future physicians acquire already during their medical studies the necessary awareness of the existing problems and conversancy with the subject matters needed for their subsequent career in medicine, and only then can the general public health system be given the impetus it needs for prevention of infections.

The → **medical licensure regulations** should therefore be amended. Furthermore, the German Medical Faculty Association is called upon to deal with the infrastructure of hygiene and microbiology in German universities and bring about improvements here.

→ **The German Medical Faculty Association is called upon to deal with the infrastructure of hygiene and microbiology in German universities and bring about improvements here.**

There is considerable need for improvements in the field of hygiene and public health at European and international level too.

The failure to teach prevention strategies is one of the reasons for the paucity of effective measures in place for control of important infectious diseases. For example, for a long time hygiene did not at all exist as a discipline in the United Kingdom, with the medical curriculum concentrating instead mainly on diagnosis and treatment of infectious diseases.

In addition to teaching infection prevention and control topics during medical studies, **advanced training** for

– Specialists for hygiene and environmental medicine
– Specialists for microbiology and infection epidemiology
– For public health physicians

must be significantly improved in terms of content and structures.

The advanced training modules for the various medical specialisms are set out in the advanced training requirements of the German Federal Medical Council (*Bundesärztekammer*). But incentives must be given to assure corresponding positions for medical specialists.

To assure an adequate supply of physicians for hygiene and environmental medicine, mandatory consultation with a hospital epidemiologist must be stipulated by hospital hygiene regulations at state level. Furthermore, provisions must be in place to ensure that e.g. water supply companies must consult a specialist for hygiene and environmental medicine. This would gradually improve the situation as regards the availability of positions.

Apart from the criteria governing **medical specialist training**, there is an urgent need to **optimise training of specialists for carrying out surveillance and epidemic management**. So far these structures are not adequately in place to meet the need for specialists in this area.

Suitable positions must also be created in the public health offices and public health service. And a stop must be put to further cuts in staffing in the public health service for such medical specialists and other specialists.

3.6 Implementation

Implementation is understood to mean the **application of prescribed structures and working procedures** within a system, while taking account of framework conditions, rules and targets.

In the Memorandum on the Threat Posed by Infectious Diseases from 1996 the lack of accurate epidemiology and surveillance of infectious diseases was identified as a serious shortcoming. As already stressed, this drawback has in the meantime been eliminated thanks to the introduction of the new Protection against Infection Act, to expansion of the spectrum of mandatory notifiable diseases and pathogens as well as to the introduction of mandatory surveillance for registration and evaluation of nosocomial infections.

There is, however, a need for improvement in

– Health promotion
– Health protection

– Organisational structures in the various federal states
– Assignment of priorities.

3.6.1 Health promotion

Here health promotion is understood to mean **all measures that enable an individual to take,** thanks to an understanding of the role of infectious diseases, **appropriate measures for himself/herself and for others aimed at prevention and control of infectious diseases.**

In Germany, infectious diseases are no longer viewed by the public as presenting any major hazard unlike in the past when people had experienced their dramatic onset within their own family circle. Furthermore, discussions focusing on the hygiene hypothesis have attenuated the motivation to observe basic hygiene practices.

However, an analysis of the notifiable infectious diseases has revealed that the majority of gastrointestinal diseases and some of the common, in some cases severe, infections could be prevented by → **simple hygiene measures in the home, in nursery school, in the school and workplace.** Instruction on the role of infectious diseases and on the effectiveness of simple, well-directed hygiene measures such as handwashing, cleaning, disinfection or good hygiene practices to avoid sexually transmitted infections, e.g. condom usage, must be provided in appropriate form and continually to the different age groups.

→
The majority of infections could be prevented in the home, nursery school, school and the workplace by providing simple, well-directed instructions on hygiene practices.

There is a growing need for proper hygiene practices to meet the rising number of persons being cared for at home and who are at increased risk for infection due to, inter alia, the increasing trend in patients being discharged home earlier from hospital; the number of such patients is also growing due to demographic trends.

Efforts must be taken to promote an understanding among the public in developed, and especially in developing, countries of the infection reservoirs among humans, animals, food, water and the air.

