

MICHIGAN STATE UNIVERSITY

The African e-Journals Project has digitized full text of articles of eleven social science and humanities journals. This item is from the digital archive maintained by Michigan State University Library. Find more at:

<http://digital.lib.msu.edu/projects/africanjournals/>

Available through a partnership with



Scroll down to read the article.

THE NATURAL HISTORY OF MEASLES

J. H. M. AXTON

Department of Paediatrics and Child Health, University of Rhodesia

YOU MAY WONDER why I have taken such a mundane disease as measles for the subject of this lecture. Most people regard it as a mild illness, often no worse than flu. Parents may welcome it as something inevitable, while for many children it means nothing more than an enforced holiday.

It is a disease of which most of us have personal experience and therefore, I hope, is of interest. Many of us possibly retain vivid memories of our own attack, and the way in which it was treated. My main recollection is of the darkened room in which I was nursed, and later of my being forced to wear a cap with a green lining, specially bought for the occasion, to protect my eyes from sunshine.

The history, and natural history, of measles can be used to illustrate the major changes in our way of thinking about diseases, and their causes, over the past two thousand years. Similarly, a study of measles helps to emphasize the two inseparable disciplines or philosophies which underly our care of children today — Paediatrics and Child Health.

Lastly, I believe that measles deserves our attention because it is one of the major problems in modern Africa, which causes a large number of deaths and leaves many survivors with life-long disabilities.

The origin of measles is unknown, although similar viruses cause distemper in dogs and rinderpest in cattle. Plague, typhus and other diseases which have changed the course of history, have a natural reservoir in animals. Measles, on the other hand, has no host except man, and so the persistence of measles in a community depends on its continual passage from infected to susceptible humans.

Thousands of years ago, man probably lived in small family groups, well isolated from his neighbours, and it would be difficult to see how the infection could persist among such groups for any length of time. We know that in isolated islands, epidemics of measles among the non-immune population spread rapidly, but came to an end equally rapidly, after which no new cases of measles occurred for many years, and only then if the virus was introduced from outside.

*An inaugural lecture delivered before the University of Rhodesia on 22 June 1978.

With the growth of villages and towns, and increased travel between them, a pool of non-immune children is always available and being added to by new births. Measles then becomes endemic — that is, it is always present within the community, moving along established lines of communication.

In this situation, we find a fairly classical two-year cycle; an epidemic year, when most susceptible children over the age of six months suffer from the disease, followed by a year when there are not enough susceptible children to sustain the epidemic. There is, however, a sufficient number who escape infection for the disease to remain endemic.

Smallpox, also with no natural animal reservoir, probably in the past followed a similar pattern, and it is interesting that for many years the two illnesses were not separated, but thought of as different manifestations of the same disease.

The earliest description of measles is attributed to Rhazes, who went some way in separating the diseases clinically but thought they proceeded from the same cause (Talbot, 1970, p.19). The prevailing theory was that the red rash associated with measles represented the mother's menstrual blood, dammed up during the child's sojourn in the womb.

Measles was therefore welcomed, as this was the only way the child could rid himself of the so-called 'poison'. For many years children were deliberately exposed to measles for this reason, much as we used to hold german measles parties, before the development of the rubella vaccine.

Thomas Phaer, in the chapter of his 'The Booke of Children' entitled 'Smallpockes and Measels' wrote: 'This disease is common . . . It is of two kinds: — varioli, ye measils; morbilli, called of us ye smal pocks. They be but of one nature and proceed of one cause.' However, after listing three humoral causes for the disease, he observed that it can 'commence [. . .] by the way of contagion, when a sick person infecteth another' (Creighton, 1894, I, p.458).

The modern history of measles begins in 1670, with Thomas Sydenham's description of his son's attack (Dewhurst, p.37). He was the first clearly to separate measles from smallpox, and he recognized complications such as *cancrum oris* and *encephalitis*.

At about the same time Mauriceau rejected the mother's blood theory, and the infectious or contagious theory became generally accepted (Debus, 1970, p.260). Mauriceau also decried the use of red curtains in the sufferer's bedroom. He suggested green would be more appropriate, though probably more on aesthetic than on scientific grounds.

Towards the end of the next century, Francis Home tried to transmit measles using blood from an infected child. In eight out of ten children he succeeded, unwittingly demonstrating the presence of an infective principle in the blood stream, a hundred years before the virus was first seen (Talbot, 1970, p.233).

The next advance came through the astute observations of Peter Ludvig Panum (Talbot, 1970, p.247). Panum was a Danish doctor, sent by his Government to investigate an epidemic of measles in the Faeroe Isles in 1846. The geographical situation of the Faeroes was ideal for an epidemiological study: seventeen isolated islands, where the arrival of a boat was noted in the local calendar and provided an excuse for the gathering of the whole population. Visits from the Danish mainland were rare, but the dates were well documented.

