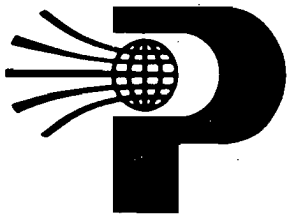

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Seminar on

SOCIO-CULTURAL DETERMINANTS OF MORBIDITY AND MORTALITY IN DEVELOPING COUNTRIES: THE ROLE OF LONGITUDINAL STUDIES

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DEATH HOUSES

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©DEATH HOUSE

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©INTRODUCTION

In many societies there is an idea that some houses or families are haunted, plagued with misfortune. One disaster rarely comes alone. People may moved to a different place or divorce to get away from misfortune and bewitching. One of the basis for such beliefs is undoubtedly the clustering of deaths as the extreme form of misfortune.

Dramatic and highly virulent and fatal infections like smallpox, cholera and plague would tend to produce a pattern of spatial clustering of deaths, attacking some houses more than others in a specific epidemic. Such infections have undoubtedly been part of reasons for beliefs about misfortune. However, the idea of clustering of misfortune or death does not only emphasize simultaneous disasters. There is an element of clustering of disasters over time in certain houses and that one may try to get away from misfortune.

Clustering of deaths over time do undoubtedly occur. Some examples from Guinea-Bissau are given in table 1. During the first year of study in Bandim, an urban area in the capital of Guinea-Bissau, it was a strong impression that deaths tended to cluster (Aaby et al 1981). To the extent such patterns do occur it would seem important to find their underlying mechanisms. It could well have implications for priorities in primary health care if these death clusters reflect behavioural patterns or environmental conditions which can be modified. Since there are good indications from studies in the UK that areas with high child mortality have high incidence of adult mortality (Barker et al), clustering of childhood deaths may reflect problems which will have an effect throughout life.

The present communication discusses different mechanisms which may contribute to clustering of death. Based on the experience from Bissau, it is shown how measles may produce clustering of death over time.

©MECHANISMS OF CLUSTERING

The are several different patterns which may produce clustering:
1) Most factors which cause perinatal or early childhood death would tend to lead to shorter spacing for the next child thus increasing its risk of dying and in thr process producing clustering over time.
2) Through a mechanism of insufficient nutrition or inaccessability of medical care, poverty could increase the risk of mortality for all children in a certain family.
3) Poor mothering due to lack of knowledge or personality may have similar effects on the survival of several children, possibly through mechanisms of lack of care, inappropriate

Table 1

1. Deaths during 1979 in [illegible] houses in zone 4, Bandim, Guinea-Bissau

Identification	Date	Death
4-18-3	[illegible]	1Y/M old child dies of [illegible]
4-14B-2a	[illegible]	1 (2) old twin dies
4-14D	23-3-79	1 case of measles diagnosed by physician
4-19B	[illegible]	1 case of measles diagnosed by physician
4-19B	[illegible]	21M old child dies of measles
4-18D-1	16-4-79	1 child diagnosed with measles same child gets paralyzed leg in August
4-22 b	11-[illegible]-79	1 child dies of measles
4-14D-2	[illegible]	1Y old child dies, cause unknown
4-20-4?	19-9-79	1 day old child dies
[illegible]-14B	10-79	mother of 4-14B-2 dies
4-19	11-79	abortion
[illegible]	13-11-79	28 year old man dies of abscess in throat
4-22 [illegible]	[illegible]-79	stillbirth
4-[illegible]-81	15-[illegible]-80	stillbirth

1). Births during 1979 in nine adjacent houses in zone 2 (houses 1, 2, 3, 7, 8, 10, 6 and 11 (houses 3 and 4), Bandim, Guinea Bissau.

