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Contents

1 Introduction

This paper presents a gender perspective on outbreaks of epidemic-prone infectious diseases. It discusses evidence of differences in the infectious disease process between males and females, and aims to show how, by taking such differences between men and women into account, it is possible to improve the understanding of the epidemiology and the clinical course and outcome of diseases, aid in their detection and treatment, and increase public participation in and the effectiveness of prevention and control activities.

Differences between males and females arise because of biological, i.e. *sex* differences and as a consequence of gender-based roles, behaviour and power. Considerable confusion surrounds the use of the words *sex* and *gender*. By and large, sex refers to biological differences between males and females whereas gender refers to differences between males and females that are determined by societal and cultural factors. It is worth noting, however, that although the distinction between these two concepts is important, it is not always easy to attribute differences in disease processes uniquely to either sex or gender, since sex and gender are not independent of one another. Therefore, the effects of both sex and gender are considered in this paper.

Despite the potential importance of differences in sex and gender for the transmission, course and outcome of some infectious diseases, little has been written about the implications of sex and gender for the surveillance of and response to outbreaks, especially for diseases that are not sexually transmitted. One reason for the lack of attention to this topic is that key contributions to knowledge about the relationships of sex and gender to infectious diseases have been made by a variety of disciplines, including epidemiology, medical and biological sciences, social sciences and demography. The fact that each discipline tends to work in isolation is a barrier to the application of research in outbreak settings. The current paper brings together findings from a broad range of disciplines so that they can be used during an outbreak. Some of the findings discussed in this paper have already been translated into recommendations for WHO operational responses to outbreaks.

The remainder of this paper is divided into two sections. The first provides a general overview of the interrelationships between sex, gender and infectious disease, illustrated with examples of how these work at each stage of the life-cycle.

Particular attention has been paid to the interaction of communicable diseases and pregnancy, where there may be special vulnerabilities, and restricted treatment options, for both mother and foetus. The second is a detailed discussion and analysis of selected examples of epidemic-prone infectious diseases (dengue, Ebola haemorrhagic fever and severe acute respiratory syndrome (SARS)).

2
Definitions and key issues

2.1 Epidemic-prone infectious diseases

This paper focuses on infectious diseases that typically lead to outbreaks and/or epidemics, including both well-established diseases such as meningitis, cholera and dengue fever, as well as newly emerging diseases such as Ebola haemorrhagic fever and SARS. The high case-fatality rates of some epidemic-prone infectious diseases and their potential for rapid spread pose particular problems. Accurate and timely surveillance and response are therefore of paramount importance for the prevention and control of epidemics of these diseases. Most countries have "early warning and response systems" for reporting and responding to outbreaks. These systems generally include mechanisms for immediate reporting of suspected cases to the next higher level, provisions for outbreak investigation and guidelines on appropriate response(s).

Unfortunately few of these mechanisms take gender or sex differences sufficiently into account. The reported data are rarely disaggregated by sex. Furthermore, information relating to the pregnancy status of women and other reproductive factors is seldom systematically collected or included in reports. This limits the possibilities for understanding the gender dynamics of disease, identifying vulnerable groups, and developing appropriate responses.

2.2 Biological (sex) differences

Fundamental differences between males and females exist at every biological level, from that of the organism as a whole, to organs and organ systems, to individual cells. These biological differences are complex, and may confer advantages either to males or females depending on the infectious agent. Anatomical and hormonal differences between males and females can influence the infectious disease process. At the cell level, a major difference is that female cells have two X chromosomes, whereas male cells have one X and one Y chromosome. Although the influence of cellular differences between males and females on the infectious disease process is not fully understood, it is known that the X chromosome governs many of the immune system responses (Institute of Medicine, 2001).

Major changes in the female body during pregnancy and lactation also affect

the infectious disease process. Some diseases are particularly severe during pregnancy, while others affect the unborn child. In addition, vaccines and other pharmacological agents may have different effects on pregnant women than on non-pregnant women, or harmful effects on the fetus or breastfed baby.

2.3 Gender-related differences

Gender influences both patterns of exposure to infectious agents and the treatment of infectious disease. For example, gender roles influence where men and women spend their time, and the infectious agents they come into contact with, as well as the nature of exposure, its frequency and its intensity. Differences in the provision of health care to males and females, as well as in accumulated scientific knowledge about the effects of treatments, influence the course and outcome of disease for those who have been infected. Examples of common gender differences that influence exposure patterns and treatment include:

- Time spent at home and away from home
  In many societies, men spend more time away from home than women. For this reason, males typically face greater exposure to infectious agents outside the home whereas females tend to face greater exposure inside the home. For example, men may go into the forests to hunt or log trees where they are more likely to come into contact with wild animals. This is known to have been the origin of a number of outbreaks of Ebola haemorrhagic fever (see section 3 below). The consequences of these different gender-related exposure patterns are complex, and differ for different infectious agents.

- Responsibility for caring for the sick
  In most societies women are more likely than men to be *caregivers for the sick* in both health-care settings and at home. In this capacity, women are more exposed than men to infectious agents. This is of particular importance for diseases that are transmitted by close contact such as Ebola haemorrhagic fever and SARS (see section 3 below).

- Responsibility for caring for livestock
  An often under-appreciated gender difference relates to the care of *livestock*. Caring for livestock is usually gendered, with either men or women responsible for different animals depending on societal norms. In many developing countries, women often care for the smaller animals such as ruminants, pigs, poultry, guinea-pigs and rabbits. Although these animals are vital sources of protein and income in some countries, they are less often the focus of attention for veterinary and extension programmes (WHO, 2002). It is possible that gender differences in providing care for animals leads to differences in the risk of zoonotic diseases – but appropriate breakdowns to investigate these possibilities are not available.

- Health care received

  There are also important gender differences related to *health-seeking behaviour* and access to health care. In some societies there are differences in the utilization of health care facilities and in the level and type of care given to males and females. A follow-up observational study in Kolkata, India, for example, found that boys with diarrhoea were more likely to be given oral rehydration fluids than girls, and were more likely to be taken to qualified health professionals for treatment. Boys were also taken for care outside the home significantly sooner than girls (Pandey et al., 2002). A similar result was found in Bangladesh where the time between the onset of symptoms of diarrhoea and hospital admission was significantly higher for girls than for boys (Mitra, Rahman & Fuchs, 2000). There is also some evidence that in many societies, adult women may face greater economic and social barriers to care than adult men (WHO, 1998).

- Scientific knowledge about treatment

  There may be differences in scientific knowledge about what is appropriate treatment for females and for males. Many clinical trials have included only male subjects, or when both sexes were included, no distinction was made between them in the analysis. Therefore, if there are differences in the way that treatment works for males and females, these cannot be taken into account. Knowledge of how certain treatments interact with stages of the reproductive cycle is scant. Pregnant women are routinely excluded from clinical trials on ethical and financial grounds; this hinders the development of appropriate treatment for pregnant women.

2.4 Sex and gender differences from a life-cycle perspective: basic questions

Discussion on the relationships between sex and gender and outbreaks of infectious disease, can be framed by two simple questions:

1. Who becomes ill?

Who becomes ill depends on both susceptibility and exposure to an infectious disease agent. Differences between males and females can be measured by calculating separate incidence rates, and can be tracked during an outbreak by plotting separate epidemic curves for males and females.

2. What is the course and outcome of illness?

The course and outcome of an illness are characterized by factors such as the nature and severity of symptoms, mortality rate and disease sequalae. These depend on both biological responses to exposure and treatment. Differences between males and females can be measured by calculating separate case-fatality rates and disability rates for males and females, and by constructing separate symptom profiles.

Examples of biological differences that influence who becomes ill and the course and outcome of illness include:

— differences in immune responses between males and females; and
— anatomical differences – particularly important for sexually transmitted infections.

Examples of gender differences that affect who becomes ill and the course and outcome of illness include differences in:

— access to immunization;
— exposures – because of gender roles;
— nutritional status;
— access to, and use of preventive and curative health care, including differences in the speed with which males and females get treatment outside the home.

In addition, the social and economic consequences of illness are often different for males and females. For example, the disfigurement that results from some infectious diseases (such as leprosy and onchocerciasis) affects marriage prospects for females more severely than for males (Vlassoff & Bonilla, 1994; Vlassoff et al., 2000). The level and types of stigma associated with some infectious diseases, such as onchocerciasis and Ebola haemorrhagic fever, also differ for males and females (Vlassoff et al., 2000; Hewlett & Amola, 2003).

Differences between males and females related to infectious diseases change over the life-cycle. For this reason, the current paper uses a life-cycle approach with separate sections for infants, children, adults, pregnant women and the elderly.

- Infancy. Infants are particularly vulnerable to some infectious diseases (although maternal antibodies have an important protective role for specific diseases). Mortality rates for male infants are generally higher for than female infants.
- Childhood. The biological differences between male and female children are diverse and disease-specific. Gender-related factors vary from country to country.
- Adulthood. As with children, differences between male and female adults are diverse, vary from place to place, and are often disease-specific.
- Pregnancy. Pregnancy induces many changes to the immune system, and for some diseases, pregnancy is a risk factor for a more serious course and outcome. In addition, the effects of infection of the mother, and/or preventive measures taken or treatment given to the mother, on the fetus or breastfed child are important considerations.
- Old age. The elderly are also particularly vulnerable to infectious diseases. In most societies this group has more women than men.

