

Session 1: World Wide Importance of Measles

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Measles as a Universal Disease

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I need hardly say how honored I am to have been asked to open the discussion at this International Conference on Measles Immunization. It is a great privilege to receive such an invitation and a great pleasure to have the opportunity of coming to this friendly country again and meeting those who have contributed so much to our knowledge of the disease. There is nothing new that I can say about measles, and I propose therefore to give a brief review of the more general features of the disease, particularly in relation to its epidemiology and immunity.

Nomenclature

There is some doubt about the origin of the name measles. Most probably it comes from the Latin term *misellus* or *misella*, itself a diminutive of the Latin *miser*, meaning miserable, which was given to the inmate of a medieval leper house. It was used in this way for the sufferer from various skin eruptions and sores by Langland, in the 14th century, in his poem "The Vision of Piers the Ploughman." Shakespeare also used it in *Coriolanus*, indicating, however, that the sores were infectious. It was John Gaddesden who identified, quite unjustifiably, the nonspecific leprous sore with the disease called in Latin *morbilli*. This term was a diminutive of *morbus*,

meaning disease, which referred to the major disease, bubonic plague, morbilli being a minor disease. In the anglicized form of *misellus*, namely *mesels*, the word henceforward became applied not to the sufferer of ill-defined skin lesions but to the specific disease morbilli. The pronunciation of the word measles presents no difficulty to Anglo-Saxons, but on the Continent it may take strange forms. Some of you will remember the consternation experienced by H. G. Wells when he was told by a doctor in Southeast Europe that he was suffering from "mee-áh-slays."

History

No accurate information is available on the early history of measles. The disease was certainly confused with smallpox, and though the Arabian physician, Rhazes, is generally credited with having drawn a distinction in the 10th century between the 2 diseases, there is no doubt that he and the Arabian school generally regarded them as intimately associated with each other. By the beginning of the 17th century the demarcation between them was becoming clearer. We find in fact that in the annual bills of mortality drawn up by the Parish Clerks of London in 1629 smallpox and measles were listed separately. The observations of the physician and epidemiologist, Thomas Sydenham, finally cleared up what obscurity was left. Subsequently, confusion, when it has existed, has been between measles and scarlet fever and between measles and rubella. Fortunately, owing to the work of Enders and his col-

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leagues, we can now say, in the face of clinical doubt, that measles is a disease caused by the measles virus and by that alone.

The mortality caused by measles has varied greatly during the past 3 centuries. In the London epidemic of 1674 it caused more deaths in the first 6 months of the year than smallpox. In the 18th century in Britain it was a comparatively mild disease, but early in the 19th century it again became more serious. The explanation offered for this by Dr. Robert Watt, a Scottish physician, was that it was usurping the place previously occupied by smallpox, which was now being prevented by vaccination. According to him smallpox had previously killed off the weakly children, so that measles, when it came later, caused only a mild disease in the more lusty survivors. In the absence of this selective effect of smallpox, the weakly children were now being exposed to measles, which assumed in them a far more serious character than it had previously had.

The substitution or usurpation of one zymotic disease by another is a phenomenon well recognized by epidemiologists and is still relevant to the world today. As Creighton¹ pointed out, the replacement in Britain of plague by typhus, of typhus by smallpox, and of smallpox by measles was accompanied by a transfer of mortality from the older ages to the younger. Probably several factors accounted for this, of which the chief was increase in the density of the population; but whatever the causes the position has now been reached that, with the exception of tuberculosis, influenza, and hepatitis, all the zymotic diseases cause their highest mortality in the first few years of life.

Epidemiological Features

The attack rate in measles is higher than for any other infectious disease. In virgin populations that have not experienced a previous visitation, susceptibility appears to be almost complete. In the epidemic in southern Greenland, for example, observed

by Christensen and his colleagues,² the attack rate was 99.9%, and in that observed by Peart and Nagler,³ among the Canadian Indians and Eskimos of the Eastern Arctic region, it was again over 99%. In populations such as those in Europe and the United States that have been in contact with the disease for some centuries, the secondary attack rate on susceptible members over 1 year of age is usually between 80% and 90%.⁴

The difference between the 100% attack rate in virgin populations and the 85% attack rate in more civilized populations raises the question of genetic immunity. Is the present increased resistance of the people of Europe and America due to the elimination of the more susceptible elements of the population during previous epidemics? Before attempting to answer this question, we have to consider the notification and the mortality rates of measles.