Identification	Date	Death
[illegible]-1A	12-79	1M old child dies of fever
[illegible]	[illegible]	3Y old dies of fever
[illegible]	[illegible]-79	1Y old dies of fever
[illegible]	[illegible]-79	1Y old dies of measles
[illegible]	[illegible]	5 cases of measles reported (information from reexamination in Dec. [illegible]
[illegible]	[illegible]	44 old woman dies of inflamation
[illegible]	[illegible]-79	1Y dies of unknown cause
[illegible]	[illegible]-79	4 days old died of suspected tetanus
[illegible]	8-79	1Y old dies of unknown
[illegible]	[illegible]	1Y old dies, now sick
[illegible]	9-[illegible]-80	8M old died of diarrhoea, vomiting
[illegible]-1A-4	[illegible]	stillbirth
[illegible]	29-2-80	10M old child died of [illegible]
[illegible]-1B	15-3-80	11 days old died of suspected tetanus

Note: When [illegible] of deaths was put together we only had observations [illegible] houses [illegible] by a physician in March [illegible] and the retrospective [illegible] of children who had participated in the [illegible] October 1979. [illegible] in all houses about [illegible] later. All houses turned out to have [illegible]

treatment of common infectious conditions, poor hygiene, refusal of preventive activities, inadequate breastfeeding and other nutritional practices.
4) Some mothers may be more likely to deliver prematurely, have difficulties during delivery or to give birth to low birthweight children. They may also be more likely to have problems with breastfeeding and conceiving early. Such differences may produce clustering of death through a mechanism of short spacing or by birth of feeble children.
5) Persisting risks of infection over several years could also produce clustering, for example, houses with bad water supply or high risk of mosquito attacks could have increased risk for several successive children. Another example would be exposure to the same environmental risk over several years. For example, we have observed in Bissau that children living in houses with pigs have higher mortality (RR around 1.5); part of this effect is related to excess mortality after cryptosporidium infection, its risk of which also being associated with having pigs at home. Thus if the family continues to have pigs that may mean higher mortality risk for several successive children in the same house.
6) Crowding living conditions would presumably also tend to increase clustering of deaths because the higher number of susceptible children increases the risk of infection for other children.
7) An infection which was both severe in the acute phase and had a latent state or could induce long-term immunological consequences increasing susceptibility to other infections would also tend to increase the clustering of deaths over time.

MEASLES AND DEATH CLUSTERING

The type of death clusters described in table 1 occurred in situation where there had been a very severe epidemic of measles killing around 7% of all children under three years of age in the community and with a case fatality ratio (CFR) of 25% (Aaby et al 1983a). It was therefore natural to examine what role measles infection or exposure to measles could have for the subsequent risk of dying. There seems to be at least four different ways that measles has contributed to the clustering of childhood deaths.

I. CLUSTERING OF MEASLES CASES AND INCREASED CFR

A common feature of most of the situations where measles has a high acute mortality is that many individuals contracted infection at the same time. In Guinea-Bissau, we found in several outbreaks that age-specific mortality was considerably higher in houses with multiple cases compared with houses with only a single case (isolated cases) (see Table 2)(Aaby 1989). This tendency has been confirmed in all other studies where it has been tested (Aaby 1988b, Aaby 1989). Though this tendency could be a result of distinguishing features between families with respectively many and few children, it has also been examined whether the difference was related to intensity of exposure. Whereas all single cases are index cases infected from someone outside the home, some of the multiple cases are

secondary cases infected by an index case in the same house (Table 2). Secondary cases have presumably been more intensively

TABLE 2
CASE FATALITY RATIO(CFR) IN MEASLES INFECTION ACCORDING TO AGE, CLUSTERING AND TYPE OF EXPOSURE. BANDIM, GUINEA-BISSAU, 1979

Age (months)	Case fatality ratio(%)(deaths/no. ill)		
		Houses with multiple cases	
	Isolated cases	Index cases	Secondary cases
0-5	0%(0/1)		24%(4/17)
6-11	14%(1/7)	0%(0/15)	42%(11/26)
12-23	11%(2/19)	21%(3/14)	33%(14/43)
24-35	0%(0/10)	14%(2/14)	38%(14/37)
36-59	0%(0/10)	5%(2/38)	13%(5/39)
60+	33%(1/3)	6%(2/36)	0%(0/50)
Total	8%(4/50)	8%(9/117)	23%(48/212)

