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Spectrum of measles complications in 942 children in Kinshasa, Zaire

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Introduction

Measles is an acute, communicable, disease characterized by cough, coryza, conjunctivitis, a confluent erythematous maculopapular rash and Koplik's spots. The measles virus is classified as RNA containing paramyxovirus with only one antigenic type known. Measles case fatality rates, for all age groups, have decreased because of improved socio-economic conditions and effective antibacterial therapy for secondary infections. In the West, death, often from respiratory and neurological complications, has occurred in 1 per 1,000 cases. In 1989 there were 41 measles associated deaths in the United States, giving a mortality of less than 1 per 500 cases (1). However, in Zaire case fatality remains as high as 10 percent.

The measles virus is not more virulent in Africa than other regions, rather it is that the socioeconomic conditions account for its high morbidity and mortality. Measles is highly contagious and overcrowding leads to early, high dosage contact with the virus, hence its early acquisition and greater severity.

The endemicity of measles is essentially world-wide. Epidemics tend to occur in large cities at 2 to 4 year intervals. In Kinshasa, the measles epidemic occurs every other year while remaining hyperendemic at all times. Infants acquire immunity transplacentally from their mothers who have had measles or were vaccinated. Although this immunity is usually complete for the first 4 to 6 months of life, it disappears rapidly thereafter. Infants of susceptible mothers have no immunity and may acquire measles in the neonatal period.

In our experience, measles complications in children has the highest hospital mortality (33%). Therefore a prospective study was designed to evaluate the clinical spectrum of complications and the causes of death in children with measles hospitalized at Mama Yemo Hospital in Kinshasa, Zaire. In this study, we reviewed all measles complications and analyzed the various parameters that contributed to the death of these children. We also present the interaction between measles and AIDS and the administration of Edmonston-Zagreb vaccine to infants at 6 months of age. To our knowledge, this is the largest series of measles complications to be reported in the literature.

Methods

There is no hospital for infectious disease in Kinshasa, therefore, children with measles are admitted to various hospitals, most of them to the 2,000 bed Mama Yemo Hospital, a teaching institution with 530 pediatric beds. The children with measles initially arrive at the Pediatric Emergency Room or the Pediatric Outpatient Clinic. Those who do not present measles complications are given ambulatory treatment and are sent home, whereas those with complications are rapidly transferred to the measles ward, a 40 bed unit with its own intensive care facilities. The staff of the measles ward serve exclusively on this ward to prevent cross infection in the hospital.

Upon admission, a complete physical examination, chest X-ray and laboratory tests were performed on each patient. Interviews with the mothers or guardians revealed that the children were treated in neighborhood dispensaries or hospitals. However, upon deterioration of the child's condition, they were referred to Mama Yemo Hospital.

Results

Between January and November 1985, 942 children were hospitalized at Mama Yemo Hospital with measles complications. There were 492 (52.2%) boys and 450 (47.8%) girls, ranging in age from 2 months to 13 years. Eighty (8.5%) infants acquired measles at 2 - 5 months, 241 (25.5%) at 6 - 9 months, 404 (43%) at 10 - 23 months, 165 (17.5%) at 2 - 4 years and 52 (5.5%) at 5 - 13 years of age. In this series, 321 (34%) of the infants acquired measles before 9 months and 725 (77%) before 2 years of age (Tab. 1). There were 3 children with Down's Syndrome and one with achondroplasia in this series.

TABLE 1

Age at onset of measles complications in 942 children in Kinshasa, Zaire

Age	No. of Cases	Percentage of case
2 - 5 mo.	80	8.5%
6 - 9 mo.	241	25.5%
10 - 23 mo.	404	43.0%
2 - 4 yrs.	165	17.5%
5 - 13 yrs.	52	5.5%

History of Measles Vaccination

Because of the high incidence of measles in infants under 12 months of age in Africa, measles vaccine is given between 9 - 12 months as recommended by the World Health Organization (2). In this cohort, 841 (89.2%) children were not immunized with measles vaccine. Of 101 (10.8%) remaining children 90 were vaccinated between 9 - 24 months and 11 after 2 years of age. It is interesting to note that the 90 younger children were vaccinated, on the average, one week before the appearance of the infection. As the measles incubation period is 10 - 14 days, it appears that these children were vaccinated during the incubation period. However, the 11 older children were vaccinated long before acquiring measles.