The epidemic originated in a single seaman from Copenhagen, who presumably left the city with no signs of measles. The sea journey to the Faeroes was sufficiently long for him to have become infectious on arrival, but not long enough for him to have recovered completely and have ceased excreting the virus. By following the course of the epidemic from village to village, and island to island, using the known movement of people and boats, Panum was able to establish four important facts:

1. the measles rash appears twelve to fourteen days after contact.
2. its greatest infectivity is during the late prodrome — three to four days before the rash appears.
3. the disease is contagious, probably spread by droplets, and not miasmatic in origin.
4. the protection from an attack is life-long. The last epidemic of measles in the Faeroes had been in 1781, and Panum found that the only inhabitants immune were those over 64 years old, who had suffered from the disease as children during the earlier epidemic.

The more recent history of measles includes the identification of the virus by Hektoen in 1910, the growth and subsequent attenuation of the virus by Enders in 1963 to produce an effective vaccine (Enders, 1963), and the discovery of the relationship between measles virus and a strange and rare degenerative disease of the nervous system of children, called sub-acute sclerosing pan-encephalitis by Payne in 1969 (Payne *et al.*, 1969).

THE PRESENT STATE OF THE DISEASE

Our present knowledge of measles is fairly complete although, as I shall show, there remain several very interesting questions unanswered.

The classical course of measles in a susceptible child is shown in Figure 1. Eight to nine days after contact with the virus the prodromal illness starts with symptoms of a common cold. After three to five days the illness becomes recognizable as measles with the appearance of a rash starting behind the ears and spreading to the face and trunk within twenty-four hours. After two to three days, rapid improvement occurs, with a fall in temperature, and fading of the rash. Within five days of the appearance of the rash most children are up and about, and have been non-infectious since the third day of the rash.

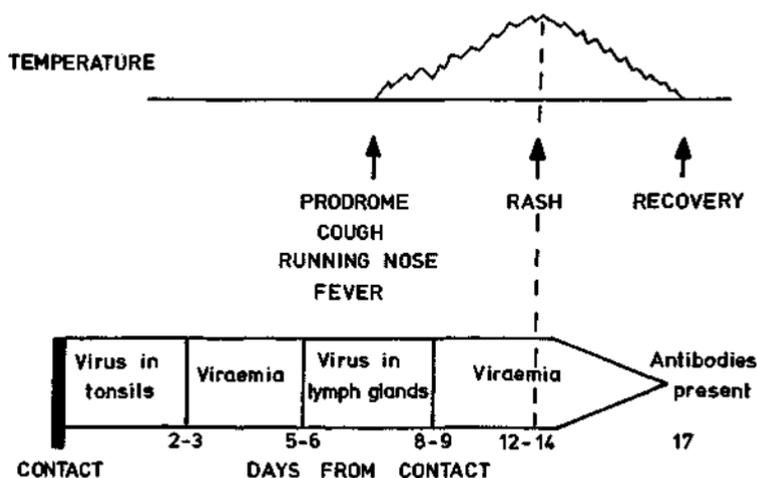


Figure 1: THE CLINICAL COURSE OF NATURAL MEASLES INFECTION

What I have described is the typical picture of measles in a well-fed child, of whatever race. This picture, however, can vary, on the one hand, from a very mild or subclinical attack to, on the other hand, the extreme of death, which occurs in one in every four to ten thousand children infected. This is illustrated in Figure 2. What determines the fatal outcome in the well-fed child is unknown, but we can presume that it is a subtle variation in the immune response, undetectable even by modern methods.