During the last 50 years or so the mortality of all the infectious diseases has fallen, in some instances almost dramatically. The notification rates have also fallen, though not so rapidly. But measles presents a striking exception to this general rule. At the beginning of this century the mortality from measles in England and Wales was 318 per million living at all ages. It is now 2 per million. In contrast to this, the number of cases of measles seems to be as high as ever. Indeed, in the present year a larger number of cases have been reported in England and Wales than in any year since the disease became notifiable in 1939. Up till the end of August nearly 750,000 cases had been recorded in a population of just over 10 million under 15 years of age.

We have here, therefore, the striking anomaly of a high degree of immunity to death associated with an apparent lack of immunity to attack. In this respect, as in certain others, measles is unique. If the immunity to death is partly due to an inherited resistance, why is there no corresponding immunity to attack?

I am going to put forward the thesis that there is some degree of inherited immunity to attack, but that it is incommensurate with that against death. The evidence I bring is based largely on the difference that I have already quoted between the attack rates on civilized and virgin populations. Why is it that in Britain 15% of children without a history of measles escape attack when they are exposed to close contact with a case? The obvious answer is that they must possess some natural immunity. The truth of this can, I think, be shown by demonstrating that these apparently insusceptible children do in fact contract the disease, but in a latent form, and as a result become latently immunized. The suggestion that this happened was put forward many years ago by Stocks and Karn⁵ and Halliday⁶ and more recently by Enders.⁷ The most suggestive evidence in its favor was brought by the School Epidemics Committee of the Medical Research Council.⁸ In 7 public schools kept under close observation, pairs of epidemics of measles occurred at an interval of 2 to 3 years. In the first epidemic the attack rate on the susceptible boys or girls ranged from 38.3% to 75.4%. Again in the second epidemic, the attack rate on those who were exposed for the first time ranged from 50.0% to 82.4%. But among the susceptible pupils who had passed through the first epidemic without contracting the disease and were still at school when the second epidemic broke out the attack rate was only 0.0% to 13.3%. This enormous reduction in susceptibility suggests not only that a high proportion of the susceptibles in the first epidemic had become latently immunized but that this immunity had lasted for at least 2 to 3 years. It is, of course, legitimate to argue that these children escaped clinical attack by virtue of a natural immunity, and that they did not suffer from even a latent infection. The general evidence, I think, is against this interpretation, but now that the development of antibodies can be followed in the laboratory there should be little difficulty in settling the question. The small amount of evidence

so far available in this respect seems to support my thesis.¹¹ Whichever interpretation is correct, it may be said that in Britain probably 15% or so of children possess a sufficient degree of genetic immunity to render them resistant to a clinical attack of measles. The enormous discrepancy, however, between resistance to attack and resistance to death still remains and, as I have already indicated, constitutes a phenomenon displayed by no other disease.

Epidemic Spread

Measles is a truly universal disease. It is present in all continents and among all peoples. Unlike influenza or cholera, which cause pandemics from time to time, measles is always pandemic. In individual countries, however, its prevalence varies from time to time and from place to place. In large cities it is common for it to show a biennial peak, dependent presumably on the accumulation of susceptible persons. The incidence of the disease is usually highest in the second, third, and fourth years of life. When, as the result of new births, the susceptible child population has reached a figure of 30% to 40%, an epidemic breaks out and continues till the susceptible population has been reduced to about a half. After that there is comparative quiet till a fresh lot of susceptible children has accumulated. This, of course, is a very generalized picture. In smaller communities, epidemic spread may bear little relation to the proportion of susceptible subjects. This was the experience of the School Epidemics Committee,⁸ though it is true to say that an outbreak seldom occurred in a school unless the proportion of susceptible children constituted at least 15%. It is interesting to note that measles was more likely than any other disease to assume epidemic proportions when infection was introduced into a school and that spread was more frequent among boys than among girls, even when the proportion of the susceptible population was higher among the girls.