Table 1 presents typical similarities and differences between males and females in disease incidence, course and outcome, and in health-seeking behaviour and

TABLE 1
Typical differences between males and females in the infectious disease process

	WHO BECOMES ILL?		COURSE AND OUTCOME	
Life-cycle	**Susceptibility and immunity**	**Exposure**	**Treatment**	**Morbidity and mortality**
Infants	Males have naturally weaker immune systems.	Exposure is similar for male and female infants.	In some countries boys are more often taken for treatment outside the home.	There is greater male mortality from infectious disease.
Children	Levels of immunization for boys and girls are similar in most parts of the world. There are lower rates of immunization of females in south-central Asia.	In some societies there are mobility differences (boys spend more time outside the home), which may account for differences in incidence and mortality for some diseases.	In some countries boys are more often and/or more quickly taken for treatment outside the home.	There are disease-specific differences in severity and outcome. For example, mortality from measles and whooping cough is greater in females. Morbidity and disability may have different consequences for girls and boys.
Adults	For most infectious diseases, differences in incidence rates between males and females are more likely to be due to differences in exposure than to differences in immunity.	Men and women have different occupational exposures. Women have greater exposure in homes; men have greater exposure outside. Women are exposed in care-taker roles within the family and in care-giving occupations.	In some societies women have poorer access to health care outside the home; access to outside care is controlled by males or other family members. Research on treatment often uses males – so there is less evidence for results for females.	There are disease-specific differences in severity and outcome. Morbidity and disability may have different consequences for males and females.
Pregnant and lactating women	Important changes in the immune system occur during pregnancy. Large knowledge gaps exist about the specific changes.	Exposures to some diseases may change during pregnancy. Pregnant women have more exposure to health care settings, so may be at greater risk for some nosocomial infections.	Some treatments and control measures are harmful to pregnant women or to fetus or breastfeeding baby. Pregnant women are excluded from research on treatment. Some treatments not given to pregnant women because of insufficient evidence of their safety.	Some diseases are particularly virulent during pregnancy. Some diseases adversely affect the fetus or breastfeeding baby.

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Table 1 *continued*

	WHO BECOMES ILL?		COURSE AND OUTCOME	
Life-cycle	**Susceptibility and immunity**	**Exposure**	**Treatment**	**Morbidity and mortality**
The elderly	Both males and females have poorer immune systems in old age.	Lack of evidence.	Diagnosis is more difficult in the elderly for both males and females due to atypical presentations.	There are more women than men in this age group. Males die younger. Very little information is available on sex and gender differences and infectious diseases in this age group.

treatment for epidemic-prone infectious diseases at different life stages. These differences, which vary with age, and from disease to disease, are discussed in more detail below. For some diseases comparison of sex differences in morbidity and mortality may lead to important insights. For example, the finding that rates of measles infection are broadly similar for males and females, but mortality rates are often higher for females has led to interesting hypotheses about how different types of exposures for boys and girls may affect the course and outcome of a disease (Aaby, 1995).

2.5 Sex and gender differences in infancy and childhood

Despite significant improvements in child survival over the past three decades, infectious diseases such as malaria, acute respiratory infection, diarrhoeal disease and measles are still responsible for the majority of deaths of infants and young children in developing countries (UNICEF, 2004).

During infancy and childhood, sex differentials in infectious disease mortality vary with age, country and disease. The relative contributions of social and biological factors have not been clearly delineated for many diseases. However, during infancy, and particularly during the first month of life, mortality rates in males are generally higher than in females, both from perinatal causes and from infectious diseases (Population Division, 1998). This observed male excess in infant mortality is consistent over time and cross-sectionally, and is generally believed to arise because of biological disadvantages of male infants relative to female infants. These disadvantages include a greater incidence of prematurity, as well as less well-developed lungs and naturally weaker immune systems (Population Division, 1998).

The female mortality advantage declines between 6 and 12 months after birth, and differences in mortality from infectious disease between males and females are disease-specific and variable among children and adolescents.

A review of mortality differentials for males and females aged 1–5 years from

82 developing countries found evidence of higher childhood mortality in females in south-central Asia, northern Africa and western Asia, China, Guatemala and Niger, and to a lesser extent in Burundi, Namibia and Togo (Population Division, 1998).

Research has found some differences between the immune systems of boys and girls that seem to confer an immunological advantage to girls, but neither the biological mechanisms involved nor the relative importance of these differences in determining morbidity and mortality have been fully identified (Population Division, 1998). This is an area of research that needs further work.

Table 2 outlines current thinking about sex differentials in morbidity and mortality for infants and young children for several common infectious epidemic-prone diseases. The picture is complex and disease-specific, often varying between age groups. For example, females have higher mortality rates from diarrhoeal disease at ages 1–5 years, despite higher incidence rates in males at those ages. Infection rates for measles are similar for girls and boys, but mortality rates are higher in females. Explanations and working hypotheses put forward by researchers as to possible reasons for these different patterns are summarized in column 4.

2.5.1 *Differences in susceptibility to infectious diseases between male and female infants and children*

Nutrition and immunization are both important determinants of susceptibility to infectious disease during childhood.

Malnutrition among infants and young children

Malnutrition among infants and young children is common in developing countries, and it makes an important contribution to the disease burden of this age group. It acts "synergistically with infectious diseases thereby exacerbating the incidence, duration and severity of morbidity" (Population Division, 1998). There is a vicious cycle whereby infections cause decreased intake and utilization of nutrients, and this in turn causes greater vulnerability to infection. Because differences in nutrition between males and females, where they exist, may be important determinants of susceptibility and resistance to infectious disease, it would be important to have sex-disaggregated breakdowns of nutritional status and feeding practices available for use during an outbreak.

There is conflicting evidence about nutritional differences between male and female children in developing countries. Although numerous small studies provide evidence of discrimination against girls in feeding practices (particularly in parts of Asia) a comprehensive review of the evidence from 41 national Demographic and Health Surveys found no single country in which female nutritional status was consistently worse than male nutritional status during childhood (Population Division, 1998). In fact,the Surveys found an excess prevalence of malnutrition among boys compared to girls in a number of African countries, and a slight excess of malnutrition among boys overall (Garenne, 2003).

TABLE 2
Sex differences in morbidity and mortality for selected epidemic-prone infectious diseases common among infants and young children

DISEASE	INFANTS	YOUNG CHILDREN (AGE 1–5 YEARS)	POSSIBLE REASONS FOR MALE FEMALE DIFFERENCES SUGGESTED BY INVESTIGATORS
Diarrhoeal disease	Incidence higher for males	Mortality rates often higher for females despite similar or slightly higher incidence rates for males.	Higher incidence rates for male children may be caused by greater male mobility. Higher female case-fatality rates found in some countries may be due to poorer health care.
Acute lower respiratory infections and pneumonia	Mortality rates higher for males	Sex differences in mortality for young children vary. Generally only small differences in incidence rates.	Mortality rates higher for males in infancy probably due to less mature lungs in boys during infancy. This disadvantage abates in early childhood.
Neonatal tetanus	Mortality rates higher for males		It is not known why mortality rates are higher for males.
Measles		Similar infection rates, but higher female mortality rates observed.	Possibly less adequate medical care is provided to girls. Possibly girls are exposed to a larger dose in the home.
Dengue		Some evidence to suggest that girls are more likely to have dengue shock syndrome than boys.	Biological reasons, related to a more aggressive immune system response have been cited as possible causes of more severe illness in girls.

Immunization of infants and young children

Immunization plays an important role in reducing susceptibility to many epidemic-prone infectious diseases, particularly childhood diseases. Therefore, differences between boys and girls in immunization status, where they exist, are likely to be important determinants of differences in susceptibility.

Data from Demographic and Health Surveys provide information on the immunization status of girls and boys in developing countries. A detailed analysis of the results of 44 of these surveys indicates that overall, there are only small differences between the sexes in childhood immunization status, favouring either boys or girls.

However, in south-central Asia, one of the areas where excess female mortality has been consistently observed, evidence points to better immunization status for boys than for girls (Population Division, 1998).

2.5.2 *Differences in exposure to infectious diseases between male and female infants and children*

By and large, the exposures of female and male infants to infectious disease are similar. Differences in exposure begin early in childhood as mobility increases. In many societies, males are allowed more freedom to move as soon as they become mobile. This may partially account for the higher incidence of intestinal infections in boys (Table 2).

The way in which differences in exposure influence infectious disease patterns is complex and may have unexpected results. For example, it has been found that for measles, an infection contracted from someone of the opposite sex is generally more severe than an infection contracted from someone of the same sex (Aaby, 1995). Furthermore secondary cases of measles within the home have two to three times greater mortality than index cases. Aaby hypothesizes that this is due to a higher infecting dose of measles inside the home compared to outside the home. This may be the reason why the case-fatality rate for measles is higher in females in some societies in which girls are kept at home more than boys, and thus are more likely than boys to become infected with measles from their siblings inside the home. Boys on the other hand have greater exposure to measles outside the home. This puts girls at the "double disadvantage" of being secondary cases and of contracting measles from someone of the opposite sex (Aaby, 1995). Greater severity has also been associated with the cross-sex transmission of both chickenpox and polio (Aaby, 1992; Nielsen et al., 2002). More research is required to understand these patterns.