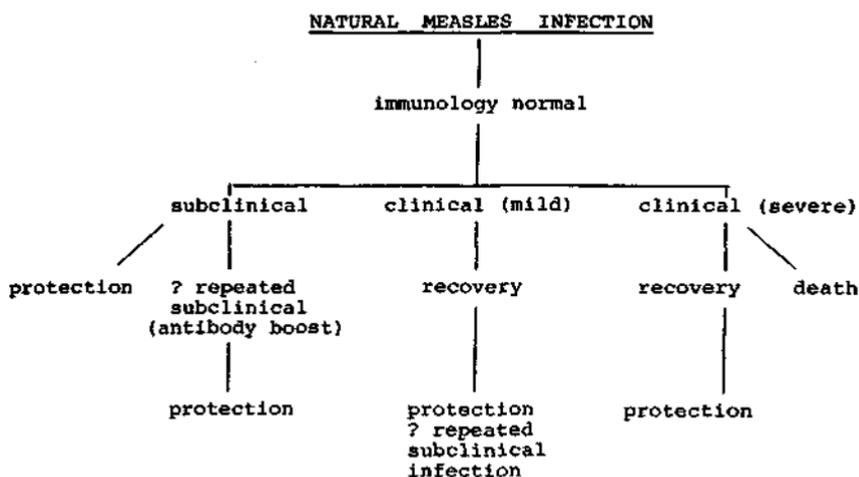


Figure 2: MEASLES INFECTION : NATURAL IMMUNOLOGICAL STATUS

Treatment of the average attack of measles in the well-fed involves no more than good nursing at home, with attention to fluid and food intake, and keeping the eyes and mouth clean. Historically, however, measles was regarded as an extremely serious disease, akin, as we have seen, to smallpox. Death rates of between ten and twenty per cent were reported from isolated communities in the seventeenth and eighteenth centuries, and in Glasgow at the turn of this century five children in every hundred died from the disease (Morley, 1969).

Table 1

MEASLES IN RHODESIA AND BRITAIN IN 1900 AND 1970

	<i>Rhodesia</i>	<i>Glasgow 1900</i>	<i>Britain 1970</i>
Pneumonia	severe, common	severe, common	rare
Laryngitis	severe, very common	severe and common	very rare
Diarrhoea	very frequent, often bloody	well recognized	unknown
Desquamation	often severe	well recognized	almost unknown
Effect on Nutrition	severe, may last for months	severe	transient (5 - 10 days)
Mortality	1 : 20 ?	1 : 20 ?	1 : 4,000 - 10,000

The clinical picture of measles in Zimbabwe Rhodesia now is very like that described seventy to a hundred years ago in Britain. The early stages in many Zimbabwe Rhodesian children are similar to those in Britain. However, when the child reaches the day when he should start to recover, that is a day or two after the rash has appeared, major differences become obvious. Instead of falling, the temperature rises, and complicating pneumonia or tracheitis supervene. A little later, diarrhoea starts, and dehydration is added to the clinical picture. Further complications develop during the next week, and by the time of admission to hospital many children are *in extremis*.

Measles is a disease which affects lymphoid tissue throughout the body, not just the skin, and we would expect, therefore, to find evidence of infection in many organs.

The external complications of measles are represented in Figure 3, and include peeling of the skin, leading to infection, and mouth ulcers, which may develop into cancrum oris. This is not a cancer, but the effect of gangrene, plus infection, on tissue round the mouth and nose. The eyes are

frequently involved, and from simple conjunctivitis there may be rapid progression to complete loss of one or both eyes. The possible internal complications of measles are represented in Figure 4.

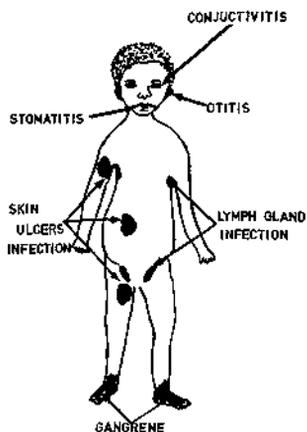


Figure 3: COMPLICATIONS OF MEASLES: EXTERNAL

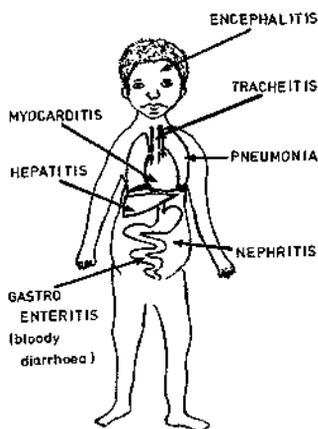


Figure 4: COMPLICATIONS OF MEASLES: INTERNAL

Although encephalitis, myocarditis, nephritis and hepatitis are well recognized, they are not common. The main killing complications in African children are tracheitis and pneumonia. In tracheitis, the upper airway narrows, which makes breathing extremely difficult and exhausting. Frequently we have to perform a tracheostomy on these children to relieve their distress. The death rate, both from this condition and the operation, is high. The early pneumonia of measles is caused by virus in the lung but later, secondary infection with bacteria supervenes. This can cause death, or irreparable damage to the lungs.

The other important complication which contributes to the deteriorating clinical situation is diarrhoea, which may be severe, blood-stained, and persist for one or two weeks. In Britain, only textbooks written before 1910 refer to blood in the stools of children with measles. In Africa, most clinicians have rediscovered the fact for themselves — and find that up to eighty per cent of children pass blood at some time during their infection (Morley, 1969; Axton, 1975a).