For example, attention is drawn in this respect to the homepage of the **International Scientific Forum of Home Hygiene** (*www.ifh-homehygiene.org*).

Despite the fact that today there is a broad range of well-tolerated and effective vaccines against a large number of infectious diseases as well as excellent systematic recommendations issued by the Standing Vaccination Committee as well as the World Health Organisation, there continue to be vaccination gaps even in highly developed countries like the Federal Republic of Germany, highlighting the need to reach the public via general practitioners and motivate people to acquiesce in vaccination. For that reason measures aimed at the following are important: development of national strategies for routine vaccination and improvement of the data available on vaccination coverage; comprehensive well-targeted communication strategies and public relations campaigns to increase public awareness of the advantages conferred by immunisation and of the risks emanating from failure to do so; regular provision of continuing professional development courses for medical personnel on vaccination. Furthermore, efforts must be stepped up to identify and reach non-vaccinees through additional campaigns, including at the time of signing up for nursery school, entry into schools, medical consultations, etc.

→
Health promotion programmes must be greatly reinforced in the future.

These types of → **health promotion programmes** must be greatly reinforced in the future.

3.6.2 Health protection

Measures aimed at improvement of health protection are those taken for the **common good** – independently of the behaviour of the individual, so as t**o assure safe health conditions,** for example water, soil, air and food hygiene, hygiene in the hospital and doctors' surgeries, in the home, in public establishments as well as the public health infrastructure.

New requirements must be met in the field of water hygiene following the identification of hitherto unknown newly emerging, drinking-waterborne pathogens which are not picked up by the classic indicator systems used for monitoring water hygiene. New prevention strategies have been formulated by WHO, but these have not yet been implemented in Germany, such as the Water Safety Programme comprising all measures ranging from the catch basin to the water distribution system and the water outlets.

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In Germany, some of the water supply structures are outdated and no longer meet present-day safety standards.

It must also be borne in mind that it is now more than a century since the introduction of a central water supply system and that as such → **there are some outdated water supply structures in Germany** which no longer meet present-day safety standards.

A negative situation of conflicting interests has arisen from the privatisation of supervisory activities and assignment of such duties to the water supply companies themselves, something that is not compatible with the principles of health protection.

There is therefore an urgent need for the following:

- Mandatory implementation in Germany of the concept set out the Water Safety Programme drawn up by the World Health Organisation
- Update pathogen monitoring in line with the latest scientific knowledge rather than confining testing to the classic indicator system based on colony forming units, *E. coli* and investigation for coliforms
- Ascribe more importance to raw water for evaluation of health safety
- Introduce new regulations for supervision and limitation of the scope of appointed bodies by independent scientific institutes, with the aim of having in place just a few, but competent, hygiene/medical institutions with special expertise, including for potential outbreak management

- Shorten monitoring intervals, in particular for the smaller and medium-sized water supply companies, to assure at least regular supervision at monthly intervals following regular hygiene/medical inspection of the water supply structures
- Record, analyse and publish on a regular basis data on waterborne outbreaks as done, in particular, in the English-speaking countries
- Step up efforts in Germany to implement the World Health Organisation's provisions within the framework of the Water Decade
- Update regularly knowledge relating to the basic measures needed for improvement of water supply
- In developing countries promote the use of simple water-treatment technologies that can be implemented by the countries themselves, and implement basic supervisory strategies in order to obtain information on the water quality.

3.6.3 Hospital hygiene

In Germany hospital hygiene can be viewed as being of a very high standard. This is due to the implementation of clear recommendations and to an infrastructure of personnel for prevention and control of nosocomial infections; this includes a hospital control infection team comprising the hospital epidemiologist, infection control physician and infection control nurses.

But the failure to introduce → **hospital hygiene regulations** into 12 federal states is not acceptable.

