The incidence of serious complications of measles is not high: it may vary in different epidemics and be reduced by the use of antibiotics. But, because of the universality of measles the total number of complications and of admissions to hospital is large enough to be important. The proportion of serious complications that lead to permanent disability can at present only be guessed, but even if small, the total number of children so affected may be considerable. Measles is, moreover, an unpleasant disease that imposes much discomfort on nearly every child and a burden of anxiety and work on parents and doctors.

These are facts which, among others, will have to be considered in any assessment of the need for universal measles vaccination. It is probable that most, if not all, the improvement to be expected in this country from raised standards of nutrition and hygiene, abolition of overcrowding and higher standards of medical care and treatment has already been achieved. Further advance is likely to come only from prevention of the disease by immunization, and on the available evidence this would seem to be well worth doing.

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## The Severe Measles of West Africa

There is evidence that measles is not a new disease in West Africa. Daniell (1852) described measles as a disease well known to the people of Accra, particularly affecting small children, as it does today. In the area of Ilesha in Western Nigeria where I worked new cases of measles have been seen every month over the last eight years. If there are sufficient new births from a population of 200,000 to maintain measles in an endemic state there is little reason to believe that the large population of West Africa was not sufficient to maintain measles indefinitely as an endemic disease once it had been introduced. In the majority of the languages of West Africa a word for measles exists and the people look on the disease with considerable fear. There is good reason for this fear. McGregor *et al.* (1962), in a village in the Gambia, recorded an 18% mortality among children under 5 during a measles epidemic. Gans *et al.* (1961) estimated a 5% mortality from measles in Nigeria, while Senecal *et al.* (1962) summed up the situation in Dakar by their statement that measles is the most killing disease of the pre-school child.

I am indebted to Dr W M Clapp, now pædiatrician at the Wesley Guild Hospital, Ilesha, for the figures shown in Table 1 of the monthly incidence of measles over the last two years. There is clearly a seasonal incidence; the epidemic starts during the dry season and declines in the wet. The range of temperature between seasons is not large; the monthly mean maximum temperature varies by 14°F and the minimum by 7°F. Humidity is high for most of the year, the mean monthly rainfall ranging between 0·5 and 9 inches. In the middle of the dry season, before and after Christmas, there is little work to be done on the farms and this is traditionally a time for family reunions and festivals. A common feature of such festivals is the gathering together of the people for an evening or night of eating, drinking and dancing, as in many societies. In this society, unlike ours, the 'baby sitter' is not required. The infants attend the party, securely fastened to their mothers' backs. This custom has many advantages; it gives security and allows the infant's needs to be known immediately by the mother. Unfortunately, it may predispose to rapid and dramatic spread of droplet infections among small children. With the onset of the rains the people return to their farms and the opportunities for infection are much reduced. The seasonal incidence of measles may depend on these movements rather than on climatic changes. The festivities offer opportunities for the spread of droplet infections among infants and about a third develop measles during the second half of the first year of life. By the age of 3 a high proportion of the children have experienced the disease.

In the early catarrhal stages the disease is similar in its manifestations to measles as now seen in England. The rash is surprisingly easy to discern on the dark skin of the African child. In a proportion

*Table 1*
**Monthly measles notifications at Ilesha Hospital, Western Nigeria**

| | *Dry season* | | | | *Wet season* | | | | | | *Dry season* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Jan* | *Feb* | *Mar* | *Apr* | *May* | *Jun* | *Jul* | *Aug* | *Sep* | *Oct* | *Nov* | *Dec* |
| 1962 | 193 | 239 | 590 | 395 | 290 | 130 | 73 | 51 | 24 | 21 | 82 | 191 |
| 1963 | 282 | 491 | 356 | 230 | 275 | 152 | 127 | 100 | 95 | 78 | 106 | 161 |

the rash progresses and darkens. This change is now rarely seen in England, but was known in the past and probably gave rise to the name of 'black measles' (Buchan 1797). The earliest reference to this change is probably that of Rhazes, who wrote, in AD 850, 'The measles which are of a deep red and violet colour are of a bad and fatal kind'. In Imesi village it was possible to watch the development of the rash closely. The rash was frequently confluent; within a few days of its appearance it often darkened in colour from deep red, through purple, almost to black. The degree of darkening indicated the extent of subsequent desquamation, which varied from a fine 'branny' desquamation to exfoliation of plaques of skin more than a centimetre in diameter. These changes usually developed in a week, but for many weeks thereafter a discoloration and scaling of the skin were apparent. It seems likely, on clinical grounds, that equivalent changes affect other epithelial surfaces of the body, for example:

*The mouth:* Soreness of the mouth is a common and frequently severe manifestation of measles in the West African child. This is important to the child's nutrition in a community where breast feeding continues for a mean period of 23 months, by which age one-half of the children have suffered from measles. The sore mouth also deters the child from eating highly seasoned food, and unfortunately any foods rich in protein which he is likely to be given are usually highly peppered.