Infection seems to occur entirely from case to case. So far as our present in-

formation goes, healthy carriers are unknown. It follows that, if the disease is introduced after a long interval of freedom into an isolated or closely circumscribed community, it attacks practically every susceptible person and then dies out. The immunity it leaves behind is almost absolute. Genuine second attacks—not those due to rubella or ECHO virus 9 or some similar infection—are a rarity. In the outbreak in the Farøe Islands in 1846 the survivors of a previous epidemic 65 years ago were found to be still immune.⁹ It is doubtful whether the immunity resulting from an attack of any other disease is quite so strong and persistent.

Vaccination

When it is possible neither to inactivate or sterilize a disease at its source nor to interfere with its transmission, reliance has to be placed on increasing the resistance of the contacts by artificial immunization. In measles the patient is usually infectious before the diagnosis can be made. Isolation of the patient, therefore, comes too late to inactivate the infection at its source. Again, transmission of the infectious material from the nose and throat by droplets and other particles carried through the air is notoriously difficult to prevent or control, particularly in infants and young children. We are forced therefore to the conclusion that to protect against measles artificial immunization in some form is the most hopeful method.

This conference is called to consider immunization against measles, and it is fitting therefore that in introducing measles as a universal disease, I should refer to the subject of vaccination. There are certain general principles that should govern the policy of vaccination against any disease:

(a) The vaccine should be harmless to the healthy child. In practice no vaccine has yet been devised that has not occasionally given rise to a severe and sometimes fatal reaction. The risk is much higher with some vaccines than with others. Unfortunately,

for any given vaccine the risk can be assessed only by experience.

(b) The disturbance caused by vaccination should not be greater than that caused by the disease itself. There is no doubt that in the prevention of smallpox the febrile eruption that follows primary vaccination is far less severe than that caused by the natural disease. In measles, however, this not so clear. Though at one time measles had a high case fatality rate resulting in a serious mortality, it has now in many parts of Europe and America become so mild that death is quite exceptional. In 1959, for example, an epidemic year in England and Wales, the total deaths from measles numbered only 98 in a total population of 45 million. Under these conditions, is the disease worth preventing, or should we concentrate on shielding infants and very young children from the risk of infection and protecting them with γ -globulin when this is impossible? It is difficult to answer this question without knowing more exactly how much permanent damage measles does to the healthy child. In the tropics, of course, the position is different. There the case fatality rate for measles is high, and a much stronger case can be made out for vaccination.

(c) If the vaccine has to be given to a high proportion of the susceptible population, then it must be easy to administer. Current practice is to vaccinate children against smallpox, whooping cough, diphtheria, tetanus, poliomyelitis, and, in many countries, tuberculosis. The successful addition of measles vaccine to this galaxy of prophylactic agents will be possible only if it can be given in a simple painless manner.

(d) There must be reason to believe that vaccination will prove of benefit to the herd as well as to the individual. One of the objections raised to attempts to eradicate tuberculosis by segregation and similar measures is that the resulting community would be left a prey to fresh infection whenever it was introduced. This, as Burnet¹⁰ pointed out, is almost certainly untrue. Our present high level of natural

resistance to tuberculosis has been gained as the result of selection over several hundred years, and to lose it would take an equally long time, even if immunity was not reinforced by vaccination. With measles the position is different. Genetic immunity, as we have seen, is not sufficiently high to protect more than a small proportion of the population against attack. Hence if the herd was to be protected against the disease, a high proportion would have to be vaccinated. How high this proportion would have to be is impossible to say, but if the chain of infection from case to case is to be broken completely, I suspect it would have to be very high indeed—perhaps 90% or more. If the policy of vaccination was successful and measles was eradicated, the new generations growing up would still be highly susceptible and, if they were to escape measles introduced into the country from one source or another, would have to be vaccinated in early life. Experience, however, has shown that mothers are reluctant to have their children vaccinated against a nonexistent disease. The chance, therefore, of ensuring a continuing herd immunity by vaccination would seem to be small.

I want to make it quite clear that I am not arguing for or against vaccination against measles. I merely want to define in general some of the problems that attend vaccination against any disease, and some of those that concern measles in particular.

(e) Lastly, the degree of immunity conferred by vaccination should be sufficiently solid to obviate the need of frequent re-vaccination.

Summary

A brief review is given of the nomenclature and history of measles.

Attention is drawn to some of the peculiar epidemiological features of measles, particularly the persistence of a high notification rate in spite of an enormous fall in

the mortality rate, and evidence in favor of latent immunization is discussed.

The general principles underlying the vaccination of healthy children are reviewed.

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