→ **The failure to introduce hospital hygiene regulations into 12 federal states is not acceptable.**

- Hospital hygiene regulations in line with the basic criteria and recommendations of the Commission for Hygiene and Infection Prevention should be introduced in all federal states.
- Regulations must be introduced in all federal states, stipulating mandatory consultation with a hospital epidemiologist, and appointment of infection control physicians and nurses in every hospital.
- Training in hospital hygiene must be given much more importance in the medical curriculum and should be examined as a quality assurance component within the discipline of Hygiene. Successful participation in hygiene seminars and practical training courses should, also for quality assurance reasons, be a precondition to be met by medical students before being allowed to attend to patients.
- Advanced training for physicians working in the field of hygiene should be promoted on a broad scale, in particular in line with the recommendations of the Commission for Hygiene and Infection Prevention.
- In homes for the elderly at least one of the treating physicians should have successfully completed the infection control course for physicians, so as to provide the competence needed in these areas and assume a coordinating role.
- Any cutbacks on cleaning and disinfection – as seen increasingly more often in recent years – should be done only following an in-depth study by a hospital epidemiologist, in view of the rising number of antibiotic resistant microorganisms that can also be spread through the patient environment.

– Controversial discussions about the pros and cons of hygiene measures among infection control experts are something that should now be consigned to the past, because these could have negative implications and, in turn, lead to the further spread of antibiotic resistant microorganisms.

The standard of hygiene in hospitals and doctors' surgeries in the various European countries, and in particular in developing countries, is exceedingly low in some cases. There is an urgent need to pass on the experiences gained in Germany to Europe and worldwide without any constraints imposed, since it has been demonstrated that poor hospital hygiene standards promote selection of antibiotic resistant microorganisms which can gradually spread worldwide (*First Epidemiological Report by ECDC 2007, see also Chapter 2.1.2*).

3.6.4 Municipal hygiene

Germany has a **very high standard of municipal hygiene** (safe, hygienic water supplies, effluent disposal, sanitary infrastructures, public facilities). The investments made here in the late 19th and early 20th centuries have paid off since numerous infectious diseases that present a threat have been reliably controlled or have now been eradicated in the developed countries.

But to date these infrastructures are lacking in many developing countries worldwide. One billion people have no access to safe hygienic water, 3 billion people live under precarious sanitary conditions. Close cohabitation of humans and animals leads to an intensive exchange of zoonoses and to selection of new pathogens with a pandemic potential, as borne out by the regular pandemic waves caused by influenza viruses.

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Germany and other developed countries bear much responsibility to invest globally in enhanced administration and in the formulation of mandatory provisions for municipal hygiene.

Globally, investment must be made in → **enhanced administration** for the formulation of mandatory provisions for municipal hygiene. Developed countries, including Germany, bear much responsibility here. Apart from countering infectious diseases in developing countries, this would also protect the developed countries against the importation of infections.

3.6.5 Infrastructure of scientific institutes and scientific networks

The much-lamented reduction in the number of hygiene institutes in the universities must be stopped in the light of the pivotal role played by hygiene measures and of the need for physicians for hygiene and environmental medicine. **To that effect, the discipline of hygiene (infection control) should be anchored in the medical licensure regulations as an independent discipline**. It must retain its independent role in teaching.

There is considerable need for research, teaching and health provision to assure public hygiene and meet hygiene needs in hospitals and doctors' surgeries. In view of the relevance of this discipline in terms of health policies, those entrusted with the formulation of such policies must show more interest in assuring the advanced training of physicians for hygiene and environmental medicine, in order to implement these insights in both the public health sector and also in other ministries. The same is true for the institutes for microbiology, virology and parasitology.

The requirements governing modern diagnostics and the provision of diagnostic/treatment consultation services to clinicians in hospitals and to doctors' surgeries have become much more stringent. There is also a need for rapid diagnosis and communication of investigation results with regard to surveillance and outbreak management.

Set against that background, it is imperative that → **there be a network of university-based hygiene institutes as well as of microbiology and virology institutes in Germany** which optimally complement each other in the field of infection prevention and control and, on the other hand, make their services available to the public health service and healthcare services.

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Retention of a network of university-based hygiene institutes as well as of microbiology and virology institutes in Germany is indispensable for a functioning healthcare system.