Clinical Complications (Table 2)

All children with measles presented multiple complications. Upper and lower respiratory tract infection and enteritis were the most common findings. Three hundred and

thirteen (33.2%) presented with croup and 652 (69.2%) with significant lower respiratory infection.

Review of the chest X-rays revealed that 616 (65.4%) children presented with bronchopneumonia, 18 (1.9%) with lobar pneumonia, 10 (1%) with empyema, 7 (0.7%) with pneumomediastinal and subcutaneous emphysema, 5 (0.5%) with pulmonary abcess and pneumatocel, 2 (0.2%) with pneumothorax and 1 (0.1%) with pulmonary abcess. Pleural aspiration was performed on all children with empyema. Culture of the aspirate grew staphylococci in 6 and Klebsiella in 4 children. The chest X-rays in children with bronchopneumonia revealed increased broncho-vascular markings, patches of opacifications, atelectasis, pleural reaction and localized pulmonary emphysema.

Enteritis in measles is a serious complication. Five hundred and eighty-eight (62.4%) children presented mild to severe dehydration. In Zaire, parents administer enemas to children with the hope of "releasing the infection". These enemas provoke diarrhea which may further aggravate an already precarious situation. Some of these products contain alkaloides which may lead to shock and cardiac arrest. Parents are often unwilling to talk about indigenous treatment, however, the staff believes that more than 10% of these children have been subjected to enemas. Eleven of these children arrived at the emergency room in a state of shock.

In children with severe measles, there is a remarkable inflamation of the skin with hemorrhage into the dermis resulting in dark staining of the rash, which is followed by desquamation. In this series, 368 (39%) children presented with massive exfoliation of the skin, 20 of them subsequently developed significant cutaneous staphylococcal infection. Koplik's spots appear on the third or fourth day of the prodromal period and rapidly spread to involve the entire buccal mucosa and gingiva, disappearing 2 to 3 days later. However, in severe cases, the gingivobuccal mucosa remains inflamed leading to ulceration of the buccal mucosa. Ulcerative stomatitis with serious feeding difficulties was observed in 112 (11.9%) children.

The central nervous system is not commonly involved in measles infection, however, the presence of an acute encephalitis carries an ominous prognosis. In this series, 41 (4.4%) children presented encephalitis. Lumbar puncture showed a mild pleocytosis with no bacterial growth in the cerebrospinal fluid culture.

Fifteen (1.6%) children presented with septicemia. Hemoculture grew *staphylococcus aureus, streptococcus* and *Klebsiella*. It is worthy to note that malnourished children are particularly susceptible to *Klebsiella* infection.

Conjunctivitis is common in children with measles. Severe conjunctivitis may be accompanied by corneal ulceration, particularly in children with vitamin A deficiency. Ulcerative keratitis and blindness were observed in 3 (0.3%) children.

Associated pathology

Anemia:

Laboratory examinations revealed that 63 (6.8%) children presented hemoglobin values (Hgb) of 5 gm% or less, 341 (36.2%) of 6 - 8 gm%, 325 (34.5%) of 9 - 10 gm% and 212 (22.5%) showed hemaglobin values of more than 10 gm%.

Malaria:

Seventy-eight (8.3%) children presented measles and malaria as *Plasmodium falciparum* malaria is endemic in the region.

TABLE 2

Measles Complications in 942 children, 2 month - 13 years old in Kinshasa, Zaire

Complication	No. cases	Percentage
Pleuropulmonary complications	652	69.2%
Enteritis	588	62.4%
Croup	313	33.2%
Ulcerative stomatitis	112	11.9%
Encephalitis	41	4.4%
Severe cutaneous staphylococcal infection	20	2.1%
Septicemia	15	1.6%
Otitis	10	1.1%
Purulent meningitis	7	0.7%
Subcutaneous emphysema	7	0.7%
Ulcerative keratitis and blindness	3	0.3%
Noma	1	0.1%
Osteomyelitis of the mandible with fistulization	1	0.1%

Other infections:

Typical cases of whooping cough were observed in 8 (0.8%) children who had not been previously immunized with DTP. Six (0.6%) children presented with tuberculosis; 5 with pulmonary tuberculosis and one with tuberculosis of the cervical lymph nodes proven by biopsy, and 2 (0.2%) children with tetanus, who were not previously immunized with DTP.

