Clinical Features and the Factors Associated with Poor Outcome of Measles Patients at Queen Elizabeth Central Hospital

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ABSTRACT

In the twelve month period from March 1992 to February 1993, 266 consecutive children with measles were admitted to the children's unit at Queen Elizabeth Central Hospital (QECH), Blantyre. During the 12 month period the overall mortality was 10.9%; mortality was highest (22.5%) in children 12-23 months age. One-third of the children admitted were under 9 months of age, not eligible for measles vaccination. Pneumonia complicated illness of 30% of cases and was the greatest clinical predictor of mortality. Among infants under 9 months of age, who were receiving inappropriate food supplementation before 4 months of age the risk of death was 6.4 times the risk of death in children who were not receiving food supplementation. Other aspects of measles epidemiology are discussed.

Introduction

Measles remains a mysterious disease although it has been well documented from ancient times by the Persian Physician Rhazes in 850 A.D. There still remain many unanswered questions concerning its pathology and the human immune response to measles. At a time when considerable attention is focused on the immuno-suppressant viruses HIV I and HIV 2 (and retroviruses in general) it is sometimes forgotten that the measles virus has long been known to cause severe immuno-suppression in children. While in the majority of patients the immuno-suppression is temporary some children develop a condition, subacute sclerosing pan-encephalitis (SSPE). In this condition the measles virus acts as a "slow" virus; after a latent period (from months to years) the virus reactivates in the central nervous system of patients. These patients, often adolescents, will usually die from progressive neurological damage within a year of onset of their symptoms. The exact trigger for this reactivation is not known; the probable mechanism is an auto-immune response against neural tissue.

In the acute illness the measles virus is well recognised to cause a significant depression of cell mediated immunity. This is manifest by loss of reactivity to tuberculin in the child and reactivation of clinical TB may occur at this time.

Vitamin A given early in the course of measles significantly decreases morbidity and mortality. Even measles patients in nonvitamin A deficient areas benefit from treatment doses of vitamin A; in South Africa mortality in measles patients given vitamin A treatment doses was 2.2% compared to 10.3% in placebo controls. Vitamin A has a direct and positive effect on the human immune response. The protective mechanism is partly due to maintenance of mucosal integrity and partly through a direct effect on the immune response. Children with low vitamin A levels have lower measles-specific antibody levels (2) and children with vitamin A deficiency (severe enough to cause xerophthalmia) have lower CD4/CD8 ratios, lower CD4 native T cells and higher proportions of CD8 cells.When children were given vitamin A supplements this effect was reversed (3-4).

The most accepted method to protect the population from measles is to immunize the susceptible population. At leash 95% of the population must have immunity for the population to develop herd immunity. In developing countries elimination of measles depends on effective herd immunity to protect nonvaccinated infants (under 9 months of age). If this is not achieved epidemics can be expected to occur every 2-5 years as the number of susceptible unvaccinated children in the population increases. In developing countries the majority of infants become susceptible shortly after the age of 4 months. Immunization is recommended at 9 months leaving a window of high risk of death from measles between 4 and 9 months.

We sought to investigate the characteristics of measles patients admitted to Queen Elizabeth Central Hospital to determine:

(*a*) the clinical outcome and factors associated with poor outcome.
(*b*) referral patterns and practices of this population and
(*c*) the contribution of preexisting vitamin A status to morbidity and mortality. In this paper we present the findings related to clinical outcome and factors associated with poor outcome to assist in the assessment of current strategies of measles eradication in Malawi.

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Materials & Methods

In the 12 month period from March 1992 to February 1993 we prospectively studied all children who were consecutively admitted to Queen Elizabeth Central Hospital with measles severe enough to warrant admission. All the children were nursed in a special ward reserved for measles cases. A questionnaire was developed and pretested prior to start of the study. Guardians of all children were interviewed within few hours of admission. This was followed by taking a vitamin A conjunctival impression cytology specimen. The que

tionnaire covered demographic, immunization and clinical information. The children were clinically reviewed on admission using a standard proforma, in most cases by the same paediatrician who assessed them at discharge. All children were given treatment doses of vitamin A on admission and, where clinically indicated, antibiotics were administered. Complications of measles were managed appropriately as clinically indicated. Data was entered on microcomputer and analyzed using SPSS-PC+.

Results

In the 12 month period there were 266 children admitted; most cases occurred in the first two months of the study period. There were 144 (54.8%) boys and 119 (45.2%) girls. 34 % of the cases were under 9 months of age and 28.4% were over two years of age.

87% of the patients were from Blantyre District. There were 29 deaths (10.9%) and 19 children absconded. Mortality was highest (22.5%) in children 12-23 months of age. Mortality was only slightly higher in girls (11.8%) than in boys (10.4%). We found no association between overcrowding and outcome (mean number of children <15 = 3.4 in both groups) however, we found that mortality was higher in singleparent households (14.8%) than in households with two or more adults (7.2%) although this difference was not statistically different. Children who were not currently breast fed had no excess risk of death compared to children who were breast fed.