2.5.3 *Differences in health care and treatment between male and female infants and children*

Appropriate care and treatment is important for reducing childhood mortality from infectious diseases. Differential treatment of boys and girls may partly explain why female mortality during childhood is greater than male mortality in some parts of the world and for some diseases, even though evidence points to similar attack rates.

There is evidence of differential treatment favouring boys over girls from studies in many different parts of the world. The data from DHS, for example, which enquire about the source and type of treatment for diarrhoea, fever and cough, can provide some insight into treatment differentials – although the questions asked were limited and retrospective. An analysis of the results of 44 national DHS from 1986 to 1994 and from the 1992–1993 Indian NFHS (a national survey similar to the DHS) reported small but widespread differences in curative services that favour boys over girls, particularly in countries in South-central Asia where there is excess female mortality

in childhood. A modest curative care advantage for male children was also found in northern Africa, western Asia, and Latin America. In contrast, in most countries in sub-Saharan Africa boys and girls received similar levels and types of curative care (Population Division, 1998).

2.5.4 *Implications of sex and gender differences among infants and children for surveillance and control of outbreaks*

- Sex-disaggregated information on nutritional status and immunization status should be part of health surveillance systems and available during outbreaks.
- Information on differential use of health care by sex should be more widely available and used during outbreaks because for many epidemic-prone diseases (including dengue haemorrhagic fever and cholera), good treatment dramatically reduces case-fatality rates. In areas where there are differences in the curative care typically provided to males and females, it is important that response efforts include a strategy to overcome these practices.

2.6 Sex and gender differences in adulthood

2.6.1 *Differences in susceptibility to infectious diseases between adult males and females*

For the most part, differences between incidence rates in adult males and females for most infectious diseases can be attributed to differences in exposure rather than to biological differences (Institute of Medicine, 2001). Sexually transmitted infections are an exception to this generalization because differences in anatomy and in local immune responses may result in different risk ratios for sexual acts. For example, women are at greater risk of (human immunodeficiency virus) HIV and gonorrhoea infections from sexual intercourse with an infected partner than men (WHO, 2000).

2.6.2 *Differences in exposure to infectious diseases between adult males and females*

Exposure to infectious diseases is related to activities that dictate where people are throughout the day, and with which infectious agents they come into contact. Males and females frequently have different activity patterns related to gender-driven differences in occupation and in family roles. Depending on the activity and the disease, these gendered differences may increase the risk of exposure either for males or females. For example, in many societies females spend more time at home than males during the day, and therefore, experience greater daytime household exposure to infections. Men, in contrast, experience greater exposures to infections transmitted in work environments outside the home.

Caring for the sick carries an increased risk of exposure, especially for diseases that are spread directly from person to person. In most societies females are more likely to care for the sick than males, be it as a nurse (in almost all countries, the nursing staff is predominantly female (Anker, 1998)) or caring for sick household

members in the home. For example, nurses as well as others who cared for the sick have been heavily infected in several outbreaks of Ebola haemorrhagic fever, and nurses were heavily infected during the SARS outbreak of 2003 (see section 3.2).

2.6.3 *Differences in health care and treatment between adult males and females*

In many countries, gender affects access to treatment. There is evidence that in many societies, males have more ready access to health care than females, especially in countries where the status of women is low. In some societies, access to health care is controlled by males and the permission of the male household head, or other family members must be granted before outside health care is sought. Poor women themselves sometimes prefer to spend the money on their family rather than on their own health.

2.6.4 *Differences in the consequences of infectious diseases between adult males and females*

The consequences of infectious diseases are often different for men and women, especially in terms of long-term disabilities. For example, the consequences of facial disfigurement resulting from skin diseases such as leishmaniasis are often more severe for young women than for men; physical appearance is more important in determining whether a female will get married or stay married than it is for men. Mumps, on the other hand, may have more severe sequelae for adolescent males due to its potential to cause male sterility.

2.6.5 *Implications of sex and gender differences among adults for surveillance and response to outbreaks*

- Epidemiological data disaggregated both by sex and by common activities and occupations is important for understanding transmission patterns.
- Local practices governing who tends to be responsible for the care of sick persons and traditional funeral practices may affect transmission. During an outbreak, the outbreak control team should be aware of local practices and their implications for transmission. The WHO outbreak alert and response teams often take anthropologists to areas where there are outbreaks to help them understand local customs. This has led to disease control practices that are more acceptable in the local setting.
- Differences in health-seeking behaviour and care and treatment of males and females need to be understood for several reasons. First and foremost, obstacles to care and treatment for either sex need to be dealt with to ensure a suitable response to an outbreak. Second, if such differences do exist, data collected from health care centres will be inaccurate as they may under-report cases and be biased in favour of the sex that has better access to health care.
- There needs to be greater understanding and consideration of the differences

between males and females in the consequences of disabilities that arise from infectious diseases.

2.7 Pregnancy and lactation

Pregnancy and lactation are atypical periods for infectious diseases. Not only are these times of major changes in the immune system of the mother, but also there are possible consequences of infectious disease and treatment on the fetus and/or breastfeeding child. Some diseases are more severe for the woman during pregnancy, and the effect of disease can vary with gestational age; the effects of influenza for example, tend to be most severe during the third trimester.

Surveillance and control efforts during outbreaks, therefore, should pay attention to pregnancy for a number of reasons including:

- the protection of pregnant women (who may have more serious illness and/or pregnancy complications);
- the protection of the fetus or breastfeeding child (who may be affected if the mother becomes ill);
- to reduce the risk of spreading infection during antenatal care, delivery, and postpartum.

It is important to monitor the effect of outbreaks of new diseases on pregnant women, because the pathogen may affect pregnant women differently from non-pregnant women, and there will be little if any knowledge about pregnancy-related outcomes at the time of the initial outbreak. For an example of this, see below the discussion of pregnancy in the section on SARS.

2.7.1 *Susceptibility of pregnant women to infectious diseases and risk of more severe complications during pregnancy*

Because the immune system undergoes considerable change during pregnancy, women can become more susceptible to some infectious diseases at this time. For example, in areas with high transmission of malaria, pregnancy reduces women's immune response to malaria, making them particularly susceptible. In addition some diseases have more severe complications for women when they are pregnant. For example, pregnant women are more prone to respiratory complications. This has been linked to pregnancy-related anatomical and biochemical changes that affect respiratory mechanics (le et. al., 2002). Among non-immune women, *Plasmodium falciparum* malaria is often more severe during pregnancy than at other times because of much higher parasitaemia. Women with leprosy have a greater risk of nerve deterioration during pregnancy and lactation than at other times.

2.7.2 *Exposure of pregnant women to infectious diseases*

Although pregnant women generally have similar exposure to infectious diseases to that of non-pregnant women, there are some notable exceptions:

- For some epidemics that are spread nosocomially, pregnancy can be a period of increased exposure because pregnant women have more contact than usual with health care settings. For example, it has been found that SARS (Zhang et al., 2003) and Ebola haemorrhagic fever have been transmitted in obstetric care settings. In these settings, there may be a low level of suspicion of the epidemic disease, because the women are coming for pregnancy-related reasons. Furthermore, because infectious diseases sometimes have atypical presentations during pregnancy, they may be more difficult to diagnose during this time. If maternal care or obstetrical procedures are performed on infected mothers without adequate infection control measures (which may be more likely if the infectious disease is not diagnosed), this could increase the risk of the disease spreading in the maternal care or obstetrical setting.
- As all obstetric procedures carry a risk of infection, pregnant women are at an increased risk of infection when undergoing them. Consequently infection control needs to be a high priority of antenatal and obstetric care systems.
- Some women change their activity pattern during pregnancy in ways that either increase or decrease their risk of exposure to infections. For example, in some societies women may have lighter workloads during pregnancy. Furthermore, sexual activity patterns sometimes change during pregnancy, thereby changing exposures to sexually transmitted infections.

2.7.3 *Access to and availability of treatment for infectious diseases during pregnancy*

As discussed in section 2.6, adult women often have poorer access to health care than men in the same settings. Access to good-quality health care can be an important factor in the outcome of many infectious diseases. The barriers to health care discussed previously in the section on adult women apply to pregnant women too.

There are additional issues that relate to more limited treatment options for pregnant and lactating women for whom some vaccinations and/or treatments are contraindicated. In addition, vector control measures, such the use of pesticides, may adversely affect the fetus. Prevention and treatment options for pregnant women can also be limited by lack of knowledge about the potential effects on the fetus.

2.7.4 *The effect of maternal infectious disease on the fetus or breastfeeding child*

There are a number of ways that the fetus can be affected by an infectious illness in the mother during pregnancy and lactation. These include:

- transmission of infection from mother to child during pregnancy, birth, and/or lactation;
- poor fetal outcome due to infectious disease (such as spontaneous abortion,

premature delivery or abnormalities in the newborn); and
- transmission of antibodies to infection from mother to child during pregnancy, birth, and/or lactation.

