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Previous studies of measles mortality in West

Subjects and methods

TABLE I—CFR BY AGE AND SEX

Age (yr)	Males		Females	
	CFR (%)	No of deaths/cases	CFR (%)	No of deaths/cases
<0·5	6	1/16	10	2/20
0·5–1·0	11	8/73	14	8/56
1	10	13/136	12	16/131
2	12	14/114	15	15/99
3	5	4/80	10	8/83
4	3	3/87	1	1/71
5–9	1	2/210	2	3/197
⩾10	0	0/62	0	0/65
Total	5·8	45/778	7·3	53/722

The Mantel-Haenszel χ^2 test and relative risk were used to combine results from individual 2×2 tables corresponding to various subgroups.[5] Approximate confidence intervals (CI) were calculated by the test-based method.[5]

Results

In 1983–86, girls continued to have higher CFR than boys (table I), although the difference was not significant; the relative risk of death from measles (girls *vs* boys) was 1·30 (95% CI 0·89–1·90), indicating the same tendency as in 1963–81 (1·52 [1·07–2·16]).[4] Analysis of the data by type of exposure (table II) showed that secondary cases had a much

TABLE IV—CFR IN HUTS WITH ONLY 2 CONCURRENT CASES OF MEASLES

—	Male		Female	
	CFR	No of deaths/cases	CFR	No of deaths/cases
2 cases of same sex				
4–5 mo	0	0/3	50	1/2
6–41 mo	8	4/49	7	2/30
42–65 mo	0	0/34	0	0/20
⩾66 mo	3	1/36	0	0/35
Total	4	5/122	4	3/87
1 case of each sex				
4–5 mo	0	0/2	100	1/1
6–41 mo	12	5/43	20	10/49
42–65 mo	4	1/25	5	1/20
⩾66 mo	0	0/22	0	0/24
Total	7	6/92	13	12/94

[1·18–3·42]) and older children (10·1 [1·96–52·2], table III). The effect of cross-sex transmission was stronger for male secondary cases (relative risk of death in comparison with same-sex transmission 2·89 [1·40–5·95]) than for female secondary cases (1·93 [0·94–3·98]). By contrast, when all secondary cases were taken together, there was no significant difference in CFR between those infected by female and those infected by male index cases (1·24 [0·77–1·99]).

In huts with only 2 cases of measles (table IV), the CFR was higher in families with 1 boy and 1 girl affected than in families with 2 boys or 2 girls affected (relative risk 2·16 [0·99–4·70]). The difference was especially pronounced for girls; the CFR was 3·15 (1·02–9·69) times higher in huts with a boy and a girl affected than in huts with 2 girls affected. For boys the relative risk was only 1·47 (0·44–4·93).

Discussion

This study suggests that measles infection contracted from a person of the opposite sex is more severe than that contracted from someone of the same sex. Even if classifications of source of infection were biased, the higher CFR in families with 1 boy and 1 girl affected than in families with 2 girls or 2 boys affected shows that contact with an infected child of the opposite sex somehow increases the severity of measles infection. In the study from Guinea-Bissau,[3] the tendency was most pronounced for girls. In this study, the tendency was strong for both sexes but significant only for boys. Whereas the Guinea-Bissau study found the effect mainly in children under 3 years old, because there were very few deaths among older children, this study found a significant tendency for both younger and older children. There seems to be no form of confounding that can explain the findings.

In developed countries, it is usually assumed that higher mortality in infectious diseases is "natural" for boys.[6] Higher mortality among girls in areas such as Bangladesh[7] is interpreted as being a result of preferential treatment of boys. Such variations, however, could also be explained by differences in the transmission pattern. There is some evidence that girls in developed countries tend to be index cases.[8,9] Thus, boys should be more likely to be secondary cases.[8] By contrast, societies with higher reported female measles mortality[7,10-12] are Muslim, and it is possible that girls stay at home while their brothers contract infection elsewhere. If individuals of one sex are more likely to be index cases owing to specific behaviour patterns, those of the other sex are at a dual disadvantage; they would be more likely to be intensively exposed as secondary cases[1] and more likely to be infected by someone of the opposite sex.

These hypotheses could be tested in Niakhar in rural Senegal, where it was known from the previous surveillance of measles infection that girls had a higher CFR than boys.[4] There was little difference in the frequency of secondary cases between the sexes. However, because of the larger number of infected boys within the area and the higher risk of girls contracting infection outside the area, there were fewer female index cases among the children infected within Niakhar. Thus, girls had a significantly higher risk than boys of contracting infection from someone of the opposite sex. This difference in exposure pattern accounted for most of the difference in CFR between girls and boys. Thus, most of the higher measles mortality among girls may be related to the pattern of transmission. Girls do not have higher mortality from all causes in the Niakhar area. The same proportions of boys and girls are taken to health centres (unpublished). Thus, differential treatment is unlikely to explain the observed pattern of measles mortality.