We are now in a position to ask what are the explanations for the difference, when we compare the present clinical picture of measles in Britain with that in Africa, and with the picture in Britain a hundred years ago.

Could it be that the virus is of a different, more virulent strain? Evidence is against this, the most telling that the children of well-to-do Africans suffer measles no more severely than their European peers.

Could there be a racial difference in response to infection by measles virus? The mortality from measles among Blacks in America has fallen at exactly the same rate as among Whites, and so this theory is not tenable.

Could the explanation lie in the nutritional state of the child, and the way in which he is looked after during the attack? There is a large volume of evidence to support this theory.

In summary, we know that under-nourished children suffer severely from measles, whatever their race. We also know that children who have an immunological deficiency — that is a congenital inability to fight infection — suffer severely and die from measles. There is, in addition, mounting evidence that one of the effects of malnutrition is to suppress the body's defence mechanisms, producing the equivalent of an immunological abnormality (Smythe *et al.*, 1971).

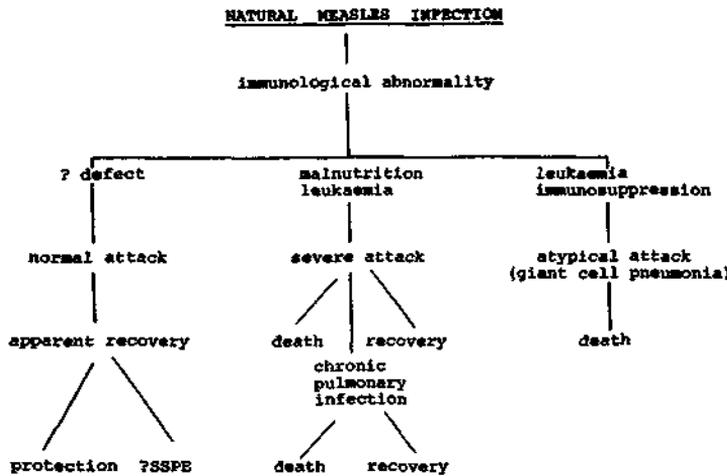


Figure 5: MEASLES INFECTION : ABNORMAL IMMUNOLOGICAL STATUS

Figure 5 shows the possible outcomes from measles in children with an immunological abnormality, whether on the basis of inheritance, malnutrition, or through a deliberate attempt to suppress the body's defence mechanisms, as occurs during the treatment of acute leukaemia or other malignancy. Again, there is a wide spectrum of possibilities, but the emphasis is on the increased severity of the attack, with a high death rate, prolongation of the attack, and in some cases an atypical clinical picture. The last is interesting in that some children with leukaemia may have a measles virus pneumonia persisting for several months, without ever developing the classical rash.

Altered immunity, brought about by malnutrition, is the most likely explanation for the severity of measles in Africa today, and this also explains why the disease was so severe in Europe in the past.

Another factor comes into play, and this is the knowledge of how to care for children while they are ill. Historically, the treatment of measles, and many other diseases, consisted of cupping, bleeding, purging, and similar empiric remedies. In the latter half of the nineteenth century, the importance of nutrition, hydration, and good general nursing care during any illness came to be appreciated and, along with the improved nutrition of children, led to better survival from measles.

These factors are as yet not well understood by many mothers in developing countries, among which we can class Zimbabwe Rhodesia. In Mali, children with measles are not allowed to eat any protein-containing food during the attack (Imperato, 1969). In Zimbabwe Rhodesia, the diarrhoea associated with measles infection is treated by withholding fluids.

Of more importance to the child is the delay in bringing him for care. There is a belief in this country that treating the disease early, especially by accepted Western methods, may prevent the rash coming out. If the rash goes inwards, so the belief runs, the child will suffer from epilepsy in later life. A second, related, belief is that a good florid rash shows the mother or the father that the spouse has been faithful. The rash is thus watched carefully, and attempts made to encourage its development. Both these beliefs imply watching the child at home, and delay the start of rational treatment, often to the point where recovery is impossible.

THE SOCIAL IMPORTANCE OF MEASLES

So far I have talked about the effect of measles on the individual child, but what are the wider, social implications of the disease?

In this country measles is one of the six major killing diseases, as Table II shows:

Table II

LEADING CAUSES OF DEATH BY FIRST DIAGNOSIS (1973)

	<i>Admissions</i>	<i>Deaths</i>
Kwashiorkor/marasmus	522	128
Tetanus	89	45
Measles	165	41
Gastroenteritis	117	21
Pneumonia	621	63
Meningitis	117	34

accounting for 280 deaths in the City of Salisbury alone in 1977. During 1973, a non-epidemic year, 41 deaths were attributed to measles at Harare

Hospital (Axton, 1977). A conservative estimate of deaths in Rhodesia as a whole in an epidemic year would be between 2,000 and 3,000.