In-utero transmission of infection from mother to child is usually harmful to the baby, while in-utero transmission of maternal antibodies can protect the baby from infectious diseases.[1]

Contracting a disease during pregnancy that has the potential to adversely affect the fetus may lead either to many months of worry for the mother – or to a pregnancy termination. Adequate information on the likely effect of illness on the course of the disease and on the course and outcome of pregnancy needs to be made available to patients so that they can make informed choices. Appropriate support services are also necessary – including support for pregnancy termination should it be necessary. Psychological support may also be required.

In the event of an outbreak of a new infectious disease, there will be no knowledge of the likely effects of the disease on the fetus. Therefore, studies that follow up infected pregnant women are required. To obtain an unbiased sample for such studies, pregnancy status (and gestational age of the fetus) should be established and recorded for all infected women of childbearing age.

2.7.5 *Implications of pregnancy for surveillance and response to outbreaks*

- During an outbreak of infectious disease, infection control in maternity settings needs careful attention, and special control measures may be required to prevent nosocomial transmission.
- If the usual treatment for the disease responsible for the outbreak is contraindicated for pregnant women, or if not enough is known about the effects of the treatment to justify its use in pregnant women, it may be necessary to design an alternative strategy.
- It is important to collect and analyse sex disaggregated data and data on pregnancy status and gestational age, particularly in outbreaks of diseases that are not well understood. Follow-up studies of infected pregnant women should be done for outbreaks of new diseases.

2.8 The elderly

Elderly people are among the most vulnerable to infectious diseases and case-fatality rates are often high. In addition, infectious diseases in older adults often have atypical presentations making them more difficult to diagnose. Treatment is also more complicated because older people are more frail and likely to have concomitant chronic conditions.

[1] For dengue, the effect of transmission of maternal antibodies is more complex. Dengue antibodies protect the baby from infection with the same strain of dengue, but may be detrimental if the infant is exposed to a different dengue strain.

The relationship of sex and gender with differences in infectious disease patterns in the elderly are poorly understood and have been little studied (Liang et al. 2003). This is surprising in view of the large sex differentials in mortality seen in the elderly, and the high mortality rates at this time of life.

2.8.1 *Exposure of the elderly to infectious disease*

Women outnumber men in the older age groups in both developed and developing countries. This disparity becomes more pronounced with advancing age. Many of those who survive into old age have lost their (marital) partners, and older women are less likely than older men to be married. In many countries, the socioeconomic status of older women, particularly widows, is poor. Women often lack the legal rights to family inheritance, and in some societies they may be resented by their in-laws with whom they live – or even be forcibly evicted from their homes upon the death of their husbands. In places where elderly women have a relatively poor socioeconomic status, this may lead to poor nutritional status, poor housing and poor access to health care, all of which increase vulnerability to infectious disease. However, there are very few studies that directly address differences between elderly men and women in exposure during outbreaks.

2.8.2 *Differences in access to curative care between elderly men and women*

Little is known about differences in access to curative care between elderly men and elderly women during disease outbreaks. Although it seems plausible that where the socioeconomic status of elderly women is poor they would lack adequate access to treatment during outbreaks, this issue has been little studied.

2.8.3 *Implications of sex and gender differences in the elderly for surveillance and response to outbreaks*

- Data on the age and sex distribution of morbidity and mortality for older people should be collected and analysed routinely.
- Symptom profiles for the elderly should be disaggregated by age and sex.
- Local customs and living conditions that could affect exposure to infectious disease, or the course and outcome of disease in the elderly, should be available to outbreak teams.

3

How sex and gender affect outbreaks of specific epidemic-prone diseases

This section focuses on the relationships between sex and gender and three specific epidemic-prone diseases: dengue, Ebola haemorrhagic fever and SARS. In addition to describing in more detail the role of specific sex and gender factors in disease transmission, the implications of such factors for outbreak surveillance and response are also presented.

All three of these diseases have caused outbreaks of public health importance during recent years. The number of cases of dengue fever, which is a vector-borne disease, has increased dramatically during the last decade, particularly in Asia and South America. Ebola haemorrhagic fever was first identified in 1976 and occurs only in Africa, whereas SARS was first identified in 2003, when it caused outbreaks in Asia and North America. Both Ebola haemorrhagic fever and SARS are spread directly from person to person.

3.1 Dengue and dengue haemorrhagic fever

3.1.1 *Introduction*

During the past two decades, there has been a dramatic increase in the number of cases of dengue fever, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). Today, dengue has become an important public health problem in tropical and subtropical areas with an estimated incidence of 50–100 million people infected annually of whom approximately 500 000 are hospitalized (WHO, 1999). Inter-epidemic periods are becoming shorter, and the proportion of cases with the most serious forms of disease (DSS and DHF) is increasing. The problem is particularly acute in Asia, South America, and, to a lesser extent, in Africa.

The severity of dengue infection ranges widely, from asymptomatic, to mild, to severe. Patients can progress to irreversible shock and death over a period of hours. The haemorrhagic symptoms of dengue fever are usually mild, but they may be severe enough in some cases to cause shock from loss of blood. Although the prognosis for dengue fever is generally favourable, a proportion of those who contract dengue develop DHF and DSS involving plasma leakage, which has a much less favourable prognosis. Case-fatality rates for DHF and DSS vary and can be as high as 10–15% in some epidemics and below 1% in others (Gubler, 2002).

Rapidly administered and carefully monitored intravenous volume replacement can be life-saving for patients with DHF and DSS. Therefore, access to health care services can play an important role in reducing case-fatality.

Dengue fever is a viral disease transmitted primarily by *Aedes* mosquitoes of the *Stegomyia* subgenus, which typically live in breeding sites in or around human habitation. There are four strains of dengue virus. Infection with one strain provides life-long immunity to that same strain and short-term immunity to the other strains. People can be infected by dengue several times if they are infected by different strains. Subsequent infections with other strains of dengue virus (secondary dengue infections) are more likely to cause severe symptoms (Cobra et al., 1995), and to progress to DHF or DSS. This is considered to be at least partly caused by an increased immune response to cross-reactive (yet non-neutralizing) antibodies from a previous dengue infection, although the exact mechanisms are not fully understood. DHF and DSS also occur in infants who have maternal antibodies to one strain of dengue virus and who become infected with a second strain.

There is as yet no available vaccine against dengue, and there are no specific drugs for treatment. Therefore, the response consists of vector control measures and good case-management. Dengue surveillance is poor in most countries, and epidemics often go undetected in the early stages, when vector control measures could do the most good.

3.1.2 *Differences in dengue incidence, severity and mortality between males and females*

Infants and children

In many countries especially in Asia, dengue is primarily a disease of children. In hyper-endemic areas (areas in which all four strains of dengue are endemic), by the time they have reached the age of 15 years, most children will have acquired antibodies to all four strains. In these areas the age distributions of the most serious forms of the disease DHF and DSS tend to be bimodal with one peak during infancy and another much larger peak during early childhood (Guzman & Kouri, 2002). This distribution pattern reflects two different risk factors for DHF and DSS, namely:

- circulating maternal antibodies coupled with primary infection during infancy; and
- secondary dengue infection during early childhood.

Several studies suggest that female children are more likely to have severe disease than male children and that this effect is age-related. A study of children admitted to a Delhi hospital during the 1996 outbreak (Kabra et al., 1996) found that although girls and boys were equally affected by dengue, girls were more likely to have severe symptoms. Based on studies in a children's hospital in Bangkok from 1962 to 1964, Halstead (1980) reported "a striking age-dependent increase in the number of girls with shock syndrome compared with boys", and concluded that this was host-related because age-stratified serological studies in Bangkok found similar

infection rates in boys and girls. Furthermore, Halstead cited Ministry of Health data for Bangkok for 1968–1977 showing greater numbers of deaths from dengue in female children from 4 to 14 years of age. A large prospective study of 712 children admitted with dengue to the Dong Nai Pediatric Center in southern Viet Nam from June 1996 to June 1998, found significantly more females requiring treatment for DSS than males (Phuong et al., 2004). However, a study of infants admitted to a hospital in Ho Chi Minh City, Viet Nam found no differences in DSS between males and females in this age group (Hung et al). Two explanations for the apparently greater severity of dengue in female children have been proposed:

— females may have increased immune responses (the more serious forms of disease are associated with an immune response to cross-reactive yet non-neutralizing antibodies); or
— female capillary systems may be "more prone to permeability than those of males" and this may put them at great risk of DHF and DSS (Halsted, 1997).

More work to quantify and understand differences between symptoms and severity in males and females is required.

Although the causes of possible male-female differences in severity and mortality may be biological, a greater awareness of a potentially higher risk to girls could lead to more girls being taken for treatment outside the home, or to girls being taken for treatment outside the home sooner. This would be particularly important in areas where gender norms such as son preference have created barriers to health care outside the home for females.

Adults

Wide variations in symptoms of dengue between male and female adults have not been suggested in the literature, although one study in Puerto Rico, which presented combined results for children and adults, found that among serologically confirmed cases, females reported body pain, joint pain and rash significantly more often than males (Cobra et al., 1995). In addition, female patients with dengue commonly experience vaginal bleeding, during both dengue fever and DHF/DSS (Gubler and Kuno, 1997). There are a number of clinical reports of patients with dengue fever experiencing severe vaginal bleeding during menstruation.

> "Severe menorrhagia has been described in women during dengue infections. Individuals with open mucosal lesions, whether pathologic (peptic ulcer) or physiologic (menstruation), who suffer dengue infections may bleed. Blood loss may be catastrophic and life threatening" (Halstead, 1997).