exposed than the index cases. The difference in severity between index and secondary cases have now been examined in several studies from both developing countries and in reanalyses of historical data from Europe. All studies have found a significantly or nearly significantly higher mortality among secondary cases, usually with at least two-three times higher mortality. In the studies from Bissau, isolated cases and index cases in house with multiple cases have had very similar mortality rates (see Table 2). This suggest that the contrast between single and multiple cases is not simply due to different socio-cultural and therapeutic practices, differences in genetic constitution or the prevalence of complicating infections between families with many and with few susceptible children. Still the difference between index and secondary cases could be confounded by higher general mortality in larger families where the proportion of secondary cases will also be higher. In the studies from Kenya (Aaby and Leeuwenburg 1990) and Copenhagen (Aaby 1988a) where this possibility has been examined, the relative risk (RR) between index and secondary cases was found to be the same in both small and large families (table 3). Maternal fatigue could also be a confounding factor if mothers would provide less care for secondary cases if they had had to care for an index case already. However, an analysis of date from several epidemics in Bissau showed that secondary cases who had the same mother as the index cases did not have higher mortality (25%(14/55) than secondary cases whose mother had not had to take care of an index case (42%(25/60) (Aaby et al 1988c). Hence, differences in maternal care due to fatigue are unlikely to explain why secondary cases have higher CFR than index cases.

Thus the indication from these studies is that the co-occurrence of several cases and in particular the increased risk of intensive exposure leads to more severe infection and this tendency is not primarily a result of confounding with poor socio-economic conditions. The implication is that deaths from

measles will cluster in families having several susceptible children at the time of an outbreak. In polygamous and/or extended families several women may loose a child at the same time, but one women may also loose two children to measles during an outbreak if the children are closely spaced or the interval between epidemics is long.

©TABLE 3
©CASE FATALITY RATE FOR CHILDREN AGED 0-2 YEARS ACCORDING TO SIZE ©OF FAMILY AND EXPOSURE. COPENHAGEN, 1915-1925

No of children in family	Case fatality rate (%) Index cases	Secondary cases	Relative risk(95%CI)
2	8%(5/64)	25%(10/40)	3.2(1.2-8.7)
3-4	7%(4/54)	31%(21/67)	4.2(1.6-11.6)
>=5	12%(4/34)	25%(8/32)	2.1(0.7-6.4)

All factors contributing to a high concentration of susceptible children in the same social units (table 4) are therefore likely to be associated with a higher frequency of clustering of deaths. For example, in rural areas there is a longer interval between epidemic and more children in the same family will be susceptible at the same time than in urban areas where children of the same family will tend to be infected in different epidemics. Assuming the same basic family size and structure in both the rural and the urban area, measles will therefore be more severe in rural than in urban environments as has also been indicated by available community studies. Following this logic, measles deaths should be more likely to cluster for women in rural areas than in urban districts.

©TABLE 4
©RISK FACTORS FOR INTENSIVE EXPOSURE

High risk	Low risk
Large compounds	Small compounds
Polygamy	Monogamy, single parent family
Extended family	Nuclear family
One-room apartments	Large apartments
Small living space	
Sleeping in same bed	Separate rooms
Multifamily housing	Separate houses
Lack of ventilations	Well ventilated rooms
Institutions (hospitals)	Families
Twins	Singletons
Short spacing	Long spacing
High birth order	Low birth order
Rural	Urban
Epidemic	Endemic

©2. DELAYED IMPACT OF MEASLES AND INTENSIVE EXPOSURE
Most studies have only dealt with acute measles mortality (within one month of the rash). However, studies from West Africa and India-Bangladesh have indicated that children