We cannot measure the cost of these deaths to the community, as children's lives are priceless. We can, however, look at the effect of measles on the work of the wards at Harare Hospital. Figure 6 shows the annual number of children admitted to the wards since 1969. There is a regular fluctuation, with about 500 more admissions during even years, coinciding with epidemics of measles in 1970, 1972 and 1974. The bottom line shows the number of admissions for measles, and the middle double line, the calculated numbers of admissions if no cases of measles had occurred. The marked variation between the years is almost totally eliminated. Most of the 500 admissions take place during the six wet months of the year, and place a very considerable strain on the nursing and medical staff.

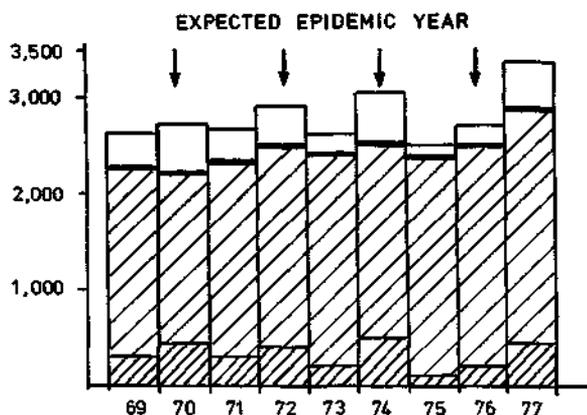


Figure 6: TOTAL ADMISSIONS TO PAEDIATRIC WARDS AND ADMISSIONS FOR MEASLES, 1969 - 77

The figures that I have given underestimate the importance of the disease by about 30 per cent, and do not include children whose malnutrition, tuberculosis or chronic chest problems had been precipitated by recent measles infection. In Table III, allowance is made for this underestimation, and the conclusion is that in epidemic years, up to 25 per cent of all admissions to the paediatric wards are associated, directly or indirectly, with measles.

It is possible to give a rough estimate of the cost to the health services of these admissions. In the five-year period 1972-7, 1,856 children were admitted to Harare Hospital, and stayed an average 8 days in hospital at a cost of ZR\$10 a day, this total works out at about ZR\$150,000.

Measles vaccine costs 35 cents a dose, and so during the same period it would have been possible to vaccinate 450,000 children for the same money as was spent on measles at Harare Hospital.

Table III

HARARE HOSPITAL, 1977

Admissions for measles		479
Admissions for malnutrition	712	
30 per cent precipitated by measles =		238
Total admissions associated with measles		<u>717</u>
Total admissions to hospital	3 000	
Percentage directly or indirectly associated with measles	24	

For the community as a whole, the cost of measles in the five years quoted was probably about ZR\$500,000 (ZR\$100,000 per year) with which approximately 1,500,000 doses of vaccine could have been bought. (These calculations are by no means exact; for, as any hospital administrator will tell you, it costs almost as much to run a ward with no patients as it does when bulging at the seams.)

With a population of 6,500,000, and a fertility rate of 5.2, roughly 338,000 children are born each year in Rhodesia. The cost of vaccine to protect every child would be ZR\$120,000, not much more than the estimated cost of measles to the hospital services each year.

MEASLES VACCINE

A safe and effective vaccine has been available for nearly fifteen years, and present evidence suggests that the protection it gives will be life-long. We may well ask why has not every child in this country received his dose.

Some parents and doctors are not yet convinced of its efficacy and safety, but the serious complications of vaccination are about two hundred times less likely to occur than similar complications after wild measles. The potential effect of the vaccine is shown by the virtual disappearance of measles epidemics in Britain and the United States of America.

The major difficulties in this country are logistical. We have a scattered population, disruption of travel in rural areas, migration from these areas to towns, and a high birth rate, all factors working against universal vaccination. The actual cost of the vaccine, in relation to these difficulties, is small.