However, the level of risk of severe blood loss posed by dengue fever for menstruating as opposed to non-menstruating women has not been quantified (Gubler D, personal communication, 2003). If there is an increased risk of severe blood loss for menstruating women during dengue infections, this would be of potential importance because of the large number of menstruating women in the population.

(At any point in time menstruating women make up approximately 15% of women of childbearing age.)

The frequency of vaginal bleeding among female patients with dengue fever or DHF/DSS is seldom reported because male and female symptom profiles are combined and because vaginal bleeding is typically grouped with other haemorrhages. For example, a clinical review of dengue in China reports severe haemorrhage occurring in 5% of patients, and includes the uterus as one of the common sites of bleeding – but does not make specific reference to the proportion of women who experienced severe bleeding of the uterus (Qui et al., 1993). The importance of vaginal bleeding is also often masked by the tendency to list symptoms in order of frequency among *all* patients. For example, in a study of dengue in Cuba (Guzman, 1984a), vaginal bleeding was listed as a symptom that occurred in 23% of patients (24/103), which made it appear much less frequent than the most common symptom petechiae (which occurred in 39% of cases) and haematemesis (which occurred in 30% of cases). If only female patients had been considered, vaginal bleeding would have ranked as being of equal importance to petechiae, because it occurred in 39% of female patients. Similarly, in China, uterine bleeding tied with gum bleeding as the fourth most common haemorrhagic symptom affecting 17.5% of patients. However, it was the second most prevalent symptom in females affecting 35% of female dengue patients (Qui et al., 1993).

The failure to study the symptom profiles of males and females separately is not limited to dengue fever, but has also hampered the understanding of sex differences in symptoms for other diseases (particularly diseases that affect males in greater numbers than females). For example, because of the failure to look at male and female symptom profiles separately, and because in the early days of the HIV/AIDS epidemic most cases studied were among males, it took many years to recognize that vaginal thrush is a typical opportunistic infection associated with HIV/AIDS in females.

Inconsistent patterns of incidence rates of dengue fever in males and females have been found. Some studies report similar incidence rates for males and females (Thaung et al., 1975, Halstead, 1980), some have found higher incidence rates in females (Kaplan et al., 1983; Guzman et al., 1984a; da Cunha et al., 1997), whereas others have found higher incidence rates in males (Goh & Yamazaki, 1987; Ooi, 2001). When differences in incidence rates between males and females have been found, they have often been attributed to differences in exposure. For example, the authors of some studies which found higher rates of dengue infection among adult females than adult males hypothesized that women have greater exposure to the bites of dengue-infected mosquitoes because they spend more time during the day (when the mosquitoes are most likely to bite) in the home (Kaplan et al., 1983: Guzman et al., 1984). Ooi attributed the higher incidence rates in males to greater exposure of males of working age outside the home.

Pregnancy and lactation

There are no estimates of the proportion of dengue cases in pregnant women. However, there is evidence of an increasing incidence during adulthood in some parts of the world (Bunyavejchevyan et al., 1997; Guha-Sapir, 2005). This shift is likely to lead to an increase in the number of pregnant women affected by dengue (Bunyavejchevyan et al., 1997). For pregnant women who are close to term and who become infected with dengue there is evidence of increased risk of haemorrhage, premature birth and fetal death (Carles et al., 2000). Furthermore, caesarean sections may pose increased risk of dangerous loss of blood for females with dengue infection.

Maternal antibodies to dengue can be transmitted vertically. In contrast to the purely protective effect of maternal antibodies against a variety of childhood diseases, the transmission of maternal dengue antibodies has both positive and negative implications. On the positive side, maternal antibodies confer protection against dengue of the same serotype as that with which the mother was infected. If only one strain of dengue virus is circulating during an epidemic, the protection afforded to the infant by the maternal antibodies is effective against the same strain as that which infected the mother, especially if the mother was infected late in pregnancy. On the negative side, these antibodies put the baby at risk for the most serious forms of the disease, namely DHH and DSS if the he or she becomes infected with a different virus type.

Anti-dengue antibodies have been found in the lipid component of breast milk and in colostrum (Chong & Lin, 1989). For the reasons given above, the risk to the breastfed baby of infection with the same strain of dengue is decreased, while the risk of DHH and DSS is increased if the baby is exposed to a different virus strain.

The elderly

The elderly have been found to be particularly vulnerable to severe disease and death from dengue, even after controlling for sex and the fact that the majority of elderly people are women. The pattern of severity among the elderly has been characterized as being similar to that of infants (Garcia et al., 2003). However, few, if any, studies have reported on sex differences related to dengue among the elderly. In settings where dengue is primarily a childhood disease, most elderly people are presumably already immune to it. However, in settings where dengue affects the old as well as the young, this is an important knowledge gap.

3.1.3 *Differences in access to treatment between males and females*

Immediate treatment with intravenous replacement fluids can make the difference between life and death in cases of severe DHF and DSS. To date, no studies have compared men and women in terms of treatment behaviour for dengue. However, in settings where males are given priority and are generally more likely than females to be taken outside the home for treatment, emphasis should be placed on persuading

families to bring females for treatment as well as males – especially because females are more likely to have severe disease and to die than males.

3.1.4 *Gender and vector control*

The elimination of mosquito breeding sites in and around the home is important for vector control. There is considerable literature to support the hypothesis that males and females have different roles and responsibilities regarding vector control activities for dengue. Although gendered roles and responsibilities vary from culture to culture, women are usually responsible for the maintenance of the containers that hold the family drinking-water, and of the water vessels for doing laundry (both of which may be prime breeding sites for *Aedes* mosquitoes). However, the responsibility for the maintenance of other potential vector breeding areas such as large water vessels stored outside the immediate living area, or disposal of discarded solid wastes may be primarily taken by men in some cultures (Whiteford, 1997). Targeting males and females separately, and being sensitive to their specific gender roles is essential when enlisting their support for vector control. Readers are referred to World Health Organization (2004) for more details on social mobilization for prevention and control of dengue.

3.1.5 *Implications of sex and gender for surveillance and response to dengue outbreaks*

- The sex distribution of cases of dengue fever, DHF/DSS and deaths from dengue should be included in the routine surveillance of dengue.
- Further work is needed to quantify the risk of severe haemorrhage for menstruating women, which has so far only been referred to anecdotally.
- There are few data on differences between males and females in health seeking behaviour specifically for dengue. Such information is important because in some areas of the world females are less likely to be taken for treatment outside the home than males or are likely to be taken for treatment later.
- Gender-related roles have been shown to be of particular importance for enlisting community support in vector control generally and for eliminating mosquito breeding sites in and around the home.

3.2 Ebola haemorrhagic fever (EHF)

3.2.1 *Background*

Ebola haemorrhagic fever (EHF) is a viral disease transmitted to people both by animal-to-human contact and human-to-human contact with infected organs, or through bodily secretions such as blood, faeces, urine, vomit, sweat and semen. Although the reservoir for EHF is unknown, contact with infected dead or sick primates is a common way in which EHF is initially introduced into human populations (index cases). Once introduced into the human population, common transmission routes include:

— contact with infected, dead or sick primates;
— contact with family members while caring for infected relatives;
— contact with dead bodies while preparing them for burial;
— amplification in hospitals and health centres (with spread to health care workers and to other patients); and
— amplification in other health care settings including traditional healers and midwives.

EHF was first identified in 1976. Since then outbreaks of the disease have occurred in seven African countries. Table 3 summarizes the salient features of each outbreak. There is neither a vaccine nor an effective treatment for EHF and case-fatality rates for clinically ill individuals vary from 50% to 90%. For this reason, outbreak control measures are concentrated on reducing exposure to infection through isolation of patients and contact tracing, eliminating unsafe burial practices and funeral rites, and on infection control in treatment settings.

To date, outbreaks have affected a relatively small number of people. Nevertheless, high case-fatality rates and dramatic symptoms in victims cause fear and panic during outbreaks. Moreover, EHF could spread to areas where it may do considerably more harm than it has done so far.

3.2.2 *Differences in exposure, infections rates and mortality between males and females*

The index cases in several outbreaks have been shown to have had contact with forest animals, including through the handling and butchering of animals found dead in the forest (Table 3). This suggests that men, who are more likely than women to go regularly into the forest as a consequence of their gendered roles, may be at greater risk of infection at the onset of an outbreak. However, as an EHF outbreak progresses, females infection rates are often higher than those of males, implying that women's exposure to the virus increases as the outbreak progresses. These incidence patterns suggest that gender-related factors are key determinants of exposure to, and infection with, the Ebola virus.

Figures 1 and 2 show how two particular epidemics of EHF progressed over time. In the 2001–2002 outbreak that occurred in the Congo and Gabon, more men than women were infected during the early stages of the outbreak, a situation that was reversed during the later stages of the outbreak (Figure 2). In contrast, the number of female cases exceeded the number of male cases for the duration of the outbreak of 2000–2001 in Gulu, Uganda (Figure 1). The reasons for these differences in the epidemic curves of these two outbreaks are not well understood.