previously infected with measles have a significant delayed excess morbidity (Bhaskaram et al 1984, Shahid et al 1983) and mortality compared with community controls after the acute phase of infection (Aaby et al 1987a). Hull et al (1983) reported an outbreak of measles in a village in the Gambia which they re-visited 3 and 9 months later to assess the impact of infection. As indicated in Table 5, after acute infection former measles patients had a significantly higher risk of dying compared to community controls (RR=9.9; 95% confidence interval (CI):4.5-21.9). The excess mortality seemed particularly high for children under one year of age. The results from Gambia could be confounded by background factors distinguishing cases from controls. For example, it seems clear that deaths mainly occurred in domestic compounds where many children lived close together (Hull 1988), and the risk of measles infection as well as mortality in general may have been greater in larger compounds. Parental attitudes could play a role since many of the controls had been immunized (Hull et al 1983). However, the relative risk was particularly high for children under one year of age where very few of the controls had been immunized prior to the outbreak and the difference in mortality in general was so large that it is unlikely to be solely due to confounding between the risk of measles infection and the determinants of child mortality in general.

TABLE 5
MORTALITY DURING 9 MONTHS OF FOLLOW-UP FOR MEASLES PATIENTS AND COMMUNITY CONTROLS. THE GAMBIA

Age at infection	Mortality of measles cases		Mortality of controls 0-9 months	Relative risk(95%CI)
	Acute	1-9 mo later		
3-11 mos	18%(2/11)	56%(5/9)	3%(3/94)	17.4(5.0-61.2)
1-2 yrs	9%(3/32)	13%(4/32)	2%(3/190)	7.9(1.9-33.7)
3-4 yrs	6%(2/31)	7%(2/29)	1%(1/182)	12.6(1.2-134.0)
5-6 yrs	0%(0/36)	6%(2/36)	1%(2/188)	5.2(0.8-35.9)
Total				9.9(4.5-21.9)

Studies from Nigeria and Burkina Faso have likewise found significantly higher risk of dying for cases in the months following measles compared with controls (Osagie 1986, van de Walle 1986). In the study from Nigeria, Osagie (1986) re-identified 106 cases of measles and 106 controls who had visited a hospital clinic the previous year. Among 106 measles cases, 11 had died (10.4%) against only two in the control group (OR=6.0 (1.5-23.4)). Acute mortality was only 1% (1/106) whereas 10 died in the 2nd-6th months. From the data available, it is difficult to assess the possibilities of biases in the selection of hospital cases and controls who could be retraced after one year. Nevertheless, the study also found a strikingly higher mortality of 31.8%(8/26) among the children who had measles before one year of age compared, for example, with the mortality opf 3.7% (1/27) for one year old children (OR=11.6 (1.8-72.9)).

In Bissau, we found excess mortality as well in the second year after measles infection. The small children under two years of age who had measles during an epidemic of measles in the beginning of 1979 had a mortality of 5.9%(7/118) during 1980 compared with only 1.3% (3/237) among the children from the same community who had not had measles (RR=4.7; CI:1.4-15.7) (Aaby et al 1984c) (table 6).

©TABLE 6
©MORTALITY 10-21 MONTHS AFTER MEASLES INFECTION COMPARED WITH ©COMMUNITY CONTROLS IMMUNIZED AGAINST MEASLES, GUINEA-BISSAU

Age (months)	Mortality(%) History of measles	Controls	Relative risk (95%CI)
12-23	6%(4/67)	1%(1/128)	7.6(1.2-47.2)
24-35	6%(3/51)	2%(2/109)	3.2(0.6-18.6)
Total	6%(7/118)	1%(3/237)	4.8(1.2-18.3)

In a subsequent vaccination study in the same area, measles infection increased the mortality ratio between 4 and 60 months two-fold when background factors were taken into consideration in a Cox regression model (Aaby et al 1992). There were 10 deaths in the group of children contracting measles, indicating that five of these were excess deaths. Compared with only one acute death, this was a very marked increase in mortality.

The available studies have been summarized in table 7 giving the excess deaths in relation to the number of acute deaths. The extent of excess mortality is clearly variable in these studies and we have no explanation of this variation. It seems likely that it is at least 50% of acute measles mortality. This figure, however, is preliminary due to the small number of studies which have been conducted so far.

©TABLE 7
©DELAYED EXCESS MORTALITY AMONG PREVIOUS MEASLES CASES.
©COMMUNITY STUDIES WITH VARIABLE FOLLOW-UP AFTER MEASLES.