Nutritional State:

In this study, 299 (31.8%) children weighed below the 3rd percentile, 229 (24.3%) weighed at the 3rd percentile, 336 (35.7%) weighed at the 10th percentile, 67 (7%) weighed at the 25th percentile and 11 (1%) weighed at the 50th percentile weight for age. In total 864 (91.7%) children weighed equal to or below the 10th percentile weight for age, indicating significant failure to thrive.

Hospital Mortality

There were altogether 310 deaths (33%) with 146 (32.4%) among the 450 girls and 164 (33.3%) among the 492 boys. Septicemia and subcutaneous emphysema had the highest mortality (100%) followed by encephalitis, toxicity with indigenous products and massive staphylococcal infection. In associated pathology, tetanus and tuberculosis had the highest mortality.

Management

Every effort should be made to improve the nutritional state of children with measles (3). This will not only improve their chances of recovery but will also prevent the much feared Kwashiorkor and marasmus which will follow in the wake of this infection.

There is no effective antibiotic against the measles virus and therefore current management is basically symptomatic and supportive. In case of enteritis, oral rehydration salt (ORS) solution is extremely effective in combatting dehydration and has considerably reduced mortality from enteritis (4).

In the tropics, stomatitis is often treated satisfactorily with the application of gentian violet. Bronchopneumonia and pneumonia are treated with penicillin or, when indicated, with large spectrum antibiotics. Laryngitis or laryngotracheitis is a serious complication associated with respiratory distress and signifies an upper respiratory obstruction. It is often associated with bronchopneumonia and requires prompt attention. Oxygen, steam inhalation in a croup tent and antibiotics are indicated. There is no treatment yet for measles encephalitis.

Discussion

Infectious diseases remain active in central Africa and are an important cause of morbidity and mortality in children. Although measles is a worldwide disease, it's severity varies geographically. In parts of Africa, it manifests as a particulary severe disease while in Europe and North America, it is relatively mild. There is no evidence of antigenic differences in viruses isolated from various regions, neither does there appear to be any racial variations in immunity as the disease manifestion in well to-do Africans is similar to Europeans.

In our experience, age at the onset of infection, nutritional status of the child, and hemoglobin level played a significant role in the outcome of measles.

Sex distribution

There was no sex predelection in measles. There were 492 (52.2%) boys and 450 (47.8%) girls with 164 (33.3%) and 146 (32.4%) hospital mortality respectively.

Age distribution

Children acquire measles at a much earlier age in Africa. The mean age, in this series, was 18 months, in sharp contrast to the mean age of 3 - 4 years in children in the West. In our experience age plays a significant role in the severity of infection; the younger the children the more critical the complications. The highest mortality was among infants under 9 months whereas the lowest mortality was in children over 5 years of age.

Nutritional State

In the tropics, malnourished children are particularly susceptible to measles and become seriously ill. On the other hand, children become prone to malnutrition following an episode of measles, especially one with prolonged complications. Children referred to Mama Yemo Hospital were predominantly from the less fortunate segment of the population, some presenting with significant malnutrition. Kwashiorkor and marasmus were common. Five hundred and twenty-eight children (56%) weighed at or below the 3rd percentile weight for age suggesting a severely compromised nutritional state. There was 68% hospital mortality among children weighing less than the 3rd percentile versus 9% mortality for children weighing more than the 10th percentile weight for age.

Anemia

Parallel with a deficient nutritional state, children with measles complications presented significant anemia. The sources of anemia in Zairian children are malaria-induced anemia, iron deficiency and sickle cell anemia. Four hundred and four (43%) children presented hemoglobin values of less than 8 gm% indicating moderate to severe anemia. In this series, all children with a hemoglobin of less than 6 gm% died, some shortly after admission, whereas those with a hemoglobin of 11 gm% had only 10% hospital mortality. This study suggests that severe anemia, in the face of an overwhelming infection, plays a crucial role in a patient's death.