During an outbreak, health officials usually compare the cumulative distributions of male and female cases. Cumulative distributions can sometimes mask potentially informative fluctuations in numbers of cases over the course of an outbreak. For the outbreak in Gulu, for example, the cumulative distribution was greater in females throughout, whereas in the outbreak in Gabon it switched from predominantly male

TABLE 3
Features of outbreaks of Ebola haemorrhagic fever (EHF)

PLACE AND YEAR	CASES	CASE FATALITY RATE (%)	FEMALE CASES (%)	CASES IN HEALTH CARE WORKERS (%)	NUMBER OF CASES AMONG PREGNANT WOMEN	COMMENTS
Yambuku, Zaire, 1976	318[a]	88	56	13 of 17 health workers in Yambuku mission hospital	82	First recognition of EHF. Amplification by contaminated needles used for vitamin injections to pregnant women. Rural area.
Nzara and Maridi area, Sudan, 1976	284[a]	53	NA[a]	26 (34% in Maridi; 3% in Nzara)	NA[b]	Began in small town of Nzara among employees of a cotton factory, spread to city of Maridi, amplified in Maridi Hospital.
Nzara and Maridi area, Sudan, 1979	34[a]	65	62	5.9	NA	Same site as previous outbreak.
Minkebe, Ogooue-Ivindo Province, Gabon, 1994	51	61	47	NA	NA	First wave in gold-mining camp in rainforest. Second wave included nosocomial amplification in Makokou General Hospital.
Kikwit area, DRC, 1995	315[a]	81	53	25	15/105 cases in Kikwit General Hospital	Index cases in charcoal worker and farmer. Nosocomial spread in Kikwit II Maternity and in Kikwit General Hospital.
Mayibout, Gabon, Spring 1996	31[a]	68	45	0.0	1	First cases linked to "butchering, transport and preparation" for eating of chimpanzee found dead in forest.
Booue, Gabon, Autumn 1996	60[a]	75	43	3.3	NA	Outbreak most likely began with a hunter in a logging camp near Booue.

Continued

Table 3 *continued*

PLACE AND YEAR	CASES	CASE FATALITY RATE (%)	FEMALE CASES (%)	CASES IN HEALTH CARE WORKERS (%)	NUMBER OF CASES AMONG PREGNANT WOMEN	COMMENTS
Gulu, Masindi, and Mbarara districts, Uganda, 2000–2001	425	53	63	7.3	NA	Amplification by nosocomial spread in hospitals, caring for sick relatives and traditional burial practices.
Zadie district Gabon and Mbomo and Kelle districts, Congo, October 2001 –July 2002	124	79	50	1.6	NA	Six or more different introductions to human population. Apparently related to epizootic in great apes.
Olloba, Congo, 2002	16	63	31	0.0	NA	
Mbomo and Kelle districts, Congo, January–April 2003	143	89	49	2.1	NA	Three independent introductions linked to hunting.
Congo October–December 2003	35	83	54	1	NA	Index case linked to dead animal in forest.

NA, not available

[a] The majority of cases in 1976 in Maridi Sudan, were male because 75% of the Maridi hospital staff were male. In Nzara there were equal attack rates in adults – and a moderate number of cases in teenagers linked to a single chain of transmission (WHO International Study Team, 1978).

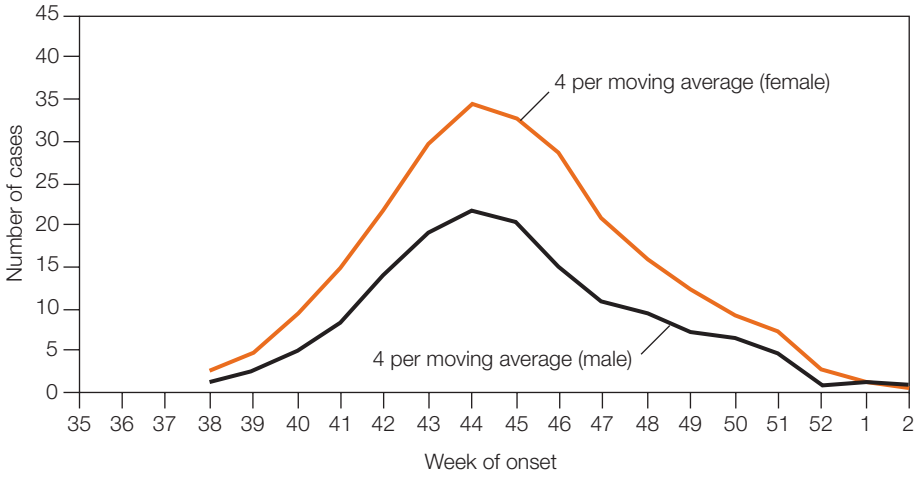
[b] The WHO International Study team indicated that pregnant females occasionally went into premature labour – but the number of pregnant females was not reported.

Sources

- CDC special pathogens branch web site (accessed 7 March 2004) for number of cases and case-fatality rate for outbreaks in Yambuku, Zaire, 1976; Nzara and Maridi area, Sudan, 1979; Kikwit area, DRC, 1995; Mayibout, Gabon, Spring 1996, Booue, Gabon, Autumn 1996, Gulu, Masindi and Mbarara districts, Uganda, 2000–2001. http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola/ebolatable.htm
- WHO International Commission, 1978 for percentage of cases in females and percentage of cases in health care workers in Yambuku, Zaire, 1976.
- WHO International Study Team, 1976, for percentage of cases in health care workers and comments for Nzara, and Maridi area, Sudan, 1976.
- Mupapa K et al., 1999 for number of cases among pregnant women for Yambuku, Zaire, 1976; Kikwit area DRC, 1996, comment Mayibout Gabon, Spring, 1996.
- Baron R, McCormick J, Zubeir O, 1983, for percentage of cases in females and percentage of cases in health care workers, Nzara and Maridi area, Sudan, 1979.
- Arthur R, 2002, for number of cases and case fatality rate in Makebe, Gabon, 1994; for case fatality rate and comment Zadie district, Gabon and Mbomo and Kelle districts, Congo, 2002.
- George A-J et al.,1999, for percentage of female cases in Makebe, Gabon, 1994.
- Khan A et al., 1999, for percentage of cases, percentage of cases in health care workers and comment Kikwit area, DRC, 1995; Mayibout, Gabon, 1996; and Booue, Gabon, 1996.

FIG 1

Four-week moving average of number of EHF cases by sex and week (n = 404), Uganda, week 35, 2000 – week 2, 2001



EHF, Ebola haemorrhagic fever.
Source: World Health Organization, Department of Communicable Disease Surveillance and Response, unpublished data, 2000–2001.

to predominately female. If only the cumulative distribution had been plotted for the outbreak in Gabon, the switch in incidence from an excess of male cases to an excess of female cases would not have been seen until later in the outbreak when the total number of females infected was greater than the total number of males infected.

Figure 3 is a scatter plot of the proportion of female cases according to the size of the outbreak. There is a general tendency for the larger outbreaks to include a larger proportion of female cases, although the relationship is not strong and is statistically significant only at the 10% level (P = 0.09). The female excess may be explained by the fact that the transmission of the Ebola virus often occurs while caring for the sick, a role that is more likely to be played by women than men.

Interestingly, the outbreaks in Sudan are notable exceptions. Although no published data are available on the proportion of female cases in a relatively large

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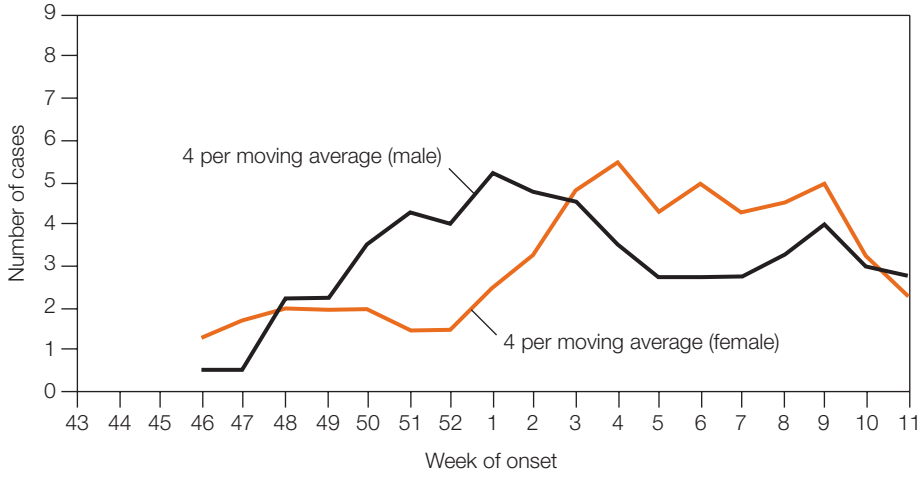
Table 3 sources continued

- Pierre Formenty, personal communication for percentage of cases in females, Booue, Gabon, 1996; all data for Olloba, Congo, 2002, and percentage of cases in females and percentage of cases in health care workers, Congo, 2003.
- Hwelett B, Amola R, 2003 for percentage of cases in females Gulu, Masindi and Mbarara districts, Uganda, 2000–2001.
- Omaswa F et al., 2002 for percentage of cases in health care workers, Gulu, Masindi and Mbarara districts, Uganda, 2000–2001.
- Formenty P, Libama F, et al, 2003 for number of cases, percentage of cases in females, and percentage of cases in health care workers, Zadie district, Gabon, and Mbomo and Kelle districts, Congo, 2001–2002.
- Anonymous, 2003 for number of cases and case fatality rate, Congo, 0ctober–December 2003.