Country	Acute deaths	Follow-up	Delayed deaths	Excess deaths	Ratio of excess to acute deaths
Gambia	7	8 mo	13	11.8	1.7
Nigeria	1	12 mo	11	8	8.0
Senegal	72	11 mo	31	22	0.3*
Bissau	1	60 mo	9	5	5.0
Bissau	2	12 mo	3	1.3	0.8
Kenya	10	12 mo	3	1.3	0.1

* This is only the excess mortality of secondary cases over index cases and not the excess of measles cases over non-infected individuals.

Since few studies have assessed the delayed impact of measles infection, it is difficult to determine its risk factors. However, it seems likely that excess morbidity and mortality is related to intensive exposure during the acute infection. For example, among the children hospitalized in Copenhagen,

secondary cases (3/152) had a higher risk of dying after the first 30 days of measles infection than did index cases (3/472) (RR=3.11; 95% CI: 0.7-14.0). In rural Senegal, the secondary cases had a significantly higher risk than the index cases of dying in the year following measles infection (OR=3.5 (1.0-12.4) (Table 8)(Garenne and Aaby 1990). Excess mortality may also be connected with the age at infection as suggested by several of the studies mentioned above.

©TABLE 8
POST-MEASLES MORTALITY RATE (6-52 WEEKS) BY AGE AND INTENSITY OF EXPOSURE. NIAKHAR, 1983-1986.

Age ©(months)	Post measles mortality (deaths/measles survivors) Index cases in compound	Secondary cases in compound
0-5	0%(0/4)	5%(1/21)
6-41	2%(2/107)	7%(25/356)
42-65	1%(1/79)	2%(3/184
66+	0%(0/122)	1%(2/275)
Total	1%(3/312)	4%(31/836)
Odds Ratio	1.0	3.5

The tendency towards increased mortality for many months and even years after the acute infection can clearly produce diachronic clusters of death. It is the families with secondary cases which will experience high acute mortality and at least the studies from Bissau and Senegal suggest that these are also the families where the risk of delayed mortality is highest. Thus the factors leading to a high degree of clustering of susceptible children will also be the risk factors for delayed mortality and death clustering.

©3. DELAYED EXCESS MORTALITY FOLLOWING EXPOSURE TO MEASLES BEFORE ©SIX MONTHS OF AGE.

In Bissau, we have found that children exposed at home to measles during the first six months of life had a mortality 3 times higher than community controls between six months and five years of age (34% vs 11%) (Aaby et al 1990a). In a Cox regression analysis taking the known background factors into consideration, the mortality hazards ratio was 5.7 times higher (95% CI:2.7-12.0) for the exposed than the control children. The difference in mortality was significant in each of the age intervals 6-11, 12-23 and 24-35 months (table 9). This delayed excess mortality was found both for children who had measles (though being below six months of age) and exposed children who did not have clinical measles. The exposed children were particularly likely to die of diarrhoea.

These tendencies have not been examined elsewhere, but have been systematic in several outbreaks in Guinea-Bissau (Aaby et al 1990a). In the subsequent three years where there were fewer cases due to measles immunization, 72 children were exposed to measles before six months of age Aaby et al 1992b). For these exposed children, five-year mortality was 34.4% against 9.3% for controls. Mortality was not different for those said to have

had measles versus those who did not report measles at time of exposure. Using an unpaired proportional hazards model controlling for age and sex, the MR for exposed children was 3.97 (1.61-9.78). The variables age at exposure (0-2 versus 3-5 months), measles infection at exposure, exposure from own versus neighbouring household and measles vaccination were not significantly associated with mortality. However, measles infection after six months of age was statistically significant, MR=4.17 (1.22-14.32)(p=0.023) adjusted for age, sex and early exposure. In the final model, the mortality ratio of early exposure was 3.84 (1.55-9.48)(p=0.004) controlling for age, sex and measles infection after six months of age. Restricting the same analysis to mortality after two years of age where 7 of 8 deaths from a total of 111 children were among exposed children, early exposure was borderline significant, MR=7.96 (0.98-64.74) (p=0.052).