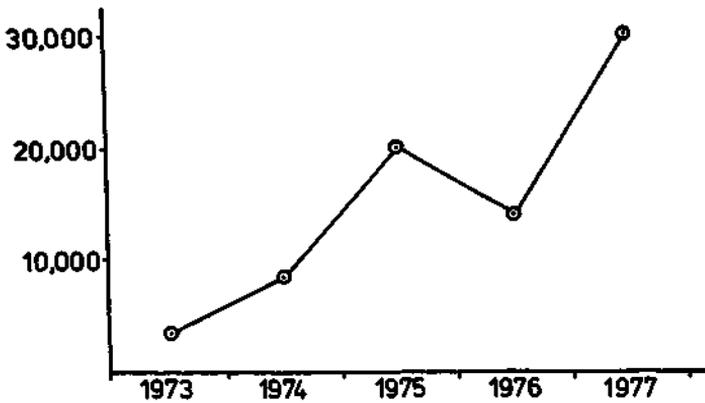


Figure 7: NUMBERS OF CHILDREN IMMUNIZED AGAINST MEASLES IN THE CITY OF SALISBURY, 1973 - 7

Despite the problems, a wide-spread campaign to control measles has been going on for several years. During 1977, in the City of Salisbury alone, 30,000 doses of vaccine were given, as shown in Figure 7. Approximately half the susceptible child population was reached, but as can be seen from Figure 8, this had little or no effect on the numbers of cases reported in the city. One factor which might explain this is that in the early part of the campaign, one-fifth of the recommended dose of vaccine, previously shown to be effective, was used. This was done in an attempt to reduce costs and increase coverage. All that we seem to have done is to postpone the expected epidemic from 1976 to 1977. We have grave doubts about the protection given by this fraction of a dose, and now recommend the full dose. It appears that the smaller dose may have given only temporary protection.

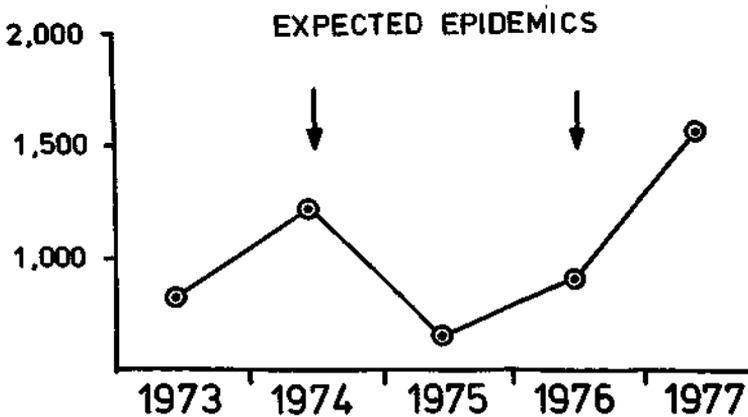


Figure 8: NUMBER OF CASES OF MEASLES NOTIFIED IN THE CITY OF SALISBURY, 1973 - 7

A second factor is that to have any real effect on the community as a whole, and not just protect the individual child, we need to keep about 85 per cent of the childhood population vaccinated. With the increased child population in the townships of Salisbury, brought about by migration from the war areas, it has been impossible to reach this level. To achieve an 85 per cent level of vaccination, we will have not only to offer vaccine at all clinics and hospitals, but also to continue with special campaigns, aimed at measles alone.

I would hesitate to recommend that measles vaccination be made compulsory, as this would remove the parents' right to decide the issue for themselves. The Americans seem to have solved the problem rather neatly: there is no compulsory vaccination, but before a child can be admitted to school evidence of vaccination must be produced.

CONTRIBUTION TO MALNUTRITION

The last aspect of measles I want to consider is its influence on the state of nutrition. I have talked about the response to measles infection in children who are already malnourished, but above this, there is a good deal of evidence to show that measles can precipitate malnutrition.

From many parts of the world, epidemics of kwashiorkor have been reported in the wake of epidemics of measles (Gans, 1961; Murphy, 1966). The time-lag is usually about two months. During epidemic years, 30 per cent of children admitted to Harare Hospital with malnutrition have suffered from measles during the previous few months. Their admission diagnosis is recorded as malnutrition, and the preceding measles infection is missed unless specific enquiry is made. The several possible mechanisms through which measles might act are listed in Table IV.

Any illness associated with fever and tissue destruction increases the body's needs for protein and energy (Scrimshaw *et al.*, 1960). Unfortunately, in most diseases, there is a simultaneous decrease in appetite. In measles there are often painful ulcers in the mouth, making feeding difficult or impossible. In some countries local custom decrees partial starvation, or at least a change in diet to a thin, non-nutritious gruel, during the attack.

Table IV

INFLUENCE OF MEASLES ON NUTRITIONAL STATE

1. Increased needs	:	any febrile illness anorexia
2. Decreased intake	:	mouth ulcers customs
3. Increased losses	:	protein/blood from the gut
4. Decreased absorption	:	effect on the lining of the gut

Another factor, recently reported from our department and confirmed by workers in Nigeria (Axton, 1975b; Dosssetor and Whittle, 1975) is the influence of measles on the gut. Plasma protein may be lost from the intestines of children with diarrhoea associated with their measles, in amounts equivalent to a quarter the normal protein intake. A second effect is that the cells lining the gut may be damaged, which impairs its ability to absorb and digest food. Thus, even if food intake is normal, nutrients may still be lost to the body through malabsorption. How long this state of malabsorption lasts is unknown, but it is probably for at least two to four weeks, and in some cases much longer.