FIG 2

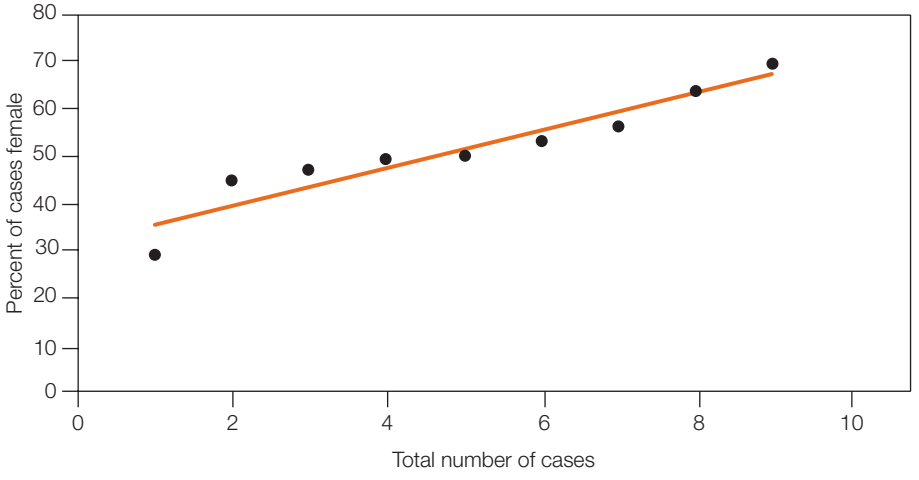
Four-week moving average of number of EHF cases by sex and week (n = 119), Gabon – Congo, week 43, 2001 – week 11, 2002



EHF, Ebola haemorrhagic fever.
Source: World Health Organization, Department of Communicable Disease Surveillance and Response, unpublished data, 2001–2002.

FIG 3

Scatter plot of the proportion of EHF cases among females to the toal number of cases



EHF, Ebola haemorrhagic fever.
Source: Table 3.

outbreak that occurred in 1976, it has been reported that males predominated because 75% of the medical staff in the main hospital was male (WHO International Study Team, 1976). The 1979 outbreak in Nzara and Yambio, Sudan was also unusual, in that despite its small size, a large proportion of those infected were female (69%). Baron et al. suggested that the transmission of cases was almost exclusively from providing nursing care for sick relatives; 24 of 29 secondary cases had provided such care.

There is anecdotal evidence that the increased burden for females caring for the sick has been well understood by some populations, and that females are deliberately asked to care for the sick to protect males from becoming sick. For example, during a recent outbreak in the Congo in October 2003, an international investigator asked a group of men how they avoided contracting EHF, and they responded that they made sure that women cared for the sick – thus protecting males from infection (P. Formenty, personal communication, 2003).

The preparation of bodies for burial has been found to play a role in the transmission of EHF. In some societies this activity is heavily influenced by gender norms. In Gulu, Uganda, for example, the paternal aunt of the deceased or another female relative on the father's side is responsible for washing the body of the deceased, a practice that is likely to have contributed to the high proportion of female cases in the 2000–2001 outbreak (Figure 1). Communal washing of hands and touching the body of the deceased during burial – traditional practices in which both males and females participate – also contributed to the transmission of EHF during this particular outbreak.

There is no indication of differences between males and females in symptoms of or mortality from Ebola, apart from the effects of Ebola during pregnancy, which are discussed below. Because Ebola is a haemorrhagic disease, in which bleeding can occur from all orifices, vaginal bleeding does occur. However, this does not appear to be of particular clinical significance.

3.2.3 *Health care workers and Ebola haemorrhagic fever*

Many of the larger epidemics of EHF were amplified in health care settings, leading to a relatively high proportion of health care workers being affected (Table 3). In Kikwit, Zaire, for instance, the attack rate was highest among the 13 medical doctors (31%), although nurses, who had attack rates of 10% (Tomori et al., 1999), accounted for the majority of cases in health care workers, because they were much more numerous than medical doctors. A breakdown by sex of the number of cases among the various categories of medical staff is not available for other outbreaks of EHF, but nursing staff generally tend to be the health care workers who come in direct contact with patients in the greatest numbers, so they have a high vulnerability. Because nurses in almost every country tend to be predominantly female, the occupational exposure of nurses can be considered a gender related exposure.

3.2.4 *Pregnancy and Ebola haemorrhagic fever*

Because pregnant women tend to have more contact with the health services than they would normally have, both for antenatal care and for delivery, like health care workers, these women experience greater exposure to infections such as EHF that are amplified in health care settings. In fact, two of the three largest outbreaks of EHF involved nosocomial transmission in maternity settings. The first recorded outbreak of EHF in Yambuku Zaire, in 1976, was spread through contaminated needles used for vitamin injections provided to pregnant women during routine antenatal visits. In 1995, there was a small unrecognized outbreak in Kikwit maternity hospital that led to a much larger outbreak in Kikwit General Hospital, when a patient was transferred there from the maternity hospital (Table 3).

EHF frequently causes spontaneous abortions with heavy bleeding, particularly during the first and second trimesters of pregnancy. However, because spontaneous abortions are not uncommon among pregnant women seeking emergency admission to maternity clinics, a person presenting with such symptoms may not be suspected of having EHF. This is likely to be especially true before an outbreak of EHF has been identified.

There is conflicting evidence as to whether case-fatality rates are higher in pregnant women than in non-pregnant women. Few of the published clinical data on EHF disaggregate cases by pregnancy status, and, therefore, clinical data on EHF during pregnancy are limited. There is, however, an excellent description of the course and outcome of EHF in pregnant women based largely on 15 pregnant patients treated in Kikwit General Hospital (Mupapa et al., 1999). The findings suggest that the course of EHF in pregnant women might be more severe than in non-pregnant women, with more severe haemorrhagic and neurological complications. The mortality rate for pregnant women was 95.5%, which was higher than the overall mortality rate in Kikwit General Hospital (77%), and in non-pregnant women (70%), but the sample size of pregnant women was small and the results were not significant at the 5% level. In contrast, the mortality rate among pregnant women in the outbreak in Yambuku in 1976 was 89%, similar to the overall mortality rate of 88%.

EHF appears to have disastrous consequences for the fetus. In Kikwit, Zaire, of the 15 pregnancies studied, 10 ended in spontaneous abortion; four women died during their third trimester; and the only baby to be born died at age 3 days. In Yambuku, the 10 live-born infants all died shortly after birth. In the Mayibout, a single case in a pregnant woman resulted in a stillbirth. There has also been documented transmission from lactating mothers to their breastfed children (Francesconi et al., 2003).

3.2.5 *Elderly women and Ebola haemorrhagic fever*

Evidence from anthropological studies of the EHF outbreak in Gulu indicates that elderly women traditionally play a crucial role in care of the sick and in the preparation of bodies for burial, a factor that is likely to increase the risk of illness

among elderly women. In Uganda, among the Acholi it is customary for the paternal aunt or an older woman in the paternal line to prepare bodies for burial. In addition, local customs call for either a survivor of disease or an elderly woman to care for the sick during outbreaks of very severe disease (Hewlett & Amola, 2003).

3.2.6 *The impact of EHF on the lives of male and female survivors*

Because of the fear engendered by outbreaks of EHF, many survivors experience difficulties in reintegrating into their families and the community after recovery. An anthropological study in Gulu, Uganda revealed a wide range of problems of this nature, which included not being able to return home and abandonment by a spouse (for example, wives were told to return to their home villages). Stigmatization was also frequently reported; some children were told not to touch survivors (Hewlett & Amola, 2003). Females reported stigmatization somewhat more frequently than males (although the sample size was small and the differences were not statistically significant). This included being feared when they returned to the community, and experiencing rejection in localities around the village such as markets, wells and boreholes, and when walking through the neighbourhood.

Some of the survivors of the 2000–2001 outbreak in Gulu told investigators that the resumption of sexual relations was problematic (M. Lamuru, personal communication, 2003). Possible reasons for these problems include weakness after the illness, and the fact that males were told to use condoms or to avoid sex for a period after recovery because of the possibility of the virus still being present in semen after recovery – but they were not necessarily told for how long they should continue to take such precautions.

3.2.7 *Implications for surveillance and response to Ebola haemorrhagic fever*

- Differences in exposure between males and females have been shown to be important factors in transmission of EHF. Therefore, it is important to understand the gender roles and responsibilities that affect exposure in the local area.
- Comparison of epidemic curves for males and females can provide information on changes in gender patterns of transmission more quickly and in more detail than the cumulative rates that are now in more general use.
- Anthropologists with a gender perspective have been shown to be very helpful in elucidating gender roles and their impact on transmission, and they are now often included in the international EHF outbreak control teams fielded by the World Health Organization.
- During outbreaks it is important that women who care for the sick outside health care settings are informed about how to protect themselves from EHF. During the most recent outbreak in the Congo, in October 2003, health education meetings targeted towards women on how to protect themselves while caring for the sick were found to be extremely useful in halting transmission.