©TABLE 9
©AGE-SPECIFIC MORTALITY RISK FOR CHILDREN EXPOSED TO MEASLES ©BEFORE 6 MONTHS OF AGE AND CONTROLS ACCORDING TO MATERNAL ©EDUCATION

Age interval (months)	No formal education		Some formal education	
	Exposed	Controls	Exposed	Controls
6-11	13.0%	3.0%	5.8%	1.3%
12-23	13.8%	2.5%	6.2%	1.1%
24-35	15.4%	1.0%	7.0%	0.4%
36-60	-	5.4%	-	2.4%
6-60	36.5%	11.4%	17.8%	5.1%

Among 12 children exposed in a rural epidemic in Quinhamel, nine died before five years of age whereas only two of the controls died. In an unpaired analysis adjusted for age and sex, the MR of exposed children compared with controls was 11.39 (1.42-91.51) (p=0.022) (Aaby et al 1992b).

Impact on mortality

Since standardization for different background factors did not affect the estimate of the mortality difference between exposed and control children in neither this nor the previous study (3), the impact on mortality can be calculated directly as the difference in cumulative mortality for exposed and control children. In the period 1980-1983, excess mortality was 25.1% (34.4%-9.3%=25.1%) for the 72 children exposed; i.e, 18 deaths. Since three of the deaths were related to acute measles, we have calculated 15 non-measles excess deaths. During the same period there were 29 acute deaths of measles among Bandim residents (unpublished observations). Thus, excess mortality related to exposure before 6 months of age contributed as much as 52% of the acute mortality from measles. During the previous epidemic, in 1979 (4), exposed children had a cumulative mortality of 45.3% from three months to 5 years of age, against only 16.2% among controls. Hence, excess mortality was 29.1% of the 86 children exposed; i.e. 25 deaths (3). Compared with the 63 acute

deaths among children over 5 months of age (4), excess mortality after early exposure to measles constituted 40% of acute measles mortality.

04. DELAYED PERINATAL AND POST-PERINATAL MORTALITY AFTER EXPOSURE TO MEASLES DURING PREGNANCY

The effect of exposure may go even further. In two outbreaks in Guinea-Bissau, it was found that children of mothers exposed to measles during pregnancy had a significantly higher perinatal mortality (Table 10)(Aaby et al 1988b) as well as increased post-perinatal mortality (Aaby et al 1990b) when background factors were taken into consideration. These analyses have taken care of a number of known background factors like size of family and mother's education. In order to assure that the tendency was not a result of a confounding that we did not know about a cohort of mother who gave birth later on in the houses where there had been exposure during pregnancy was also followed. The subsequent children from these houses had the same mortality as the controls had had. Thus it is unlikely that the tendencies are just related to bad mothering.

TABLE 10
PERINATAL MORTALITY AMONG CHILDREN OF MOTHERS EXPOSED TO MEASLES DURING PREGNANCY. BANDIM, GUINEA-BISSAU, 1979

Type of mortality	Perinatal mortality risk(deaths/at risk) Exposed	Controls	OR(95%CI)*
Stillbirths	6.5%(7/107)	1.4%(5/346)	4.8(1.7-13.8)
Died 1st week	9.0%(9/100)	2.6%(9/341)	3.6(2.3-5.6)
Perinatal	15.0%(16/107)	4.0%(14/346)	4.2(2.1-8.5)

In the major epidemic in Bandim, there were 12 excess perinatal deaths among women exposed to measles during pregnancy. Compared with the 63 acute deaths, this constitute an excess of 19% of the acute mortality. The same cohort of children exposed during pregnancy had a two fold higher post-perinatal mortality to the age of five years. Thus 10 of the 20 deaths in the exposed group may be considered excess deaths. This is another 16% excess mortality over the acute deaths. Similar increases in perinatal and post-perinatal mortality were observed in a rural epidemic (Aaby et al 1988b, 1990b).