Other complications

The upper respiratory tract is the first site of measles virus invasion. With the spread of the virus to adjacent cells, the infection extends to the lower respiratory tract, paralyzing the cilia of the respiratory epithelial cells and rendering the patient susceptible to secondary bacterial pneumonitis. The virus will eventually enter the circulation and spread throughout the body producing multiple complications.

We observed 10 children with otitis, 112 with ulcerative stomatitis and 313 with croup. Laryngitis or laryngotracheitis are associated with respiratory distress and are indicative of an upper respiratory obstruction. Of particular interest were 7 children with pneumomediastinal and subcutaneous emphysema of the upper thorax, neck and face. These lesions are caused by a severe upper respiratory infection which perforates the trachea and releases the air into the mediastinum. Subcutaneous emphysema has a poor prognosis. All 7 children with this complication died within 1 - 3 days.

Lower respiratory measles complications manifest as bronchopneumonia, pneumonia, empyema, pneumothorax, atelectasis and pulmonary abscess. It is difficult to distinguish bronchopneumonia from interstitial pneumonitis caused by the measles virus. However from the clinical point of view, bronchopneumonia, due to secondary bacterial invasion, appears after the measles rash has disappeared. At this time, viral pneumonitis should have also subsided. In this series, there were 616 children with complications due to bronchopneumonia.

Persistant measles virus infection may cause subacute sclerosing panencephalitis (SSPE), a rare degenerative central nervous system disease, characterized by behavioral and intellectual deterioration and convulsions. Worldwide measles vaccination has greatly eliminated this complication. In 16 years experience in Zaire, the author observed only one case of SSPE. This is a slow developing complication taking, on an average, 10 years to become clinically manifest.

HIV-infection and measles

In 1987, a study was designed to determine whether HIV infection increases childhood measles mortality in Kinshasa. A total of 314 children with measles hospitalized at Mama Yemo Hospital were studied. Sixteen (5.1%) were seropositive with HIV-ELISA and Western blot tests. There was no apparent difference in the measles fatality rate between HIV seropositive and seronegative children. Among HIV seropositive children older than 9 months, there was a trend towards a lower mortality among vaccinated children (0/3) as compared to unvaccinated children (4/5) (5). This study suggests that there is no interaction between HIV infection and measles.

Prevention of measles

Socio-economic factors

CHALMERS first demonstrated the relationship between the severity of measles and the socio-economic status of the patient in 1908 (6). He observed that the nutritional state of the child was the most important adverse condition influencing both the severity and the outcome of the disease. Improving the diet reduces the incidence of severe measles, however this is a solw process involving improved home economic and agricultural education and must be viewed as a long term goal. Due to the loss of maternal antibodies, measles transmission usually occurs between 5 - 11 months of age. For this reason, the World Health Organization (WHO) recommends that children in developing countries be vaccinated at 9 months of age (7).

An epidemiological evaluation of measles in Kinshasa, Zaire in 1983 estimated that 50% of susceptible children would contract measles by age one year, 80% by age 3 years and 100% by age 5 years, with a vaccine efficacy of 85%. Following a 1977 vaccination campaign, 70,000 - 80,000 measles vaccines were administered each year to children 9 - 23 months of age; 90% of them being vaccinated between 9 - 11 months of age. Measles vaccination coverage among children 12 - 23 months of age increased from 37% in 1977 to 62% in 1983.

Despite this coverage, measles epidemics occurred every other year between 1980 and 1985 with 49,055 cases of measles and 3,277 deaths reported. The incidence rate ranged from 23.9 to 35.4 per 10,000 population without any noticeable trend. While the proportion of measles cases among children 12 - 23 months of age declined from 52% in 1976 to 26% in 1983, the proportion in younger and older children increased. Of 565 children under 9 month old hospitalized with measles in 1982, 85% were between 6 - 8 months of age.

It was estimated that 175,200 cases of measles occurred in Kinshasa in 1983 and 1984. During this same period, 16,982 cases and 1,339 deaths were reported. This represents 9.7% of the estimated number of cases. Approximately 286,900 cases of measles would have occured during this period if vaccine had not been given.