*The larynx:* Laryngitis was common in Nigeria, as it was in the past in England. In London, Balme in 1904 recorded it in 8% of 227 children seen with measles in a London clinic.

*The bronchi:* Even though treated with modern antibiotics more than a fifth of children in all age groups admitted to the hospital in Ilesha with measles bronchopneumonia died. In the past Sydenham (1674) and Trousseau (1869), among many others, had good reason to fear the bronchopneumonia that followed measles.

*The intestine:* The frequency and severity of diarrhœa are outstanding characteristics of the severe form of measles seen in West Africa. Daniell (1852), in describing measles in Accra, laid particular stress on diarrhœa. At Ilesha, diarrhœa with measles was severe and about a third of the children admitted with measles and diarrhœa died. The diarrhœa was most common in the period of desquamation and in the weeks that followed. In an article by Dawson Williams (1906) there is ample evidence of the severity of the diarrhœa that followed measles in this country in the past.

All these aspects or 'complications' of measles arise during, or after, the period of skin exfoliation, suggesting that other epithelial surfaces may be undergoing equivalent changes. The skin itself is liable to infection and a syndrome of multiple boils in the weeks succeeding measles was not uncommon. A similar condition was described by Willan (1821) and others in England.

Of particular importance is the effect of measles on the child's nutrition. Frequently there is a dramatic loss of weight. Several children were observed who lost a quarter of their weight after measles. This loss is likely to be particularly severe if measles coincides with the period when the child comes off the breast. Almost one in four lost 10% of their weight. One-half of the children took more than a month, and 15% took more than three months, to regain their original weight (Morley *et al.* 1963). Measles precipitates kwashiorkor in this part of Nigeria more often than any other acute infection. The loss of weight and the occurrence of kwashiorkor after measles are due to a sore mouth, which impairs the child's ability to suck and eat, to a reduction in the amount of food offered to it, to loss of appetite, and to the additional drain which the disease imposes on a child existing on a diet poor in protein. The skin changes due to the rash may blend with the skin changes of kwashiorkor. They are different from those that appear in kwashiorkor unrelated to measles.

*Vaccination against Measles*

Because of the severe morbidity and mortality from measles in this community, the possibility of using measles vaccine was welcomed. Trials of the Enders 'attenuated live vaccine', with and without $\gamma$ globulin, were made (Morley 1963) and, more recently, the newer 'further attenuated vaccine' developed by Schwarz has been used (Morley 1964). The village experienced severe measles epidemics in 1960 and 1962. Since 1962 the majority of children have been vaccinated and it is hoped that this may be the first community to be artificially freed from measles by vaccination.

### *World-wide Survey of the Extent of Severe Measles*

It seems clear that measles as now seen in West Africa and probably in many other tropical areas is a much more severe disease than measles as it occurs in Europe and North America today. This severity can only in small part be explained by the younger age incidence in some tropical areas. With the assistance of the World Health Organization, I am making an attempt, in association with Dr W J Martin and Miss Irene Allen of the MRC Statistical Research Unit, London School of Hygiene and Tropical Medicine, to collect information on the distribution of the severe type of measles throughout the world. A questionnaire has been sent to doctors in about 70 countries, the majority of these being doctors in charge of mission hospitals. Answers have been received from 600 doctors; of these some 350 have agreed to undertake a year's study of measles in their hospitals. This study should give some useful indications of the age incidence, seasonal incidence and severity of measles. The results will not, however, be available for about two years. A preliminary analysis of some of the replies already received is presented in Tables 2 and 3.

Table 2 gives some indication of the severity of the disease in 7 different regions. It is doubtful whether measles is as mild in India and Pakistan as the replies suggest, owing to the fact that in these countries the proportion of children with measles kept at home and not brought to the doctor is exceptionally high. The beliefs underlying this practice have been reported by Taneja *et al.* (1962). Table 2 also indicates that the intensity of the different signs varies with the general severity of measles which in turn suggests that the marked epithelial changes observed in measles in West Africa also occur in other regions where the disease is severe.

*Table 3*

**Correlation between severity of measles and incidence of kwashiorkor: results from retrospective questionnaire**

| | *Incidence of kwashiorkor* | | | |
|---|---|---|---|---|
| *Severity of measles* | *Commonly seen* | *Occasionally seen* | *Very rarely or never seen* | *Total* |
| Severe: | | | | |
| Observed | 170 | 80 | 11 | 261 |
| (Expected) | (136·8) | (82·8) | (41·4) | |
| Moderate: | | | | |
| Observed | 85 | 55 | 31 | 171 |
| (Expected) | (89·6) | (54·3) | (27·1) | |
| Mild: | | | | |
| Observed | 29 | 37 | 44 | 110 |
| (Expected) | (57·6) | (34·9) | (17·4) | |
| Total | 284 | 172 | 86 | 542 |

$\chi^2 = 86{\cdot}2227$, $P < 0{\cdot}00001$

In the final question the doctor was asked to state whether kwashiorkor was common in his area. From Table 3 it appears that in general the areas where measles is severe are also areas where kwashiorkor is prevalent. If a geographical association between severe measles and kwashiorkor were established, this could suggest that malnutrition enhances the severity of measles and also the possibility that lack of essential nutrients plays a part in the pronounced epithelial changes by making the epithelium more 'vulnerable'.