While these tendencies have not been studies elsewhere, there are some indications that exposure at an early age may have consequences for health in later life. The delayed fatal form of measles known as subacute sclerosing panencephalitis (SSPE) occur mostly among children who had measles early in life. This suggests that the children are more likely to have been intensively exposed as secondary cases (Aaby et al 1984d). A study from Denmark found that adults with no history of measles in childhood had four times higher frequency of cancers and immunoreactive diseases than controls reported to have had measles in childhood (Rønne 1985). The most likely explanation of not reporting a measles infection would be that they were

exposed to measles when still partly protected by maternal antibodies or immunoglobulin. Early exposure therefore seemed to be connected with their excess morbidity in later life.

05. TOTAL IMPACT AND THE RISK FACTORS FOR LONG-TERM CONSEQUENCES

With the few studies available at the moment it is difficult to give a precise estimate of the contribution of the different forms of long-term consequences following measles infection. Since several studies indicate several fold higher mortality rates over the months following acute measles and few studies have measured more than the effect during the first year after measles, it is probably not exaggerated to suggest that the delayed excess mortality following clinical measles infection is at least 50% of acute mortality. Since children with exposure to measles before six months of age have had an increase in mortality of the order of 40-50% of the acute CFR, it seems reasonable to estimate that the impact of exposure to measles before six months of age is at least 25% of the acute measles mortality. Thus is seems likely that the different forms of delayed mortality may constitute at least 75%-100% of acute measles mortality. (This would increase the current estimate of the impact of measles globally from 1,385 million annually to 2,423 million). In this estimate we have not included the effect of exposure during pregnancy.

There is naturally an element of random variation in who happens to be exposed early or during pregnancy. However, exposure before six month of age and during pregnancy as well as the long-term impact of previous measles infection would tend to have the same risk factors as severe acute infection. The risk of exposure during pregnancy or the first six months of life are going to be higher in families with many susceptible children where the risk of someone bringing the infection back home will be higher. Both types of exposure are necessarily intensive, since it will not be the individual itself who contract infection outside the home. Known risk factors like higher birth order or short spacing would tend to be associated with these forms for early exposure and they may derive some of their strength from the effect of such exposure.

It is to be noted that the delayed impact last for several years. Among the children with exposure before six months of age, where the best analyses have been made, this effect lasted at least 2-3 years. Hence, clustering of death may stretch over long periods.

There has been no study of the pathogenic process leading to the long-term consequences of measles infection and exposure early in life. It seems likely that some form of latent virus and immunosuppression is involved. The importance of intensive exposure may well be that it provides a larger dose of infection. The dose of infection is likely to be determine how much virus become latent and this may be important for the long-term consequences.

OCONCLUSION

There may die as many of the long-term consequences of measles as during acute infection. Acute and delayed mortality

both seem to depend on the intensity of exposure and would therefore tend to have the same socio-cultural risk factors (table 4). Death clustering seems an inevitable consequence of the different forms of delayed consequences following measles infection. Severity of a number of other infections,e.g. whooping cough and meningococcal meningitis, seem to depend on the intensity of exposure and may therefore also produce temporal clustering of deaths in families with many susceptible children (Aaby et al 1985). Whether they also produce delayed consequences during childhood is probably unknown, but there are for example whooping cough during childhood is related to adult mortality (Barker et al 1991). When smallpox was a severe disease before general vaccination it seems also to have been capable of producing delayed consequences for the infected individual (consumption) as well as for the fetus (Mercer 1985). Infections like tuberculosis and retrovirus, while they have no high acute mortality, may produce clustering of death because they weakens many individuals in the same family. It should be worthwhile to examine if other infections have the same capacity as measles to produce both synchronic and diachronic clustering through a process of increased severity and viral persistence/ latency or immune damage.

Since the public health consequences of death clustering are likely to be different depending on whether the underlying mechanisms are related to maternal health, care and nutrition behaviour, persistent environmental risks of infection or chronic infection and immune damage, it should be important to undertake studies where the different mechanisms can be compared. Since this will require correct data on the timing of events like birth, infection, care, treatment, environmental risk factors and deaths, it is probably only within longitudinal studies that the necessary data can be obtained.

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