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The commonest complication of measles were predominantly of the respiratory system. Pneumonia complicated the illness of 79 children of whom 21 died. Laryngitis and croup occurred in 70 children of whom 15 died. Pulmonary TB was found in 4 children and one died. Otitis media occurred in 127 children (13 died). Ulceration of the mouth occurred in 75 children. Most of these were aphthous ulcers and we found surprisingly few cases of herpes labialis infection. Mortality was associated with pneumonia and laryngitis. (Table 1) Pneumonia was more commonly reported in secondary cases (40%) than in primary cases (28%). Although viral conjunctivitis was a presenting symptom in most children, no child had obvious xerophthalmia and no child developed severe eye complications.

Of 146 children over 9 months of age, 26 children (17.8%) had no immunization card or the card that has been lost, 76 children (52.1%) had no record of immunization and 44 children (30.1%) had record of being immunized. Only 5 children had documented vitamin A supplementation in the prior six months.

Discussion

There is very little remarkable about our data that cannot be reproduced in nearly every district hospital in Malawi. We present it to review present measles eradication strategies.While the contribution of treatment doses of vitamin A to reducing mortality is well documented, the contribution of periodic (biannual) vitamin A supplementation on the causes of measles remains unclear.

There were too few children in this study who were supplemented periodically prior to measles onset to assess the contribution of periodic vitamin A supplementation in our patients.

Pneumonia is the greatest contributor to measles mortality in developing countries.

None of our patients had evidence of obvious vitamin A deficiency as manifested by xerophthalmia. It has been suggested that children who are vitamin A deficient at immunization will not have a sufficient rise in measles antibody to offer adequate immunity. Decreased measles antibody response has been noted in children with common colds at time of vaccination. (5)

Most children who develop measles under 9 months will have protection from waning maternal antibodies. These children will also be receiving vitamin A through breast milk and are more likely to be vitamin A sufficient. The higher mortality in the 12-23 month age group that we observed may be due to lack of antibody protection, poor vitamin A status, and early introduction of waning foods, as suggested in our results. it has been demonstrated that severity of measles is associated with prolonged exposure and dose of measles virus. (6-8). This is demonstrated by increased severity in the secondary cases. In our population there was no increased risk of death in children exposed in the household compared to those not exposed in the household however, there was an increased risk of severe complications (pneumonia) in secondary cases. It should be noted that among children who were exposed in the household (n=45) all patients who died (n=S) had been exposed to a different sex sibling. Of those who survived (n=40) 21 were exposed to a different sex sibling. This finding confirms population-based results from West Africa (9-10) suggesting that measles cases exposed to different sex siblings are more likely to be intensively exposed, as in secondary cases. Similar to the findings in these studies patients who died were likely to have acquired measles from a sibling older (mean age interval = 62.4 months) than among patients who survived (mean age interval 43.8 months).

Pneumonia is the greatest contributor to mortality in developing countries (11) and in our study population. Mortality, at 10.9% in our population, is likely to be an under estimate since many deaths occur six to eight weeks after onset of symptoms and after discharge from the hospital. Delayed mortality is higher in children who acquire measles before one year of age. (12) These findings suggest that secondary exposure in the household does contribute to a poor outcome.

The definitive way of preventing measles is immunization of children with the live measles vaccine. In Malawi and most developing countries children are vaccinated at 9 months of age with the standard Schwartz vaccine. The time of vaccination is an attempt to balance the risk of acquiring infection against the risk of poor vaccine uptake because of interference from maternal antibodies.

Table I

Risk of Death According to Clinical Complication of Measles

Clinical Sign	%Died	%Survived	Relative Risk (95% Confidence Interval)	p value
Otitis media	46.4%	521.3%'	0.89 (0.58, 1.35)	NS
Pneumon4-a	75.0%	26.6%	2.82 (2.07, 3.83)	<0.001
TB	3.6%	1.4%	2.59 (o.28, 24.1)	NS
Post measles syndrome	10.7%	7.9%	1.37 (0.43, 4.39)	NS
Laryngitis	53.6%	25.2%	2.12 (1.40), 3.21)	0.003
Mouth ulcers	42.9%	28.9%	1.48 (0.92, 2.39)	NS

NS = not significant

In Malawi where crowded conditions are common in urban areas we can anticipate a proportion of measles cases to continue to be under 9 months of age.

In a highly immunized population a large proportion of cases is expected to be among immunized persons. Thus, the 44 immunized, yet infected children represent expected vaccine failures. Measles vaccine failure can range from 1.7-10% and we cannot attribute the Malawian cases to either loss of immunity after initial seroconversion (secondary vaccine failure) or inappropriate handling techniques. In our immunized patients >8 months of age 20.4% had been immunized before 9 months and an additional 22.4% had been immunized at 9 months. Secondary vaccine failure is not uncommon in patients vaccinated too early.

The timing of vaccination of 9 months is an attempt to balance the risk of acquiring infection against the risk of poor vaccine uptake

Our results, although hospital-based and probably not representative of the population as a whole, suggests that there is much we still need to understand about the epidemiology of measles in Malawi. Patterns of transmission, severity, and mortality will continue to change as immunization coverage changes, as the population grows and becomes more urbanized, and as the impact of the AIDS epidemic continues.

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