In summary, it is hoped that the enquiry may throw light on the following questions:

(1) Whether the severity of measles in an individual depends on the epithelial reaction to the virus infection.

(2) Whether the epithelial reaction is determined by virus virulence, inherited resistance, or by environmental factors.

(3) The possible importance, as an environmental factor, of the state of nutrition of the child before and during the infection.

*Table 2*

**Severity of measles: results of retrospective questionnaire**

| | | *Percentage of doctors recording the following information* | | | | | |
|---|---|---|---|---|---|---|---|
| | *Total no. of replies* | *'Measles a severe and at times a fatal disease'* (%) | *'The rash sometimes turns deep red'* (%) | *'Severe desquamation'* (%) | *'A sore mouth is a common complaint'* (%) | *'Diarrhœa is common'* (%) | *'Kwashiorkor is common in my area'* (%) |
| West Africa (Senegal to Cameroons) | 132 | 91 | 76 | 64 | 72 | 82 | 62 |
| South-West and South Africa (Congo southwards) | 71 | 63 | 40 | 33 | 49 | 57 | 71 |
| East Africa (Sudan to Rhodesia) | 110 | 55 | 31 | 27 | 44 | 63 | 60 |
| Central and South America & West Indies | 32 | 47 | 34 | 22 | 22 | 38 | 42 |
| Middle East & North Africa | 31 | 35 | 36 | 17 | 41 | 43 | 32 |
| Pacific (including Burma, Thailand & Vietnam) | 72 | 17 | 29 | 6 | 20 | 26 | 14 |
| India & Pakistan | 115 | 14 | 25 | 9 | 27 | 37 | 52 |

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## Control of Measles by Vaccination

It seems likely that the future control of measles will largely depend upon the development of vaccines capable of producing immunity without reactions. Considerable progress has in fact been achieved along these lines and at present it looks as though suitable vaccines may soon be available.

### *Qualities of a Measles Vaccine*

The two basic requisites of a measles vaccine are that the vaccine should be safe and effective. It should not give rise to serious sequelæ, and any reactions which it may produce will require to be of a transitory and minor character if it is ever to become popular. Moreover vaccination must be followed – certainly in the majority of cases – by life-long immunity. Besides these basic qualities it will be an advantage if immunity can be conferred by a single rather than by repeated injections, and if the vaccine is cheap to produce, has good keeping qualities and can be conveniently given concurrently with other vaccines in routine immunization regimes.

### *Assessment of Measles Vaccines*

Most of these qualities can only be assessed by field trials, which have accordingly come to play a prominent part in the development of measles vaccines. In most trials four criteria have been used to assess the degree of vaccination reaction: the degree and frequency of pyrexia, the presence and extent of rash, the degree of constitutional disturbance, and the presence of complications. Protection has been assessed by the presence of measles antibody sometimes supplemented by a comparison of incidence of measles in vaccinated and unvaccinated children.

In considering such assessments three points should be borne in mind:

(1) Unless the vaccinated participants are compared with an adequate control group there may be a tendency to impute to the vaccine malaise and pyrexia which are in fact due to other unrelated causes; this is especially so in tropical countries in which it seems quite common to record appreciable pyrexia, attacks of diarrhœa and other symptoms during the period of observation.

(2) Care should be exercised in drawing conclusions about the severity of vaccination reactions when vaccines are tested in different trials. For example, reports of the early vaccines tested outside the United Kingdom indicated that the high temperatures which frequently followed vaccination were not usually associated with pronounced constitutional disturbance, but this was not our experience when similar vaccines were tested here. Differences in the epidemiological background and observation may, of course, have been responsible for the discrepancy. If the relative merits of vaccines or vaccination methods are to be compared the vaccines must be tested in parallel in the same trial.

(3) Although there is abundant evidence of the immunity produced by measles vaccines, field trials have not been in progress long enough to provide authoritative information about the long-term duration of the immunity. Although it is hoped that immunity would be life-long – certainly with living vaccines – there can be no assurance of this at the present time.

### *Vaccination Procedures*

Four main vaccination procedures are now available: (1) Living attenuated vaccine given alone. (2) Living vaccine given with $\gamma$ globulin to modify the vaccination reactions. (3) Killed vaccine given alone. (4) Killed vaccine followed by living vaccine.

*Living attenuated vaccine:* Living vaccines have been extensively tested in several countries. At Beckenham the first batches were produced in 1960, and since then the work of developing an effective measles vaccine free from reactions has followed a simple basic pattern. Virus of the Edmonston strain has been subjected to repeated