- The introduction of barrier-nursing methods (coupled with contact tracing and isolation of patients) has been key to ending EHF outbreaks in several settings. However, nursing staff often are not empowered to initiate barrier-nursing procedures if they suspect a case of EHF. The need to provide nurses with better training in infection control and to empower them to initiate protective measures are, therefore, key lessons to be learned from these outbreaks.
- Surveillance of complications of pregnancy suggestive of EHF and of deaths in maternity clinics is important for contact tracing, particularly at the beginning of an outbreak.

3.3 Severe acute respiratory syndrome (SARS)

3.3.1 *Introduction*

Despite significant differences in locations and clinical profile, there were many similarities between the outbreak of SARS that occurred in 2003 and outbreaks of EHF. Both are severe viral diseases with high case-fatality rates, although the crude case-fatality rate of SARS (9.6%) is not nearly as high as the crude case-fatality rates of EHF (normally between 50% and 90%). Both diseases have been identified recently and, as yet, their natural reservoirs are unknown. Their spread in the community has resulted in fear and large-scale disruptions, and both diseases have been amplified in health care settings. Outbreaks of both diseases have been controlled by introduction of better infection control procedures in hospitals, isolation of cases and contact tracing.

3.3.2 *Differences in incidence and mortality between males and females*

A total of 8098 probable SARS cases, of which slightly more than half were female[1] (World Health Organization, 2003), have been reported to WHO from 30 different countries and areas. Age was the most important predictor of mortality from SARS; the few children infected had the lowest mortality rate, whereas the oldest patients had the highest. For reasons that are not yet understood, females had lower mortality rates from SARS than males, a pattern that is maintained after adjusting for age. For example, according to data reported to WHO from China, Hong Kong, Special Administrative Region (Hong Kong SAR), the mortality rate for males was 21.9%, which was substantially higher than the mortality rate for females of 13.2%.

Health care workers

Considerable transmission of SARS took place in health care settings, and consequently, health care workers bore a disproportionate burden of disease. The proportion of cases that occurred among health care workers ranged from 8% in countries with relatively few cases to 57% in Viet Nam, with an overall average of

[1] The sex of 46 cases from China was not determined. These cases were not considered when calculating the percentage of SARS cases that occurred in females.

21% (World Health Organization, 2003). Gender roles are such that health care workers tend to be predominantly female, a factor that would have contributed to higher infection rates for females than males in most countries.

Pregnancy and SARS

The SARS epidemic provides important insights into the extent to which the surveillance and response system for serious new diseases takes sex and gender considerations into account. During the SARS outbreak, pregnancy status was generally ignored by the surveillance and response system, and pregnancy was treated like any other concomitant condition. Thus, pregnancy status was not systematically established and recorded in several of the countries with sizeable numbers of SARS cases. Nor was pregnancy data included in line-listings of cases provided to WHO. This has made it difficult to identify pregnant cases and hampered our understanding of the clinical manifestations of pregnancies complicated by SARS.

Partly because information on pregnancy status was not systematically collected, there is very little information on the outcome of SARS infection during pregnancy for the women or for the fetuses. However, other causes of pneumonia have been associated with increased complications and hazards for the fetus, and greater mortality during pregnancy (Dumont, 1989; Rodrigues & Niederman, 1992; le et al., 2002), so one could reasonably also expect SARS to be associated with poor outcomes.

To date, there are published reviews of the clinical course and outcome of SARS-complicated pregnancies from five cases in China (Zhang et al., 2003), 12 cases in Hong Kong SAR (Shek et al., 2003; Wong et al., 2004; Lam 2004), two cases from the USA (Robertson et al., 2004; Stockman et al., 2004) and one case from Canada (Yudin et al., 2005). These reports provide an indication of the ranges of outcomes that have occurred following pregnancies complicated by SARS. However, they cover a total of only 20 cases.

Despite the small number of cases, there is some evidence from Hong Kong SAR and China that SARS had a more severe course in pregnant women than in non-pregnant women. In addition, mortality rates were greater in pregnant SARS patients in Hong Kong SAR than non-pregnant female patients of childbearing age. Furthermore, pregnant women who recovered from SARS, and remained pregnant, faced psychological problems. Indeed in China, two pregnant SARS patients developed mental disorders – attributed by the authors to the psychological stress of being pregnant and contracting a new infectious disease whose potential effects on the fetus are unknown.

The limited evidence available also raises concerns about the outcome of SARS for the fetus. In Hong Kong SAR, there was a high incidence of spontaneous abortion involving four of seven women presenting with SARS during their first trimester, and a high incidence of pre-term delivery involving four of five patients who presented after 24 weeks of gestation in Hong Kong SAR (Wong et al., 2004).

In addition two of the five infants born in Hong Kong SAR to mothers who had SARS developed severe gastrointestinal complications. In China, one twin was lost from a twin-pregnancy. There was one pre-term delivery at 31 weeks, and fetal distress occurred in two deliveries (Zhang et al., 2003). In the USA and Canada, all mothers delivered healthy babies with no apparent effect from the mothers having SARS (Robertson 2004; Stockman 2004; Yudin et al., 2005).

There is no evidence of SARS transmission to health care staff during obstetrical procedures, but it is highly unlikely that all pregnancies complicated by SARS have been identified. Because the modes of transmission of SARS were not fully understood, stringent infection control measures were used for deliveries following pregnancies complicated by SARS and described in the literature on Hong Kong SAR (Ng et al., 2003), China (Zhang et al., 2003) and on the USA (Robertson et al., 2004). Descriptions of the infection control methods used during these deliveries may become important should there be another outbreak of SARS, or an outbreak of another new infectious disease with unknown routes of transmission.

3.3.3 *Implications for surveillance and response*

- There was a small excess of female SARS cases, especially in countries with large outbreaks, which can be attributed to the predominance of female health care workers in those countries. However, even after controlling for age, females had lower mortality rates than males. The reasons for this are not understood.
- It is important to record the pregnancy status of every female patient of child-bearing age during outbreaks of new infectious diseases. In addition, an informal network of clinicians who have treated pregnant women with SARS can be very useful for sharing ideas and information on pregnancy. During the SARS outbreak WHO convened an informal network of clinicians who had treated such patients. This network held several telephone conferences to discuss clinical issues relating to SARS and pregnancy, with the aim of consolidating available information and sharing experience. A clinical database of all known cases of SARS and pregnancy status should be established and analysed. This is especially important for assessing the success and failure of potential treatment.

3.4 Conclusions and implications for surveillance and control

This paper has been concerned with epidemic-prone diseases and the extent to which gender and sex play a role in their transmission. The available evidence for three important epidemic-prone diseases – dengue, EHF and SARS – were used to illustrate the importance of gender and sex in spreading disease and controlling outbreaks. Four aspects of relevance should be noted:

1. There is a scarcity of systematic evidence on sex and gender differences, even to the point where basic information, for example, on incidence, case-fatality rates and pregnancy status, is not always available for women.

2. Despite the scarcity of information, there are strong indications that sex and gender are important for transmission and control of epidemic-prone diseases.
3. The ways in which sex and gender affect outbreaks of epidemic-prone diseases are complex and disease-specific. For example, there are indications that severity may be greater for female children with dengue, and for males with SARS. Exposure to EHF is sometimes greater for male hunters at the onset of the outbreak and for female caregivers later on.
4. There need to be changes in the information that is routinely collected during outbreaks because information on sex, occupational status and pregnancy status cannot easily be collected retrospectively. This is particularly important for outbreaks of new diseases.

Some other general conclusions and suggestions are provided below to help improve surveillance and control of outbreaks of epidemic-prone infectious diseases.

Gender factors related to transmission and control in the community

- It is important to identify differences in patterns of exposure of females and males and to understand why such differences exist.
- Both males and females need to receive gender-sensitive messages related to outbreak control. The content of the message should vary by disease. For example, for EHF the message may deal with protection from infection, whereas for dengue it may deal with elimination of mosquito breeding sites.
- Reported data should be disaggregated by sex, occupational status and pregnancy status and subjected to careful statistical analysis, such as comparing epidemic curves for males and females.

Gender factors related to transmission and control in health care settings

- Preventing the spread of infection in hospital and health care settings has been a recurrent theme, and its importance was dramatically illustrated during the outbreaks of SARS and EHF.

Factors related to pregnancy

- Pregnancy is a period of special vulnerabilities and potential risk; therefore it is particularly important to consider pregnant women during an outbreak of an unknown disease. Pregnant women face changes in the immune system throughout pregnancy, increased exposure to health care settings, limitations on treatment options and concerns for the fetus as well as for themselves.
- During outbreaks, close links are needed between the outbreak control staff and health care workers who treat pregnant women. Additional surveillance is required in obstetric care settings to raise awareness, as suspicion of infection may be low for pregnant women, and obstetric care workers may be at higher risk – especially if the disease causes pregnancy complications.

- International protocols should be developed for sharing clinical data during an outbreak of a new infectious disease, including the disaggregation of such data by sex and pregnancy status. The procedures for doing this need to be worked out in advance.

In conclusion, this paper has presented evidence that gender and sex are important for the transmission of three infectious epidemic-prone diseases, although gender-related aspects of these diseases have so far received little attention. It is clear that sex and gender-related aspects of infectious diseases need to be understood better and should become an integral part of the thinking of public health officials. This would benefit both men and women as it would lead to improved outbreak control.

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