3.6.6 The public health service

The public health service plays a key role in **coordination of measures for infection prevention, detection and control.** The public health service has been given extensive powers to that effect by the legislator, which when properly used will have sustained implications for infection prevention and control. The public health service is dependent on clear guidelines, provisions and on an adequate and well-qualified human resources' structure. The primary role of the public health service is not to carry out independent research but rather, first of all, to implement in a consistent and circumspect manner the existing guidelines, regulations and directives coming within its purview. This by no means rules out conductance of a greater number of scientific studies by the public health service in cooperation with scientific institutions. Excellent examples of such cooperation are the successes scored by the Frankfurt Public Health Office where, after providing training and support to the respective hospitals and doctors' surgeries, systematic inspections were carried to assess the standards of hygiene in hospitals and in doctors' surgeries, while evaluating their scientific merits. This helped to bring about marked improvements in the standard of hygiene, infection prevention and control.

What is of decisive importance is that there should be no further → **cutbacks on staffing in the public health service.** Rather, more positions should be created in public health offices for medical specialists for hygiene and environmental medicine, microbiology and infection epidemiology as well as for infectiology. The public health offices should also fund short-time training courses at hygiene institutes or at medical microbiology institutes for their physicians in training. This would help to meet the need for qualified personnel in a rapid and sustained manner.

→
Cutbacks on staffing in the public service must be stopped and measures taken to ensure continuing professional development of the physicians working there.

3.6.7 Developing countries

There are glaring deficits in the field of hygiene, public health and microbiological diagnostics in developing countries.

Development aid programmes should focus more on the needs of developing and economically less developed countries to improve hygiene, training and, in particular, training of medical specialists and, in turn, improve the situation as regards specialist know how, while taking account of the specific needs of these countries. To that effect, medical specialists from less developed countries should be given scholarships to study in Germany and implement their expertise in their own countries. The decision taken by the German Research Foundation (*Deutsche Forschungsgemeinschaft* – DFG) in 2006 to promote Africa research in the life sciences is an encouraging sign.

In May 2007 an international conference “Towards Sustainable Global Health” was held in Bonn which was organised by the UN institutions based in Bonn, the International Labour Organisation and the Institute of Hygiene and Public Health at Bonn University. A position paper, the **“Bonn Call for Action and Awareness on Promoting Sustainable Global Health”,** was published, stressing the importance of mutual support through hygiene and public health against a background of a dramatic global situation (*www.hygiene-und-oeffentliche-gesundheit.de*).

In a similar vein, the World Health Report 2007 focuses on the importance of strengthening resilience through international cooperation.

The UN General Assembly has declared 2008 the **“International Year of Sanitation”** with the general aim of advancing processes for hygiene improvement so as to save lives and to accelerate economic and social developments.

In the person of, in particular, Robert Koch, Germany laid the foundation for a rich tradition in prevention and control of infectious diseases through hygiene, microbiology, health protection and research in the 19th century. And precisely for that reason, Germany has also a duty to support the World Health Organisation in this field.

FINAL REMARKS

Looking back on his professional life, Prof. Dr. John M. Last (University of Ottawa), Canadian emeritus professor of epidemiology and community medicine, stated that the following sequence was needed to solve any public health problem:

- Note that a problem exists
- Understand the cause of the problem
- Be able to deal with the problem
- Observe values that must be borne in mind when solving the problem
- Have the political will to solve the problem.

It is to be hoped that in the spirit of that sequence, this Publication has made a contribution to:

- Highlighting that infections continue to be a challenge of considerable proportions globally, and in Germany
- Providing insights into the cause of current infection problems
- Showing how these problems can be overcome
- Pointing to the need for a system of values in bearing responsibility for public health protection, rather than paying attention only to economic aspects
- Ensuring that the political will will be influenced to bring about, finally, fundamental changes so that Germany will be able in the future, too, to demonstrate the necessary resilience where old and new infectious diseases are concerned.

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Despite the enormous successes scored worldwide, **infectious diseases** continue to pose a serious health threat. They are characterised by dynamics for which no prognosis can be ventured and represent a major economic burden not only for the health services but also for the overall national economy. Hence combating them presents a continual medical, ethical, political and social challenge.

This publication, like the "Memorandum on the Threat Posed by Infectious Diseases" published in 1996, has been published on behalf of the Rudolf Schülke Foundation in cooperation with the professional societies and medical associations for hygiene and public health. This completely revised edition includes a risk assessment of the current situation and, based on this evaluation, presents strategies aimed at minimising risks posed by infectious diseases.

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