A change in the epidemiology of measles would be expected after a vaccination program. There are several factors which influence herd immunity; the pattern of population mixing, the number and distribution of susceptibles, and the rate of contact between the infected and the susceptible (8). It has been estimated that 98% of each birth cohort must be vaccinated by 12 months of age to eliminate measles from a population (9). However, this goal is not yet attainable in developing countries as measles control has not been achieved (10). An intermediate level of vaccination coverage could also reduce the circulation of the virus in a community and thereby reduce measles (11).

Efforts to control measles in Kinshasa have been complicated by the elevated proportion of cases in infants under 9 months and failure to obtain the protective effects of herd immunity. Its continued significance is reflected in the estimated 87,600 cases per year inspite of a vaccination coverage of 60% and a reduction in the incidence rate by 39%. Three factors are responsible for this effect; the large proportion of measles cases in children under age 9 months which constitutes an important reservoir of virus, the non-uniform vaccination coverage leaves areas of susceptible children open to continued transmission and crowding and mobility within the urban population which constitutes a high risk for an unvaccinated child.

Encouraging results have been reported when vaccinating children 4 - 6 months of age with the Edmonston-Zagreb human diploid cell measles vaccine (12). With an effective vaccination of children under 9 months of age in Kinshasa, 18% of the cases could be prevented. Increasing urbanization in Africa has increased the spread of measles (13), and therefore, vaccinating younger infants can contribute significantly to the control of the disease throughout Africa. Edmonston-Zagreb vaccination at 6 months of age began in Kinshasa in September, 1989 and continues to the present with excellent results.

Severe measles have been reported in symptomatic HIV-infected children. Since there have been no serious or unusual reactions to the Measles-Mumps and Rubella vaccine (MMR), it is recommended for HIV-infected children. To save children with perinatally acquired HIV infection from early acquisition of measles and to evaluate the safety and efficacy of Edmonston-Zagreb (EZ) vaccine, 187 children of HIV-seropositive mothers and 171 children of HIV-seronegative mothers at Mama Yemo Hospital in Kinshasa

received high-dose (10^5 PFU/dose) EZ vaccine at 6 months of age and were seen at 7 and 14 days post vaccination. Following vaccination, there was no difference between the children of HIV+ and HIV− women in cough (23% vs 22%), fever (10% vs 11%), diarrhea (24% vs 18%) or rash (1% vs 0%). No serious complications or deaths were attributable to the vaccine. Seroconversion was assessed by EIA in pre- and 3 month post vaccination sera which revealed that seroconversion rates were similar in children of HIV-seropositive (87%) and HIV-seronegative (90%) women. However, seroconversion rates (76% vs 89%) and mean titres were lower in a sample of 21 children known to be HIV-infected than in children not infected by HIV. In the HIV-infected children (some determined by viral culture), lower T4 lymphocyte levels were associated with lower seroconversion rates and lower mean antibody titres ($P < 0.05$). However, there have been no cases of measles after vaccination. It was concluded that EZ vaccine was safe and effective in HIV-infected children (14). Similar results were reported from a study in Kigali, Rwanda (15).

Summary

Measles is an acute, infectious disease with worldwide epidemics. Although its case fatality rate has decreased, it remains an important cause of childhood morbidity and mortality in Africa. Inspite of tremendous progress in the enlarged programme of immunization in Zaire, vaccination coverage in the urban areas remains below 80%. In a city like Kinshasa, with 3.5 million people, a large number of children continue to acquire measles and suffer serious complications. This study shows that younger age at the onset of infection, malnutrition and anemia are major contributing factors to the mortality of these children. In this series, 34% of the infants acquired measles before age 9 months, therefore, with the administration of EZ vaccine at 6 months of age, the majority of these children can be saved.

Key words

Measles infection, complications, age of infection, risks, vaccination against measles.