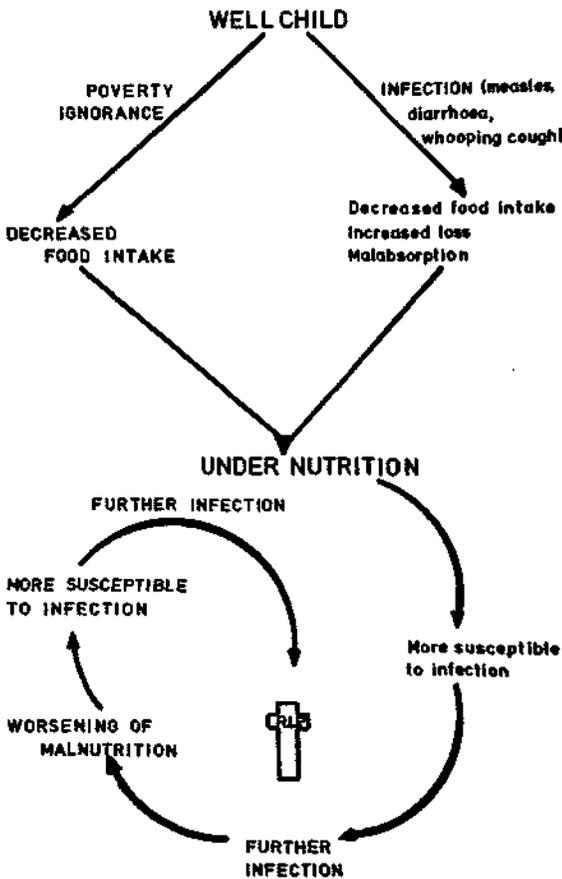


Figure 9: THE VICIOUS CIRCLE : MALNUTRITION AND INFECTION

Taken together, these factors explain how measles may initiate a vicious circle of malnutrition and infection, shown in Figure 9. We start with a

well child. Following the right-hand pathway, he may become undernourished through suffering from any acute infectious illness, including measles. In this undernourished state, the child is more susceptible to other infections, and to suffer from them more severely than normal. It is then only a few steps to the grave.

I mentioned earlier how malnutrition depresses the body's defence mechanisms, so predisposing to severe measles infection. From several centres, but principally from Durban, have come reports that measles itself will depress the immunological system for as long as six to eight weeks (Coovadia, 1977). This emphasizes still further the importance of measles as one initiator of the vicious circle.

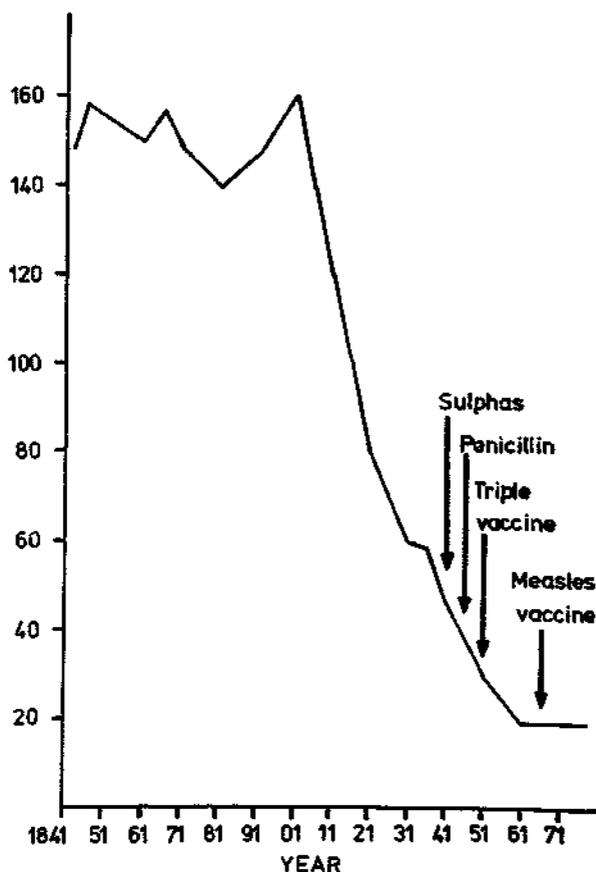


Figure 10: INFANT MORTALITY : ENGLAND AND WALES

In discussing the inter-relationship between malnutrition and infection, we are at the heart of the most important problem facing children in every developing country.