The phenomenon of greater severity after cross-sex than same-sex transmission has been found in several studies of measles.[3,13-16] This unexpected tendency may not be limited to measles infection; we have found in Guinea-Bissau that male/female twins have a higher risk of postneonatal mortality than same-sex twins.[17] Furthermore, my examination of case-reports of severe and fatal chickenpox infection suggests that cross-sex transmission increases severity. However, preliminary observations of a severe whooping-cough epidemic in Guinea-Bissau with a high CFR suggested that cross-sex transmission was less important in pertussis infection (unpublished). Hence, the phenomenon may be associated mainly with viral infections.

Why is infection contracted from someone of the opposite sex more severe? The simplest explanation would be that close contact (eg, kissing), which increased the dose of virus or the risk of complicating infections, was more common between a boy and a girl than between 2 children of the same sex. No such difference in contact patterns has been documented in studies of child behaviour.[3] However, it may be necessary to look more specifically at interaction patterns during times of illness. Since the same tendency has been found in widely differing societies,[3,13-17] it seems unlikely that culturally determined behaviour patterns are the cause, but biologically based behaviour patterns could mean that transmission of a high dose is more common from someone of the opposite sex.

Basic mechanisms at cellular level should also be considered. The simplest possibility is that passage through cells of the opposite sex enhances infectivity and increases viral load or interferes with the immune system.[3] The plausibility of sex-specific interaction is supported by findings that different measles vaccines are related to sex-specific mortality patterns;[18-20] high-titre measles vaccine was associated with higher female mortality, whereas Schwarz standard measles vaccine was especially beneficial for girls.[19] Although the underlying process is not understood, an expert panel convened by the World Health Organisation has recommended that routine use of high-titre measles vaccine be stopped.[20] Further studies of the biological basis for such interaction between (vaccine) virus and sex are clearly warranted.

Sex-specific patterns of exposure and cross-sex transmission should be examined further for two reasons. First, they offer another explanation for variation in mortality by sex in different societies. This information could affect the general cultural understanding of the relative biological strength of the sexes and might ultimately

have consequences for research on sex and infections. Second, observations on cross-sex transmission point to an important and hitherto unnoticed mechanism for aggravating infections. Whether the cause is behavioural or biological, it is likely that a better understanding of the underlying mechanism will lead to improved control of severe and potentially fatal infections.

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Chromosome status of untransferred (spare) embryos and probability of pregnancy after in-vitro fertilisation

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Many spontaneous abortions are associated with chromosomal abnormality of the fetus. In in-vitro fertilisation (IVF) the chromosome status of untransferred ("spare") embryos and subsequent fate (pregnancy or not) of the transferred sibling embryos might be related. Since the spare and transferred embryos of a patient's cycle genetically are full siblings, the inherited chromosomal abnormalities in spare embryos have a 50% probability of also appearing in transferred embryos. We have tested whether chromosome analysis of spare embryos has predictive power for transferred embryos.

48 couples with a total of 437 embryos were selected because their spare embryos (1–4 per couple; 76 total) were successfully analysed for chromosome status. 16 patients became pregnant. These women produced a higher proportion of chromosomally normal spare embryos (9/24; 37·5%) than those who did not achieve pregnancy (1/52; 1·9%). The proportion of patients who had only normal embryos was significantly higher ($p=0·012$) in the pregnant group than in the non-pregnant group, and the proportion of patients who had only abnormal embryos was significantly higher ($p=0·001$) in the non-pregnant group. Patients with preclinical and clinical pregnancy losses had only chromosomally abnormal spare embryos; by contrast, 50% of spare embryos from patients with ectopic pregnancies were normal. The proportion of spare embryos that were normal (13%, 10/76), was similar to the livebirth rate of 11% per transferred embryo (19 infants from 171 transferred embryos).

These results suggest that chromosome analysis of spare embryos may have predictive value for their transferred sibling embryos. We conclude that improving detection of chromosomally normal embryos for transfer should improve the success rate in IVF.

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Introduction

Reproductive failure is closely associated with chromosomal abnormalities. A major cause of spontaneous abortion among clinically recognised pregnancies is a grossly abnormal chromosome complement (chromosome numbers departing from the normal 46—ie, aneuploidy).[1] Estimates of overall rates of chromosome abnormalities in spontaneous abortions and fetal deaths, adjusted for gestational age, are around 32%.[2] The frequency of chromosomal abnormality before week 8 of gestation (as measured from the onset of

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