Zusammenfassung

Spektrum der Masernkomplikationen bei 942 Kindern in Kinshasa, Zaire

Masern ist eine akute, weltweit verbreitete Infektionskrankheit. Obwohl die Mortalität dieser Erkrankung auch in Afrika in der letzten Zeit stark zurückgegangen ist, bleibt sie eine wichtige Ursache für Krankheit und Tod bei afrikanischen Kindern. Trotz eines beträchtlichen Fortschritts beim Expanded Programme on Immunization in Zaire, liegt die Durchimpfungsrate bei Masern in den Stadtgebieten jedoch noch unter 80%. In Kinshasa, einer Stadt mit 3,5 Mio. Einwohnern, erkranken daher nach wie vor viele Kinder an Masern. Diese Studie zeigt, daß frühes Erkrankungsalter, Malnutrition und Anämie wichtige Risikofaktoren hinsichtlich Komplikationen und Mortalität sind. Etwa ein Drittel (34%) der Säuglinge werden vor dem Erreichen des 9. Lebensmonats infiziert. Durch die Verarbeitung der Edmonston-Zagreb-Vakzine mit 6 Monaten könnte die Mehrzahl dieser Kinder geschützt werden.

Schlüsselwörter

Maserninfektion, Komplikationen, Infektionsalter, Risikofaktoren, Masernimpfung.

References

1. Committee on Infectious Diseases, American Academy of Pediatrics (1991):
Report of the Committee on Infectious Diseases Twenty-first Edition, 308-323.

2. World Health Organization (1979):
Expanded Programme on Immunization.
Wkly. Epidemiol. Rec. 54, 337-339.

3. SCRIMSHAW, N. S., TALOR, C. E., GORDON, J. E. (1986):
International Conference of Nutrition and Infection, WHO.
Mongram. Ser. 57, Geneva.

4. DAVACHI, F., BONGO, L., MUTOMBO, M., MOORE, M. (1989):
The Impact of Oral Rehydration Therapy on the Treatment of Diarrheal Diseases in Kinshasa, Zaire.
Mitt. Österr. Ges. Tropenmed. Parasitol. 11, 197-201.

5. DAVACHI, F. (1991):
Review of epidemiology of HIV-1 infection in Children:
Zaire experience. Biomedical and Social Developments in AIDS and Associated Tumors.
Antibiot. Chemother. Giraldo, G., Salvatore, M., Piazza, M., Zarrilli, D., Beth-Giraldo, E. (Ed.).
Basel, Karger, Vol. 43, 14-36.

6. CHALMERS, A. K. (1930):
The Health of Glasgow 1818 - 1925.
Bell and Bain, Glasgow, 340.

7. World Health Organization (1979):
The optimal age for measles immunization.
Wkly. Epidemiol. Rec. 54, 337-339.

8. FOX, J. P., ELVEBACK, L., SCOTT, W. et al. (1971):
Herd immunity: basic concept and relevance to public health immunization practices.
Am. J. Epidemiol. 94, 179-189.

9. HETHCOTE, H. W. (1983):
Measles and rubella in the United States.
Am. J. Epidemiol. 117, 2-13.

10. MITCHELL, C. D., BALFOUR, H. W. jr. (1985):
Measles control: so near and yet so far.
Prog. Med. Virol. 31, 1-41.

11. BLACK, F. L. (1982):
The role of herd immunity in control of measles.
Yale J. Biol. Med. 55, 351-360.

12. WHITTLE, H. C., ROWLAND, M. G. M. (1984):
Immunization of 4 - 6 month old Gambian infants with Edmonston-Zagreb measles vaccine.
Lancet 2, 834-837.

13. LEONING, W. E. K., COOVADIA, H. M. (1983):
Age-specific occurrence rates of urban, peri-urban and rural environments: implications for time of vaccination.
Lancet 2, 324-326.

14. MANDALA, K., MAYALA, B., CUTTS, F., BROWN, C., DAVACHI, F., OXTOBY, M., ST. LOUIS, M. E. (1991):
Edmonston-Zagreb measles vaccination in HIV-infected children.
Seventh International Conference on AIDS, Florence.
Abstr. WB 2040, 192.

15. DABIS, F., MSELLATI, P., LEPAGE, P., HITIMANA, D. G., De BOUVER, J. L., Van de PERRE, P. (1991):
Vaccination of HIV-infected infants with the Edmonston-Zagreb strain of measles vaccine:
A cohort study in Kigali, Rwanda.
Seventh International Conference on AIDS, Florence.
Abstr. WC 3274, 364.

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