The answer to malnutrition is not simply the provision of food; it involves preventing infection. Conversely, the prevention of infection, and more specifically the amelioration of its effects in terms of mortality and morbidity, depends on improving the nutritional state of children.

For all those involved in child health, the importance of these ideas is far-reaching. We cannot hope to tackle the problem by concentrating our work in hospitals and clinics, nor can we tackle the problem alone. Only the short-term solution for the individual child can be provided by doctors or nurses. The long-term answer lies in overall change and improvement in the environment, which can only be brought about by integrated development on many fronts. Here, the doctor takes his correct place in a team, the other members of which will be agriculturalists, politicians and hydrologists, to name a few.

It is salutary to remember that the greater part of the decrease in infant mortality in Britain and Europe took place through social revolution, which improved nutrition, housing, and child care, before the discovery of vaccines and antibiotics (Figure 10). We should also recognize that a falling child mortality in Europe was followed, after an interval of fifteen to twenty years, by a fall in fertility.

In Zimbabwe Rhodesia we are fortunate in having, first, an understanding, through hindsight, of those factors which will improve child health, and second, the availability of vaccines and drugs which were not known in Great Britain in the early twentieth century.

We have the ability to reduce mortality and improve the quality of children's lives more rapidly than at any other time in history. Some may plead that a population growth of 4 per cent per year will negate all our efforts; but until we can demonstrate that most children born will survive to adulthood, we have no hope of inducing people to limit their families.

This, I believe, is one of the most fundamental problems which the Government of the day will have to face in the future.

Acknowledgements

It gives me great pleasure to thank Mrs M. Sapseid, secretary to the Department of Paediatrics and Child Health, who patiently typed numerous drafts, and the final manuscript, and helped collate the references and illustrations.

References

- AXTON, J. H. M. 1975a 'Gut Structure and Function during and after Measles in Undernourished Children' (Salisbury, Univ. of Rhodesia, unpubl. M.D. thesis).
- AXTON, J. H. M. 1975b 'Measles — a protein-losing enteropathy', *British Medical Journal*, iii, 79—80.
- AXTON, J. H. M. 1977 'Analysis of medical paediatric admissions to Harare Hospital, 1973', *The Central African Journal of Medicine*, XXIII, 193 - 201.
- COOVADIA, H. M. 1977 'Host Allergic Response Variation in Children with Measles Infection' (Durban, Univ. of Natal, unpubl. M.D. thesis).
- CREIGHTON, C., *A History of Epidemics in Britain* (Cambridge, Univ. Press, 2 vols, 1894).
- DEBUS, A. G. 1970 *Medicine in Seventeenth Century England* (Los Angeles, Univ. of California Press).
- DEWHURST, K. 1966 *Dr Thomas Sydenham (1624 - 1689) : His Life and Original Writings* (London, Wellcome Historical Medical Library).
- DOSSETOR, J. F. B. and WHITTLE, H. C. 1975 'Protein losing enteropathy and malabsorption in acute measles enteritis', *British Medical Journal*, ii, 592 - 3.
- ENDERS, J. F. 1963 'Vaccination against measles', *Australian Journal of Experimental Biology and Medical Science*, XLI, 1467 - 80.
- GANS, B. 1961 'Paediatric problems in Lagos', *The West African Medical Journal*, X, 33 - 46.
- IMPERATO, P. J. 1969 'Traditional attitudes towards measles in the Republic of Mali', *Transaction of the Royal Society of Tropical Medicine and Hygiene*, LXIII, 768 - 80.
- MORLEY, D. C. 1969 'Severe measles in the tropics', *British Medical Journal*, i, 297 - 300, 363 - 6.
- MURPHY, E. la C. 1966 'Measles in Accra, 1961 - 1962', *Ghana Medical Journal* V, 58 - 60.
- PAYNE, F. E., BAUBLIS, J. V. AND ITABASHI, H. H. 1969 'Isolation of measles virus from cell culture of brain from a patient with S.S.P.E.', *The New England Journal of Medicine*, CGLXXXI, 585 - 9.
- SCRIMSHAW, N. S., WILSON, D. AND BRESSANI, R. 1960 'Infection and kwashiorkar', *Journal of Tropical Paediatrics*, VI, 37 - 43.
- SYMTHE, P. M., SCHONLAND, M., BRERETON-STYLES, G. G. *et al.* 1971 'Thymolympathic deficiency and depression of cell-mediated immunity in protein-calorie malnutrition', *Lancet*, ii, 939 - 44.
- TALBOT, T. H. 1970 *A Biographical History of Medicine: Excerpts and Essays on the Men and Their Work* (New York, Grune and Stratton).