The Role of Immunization Status and Vitamin An in Outbreak of Measles among Patients Admitted in Al-Yarmouk Teaching Hospital October 2010-April 2011

Rafid .A. Alkhuzuie (MBcHB)[1]

Abstract

Background: Measles is a highly contagious viral illness; it is endemic in Iraq and worldwide developing countries. Measles is carrying many complications with morbidity and mortality.
Objective: To determine the role of previous immunization agonist measles and the use of the vitamin A to decrease the mortality and morbidity of disease.
Patients & Methods: A cross-sectional study was conducted at Al-Yarmouk Teaching Hospital included 632 patients (318 males at age 15-42 years & 314 females at age 17-42 years) whose admitted to hospital for the period between October 2010 to April 2011. Diagnosis was according to the clinical manifestation and confirmed by ELISA for detected antibody (IgM & IgG).
Results: The study shows the role of immunization against measles. It is very important to control out break and decrease mortality and morbidity of the disease, therefor must be re immunization against measles in booster dose in the 18th & 30th years old, and in premarital program in Iraq to decrease the outbreak in pregnants women's to decrease mortality and morbidity among mothers and babies.
Conclusion: The use of vitamin A in treatment of measles patient to decrease mortality and morbidity of disease, and must be supplement to child and scholar in outbreak season of disease.

[1]Department of Medicine - College of Medicine - Al-Mustansiriya University – Baghdad-Iraq.

Introduction

Measles is a highly contagious viral illness characterized by fever, Malaise, rash, cough, coryza, and conjunctivitis. There are unknown measles virus reservoirs outside of humans [1]. Parmyxovirus infection is endemic world-wide. It is probably the most infectious of all microbial agents. Before immunization campaigns, measles occurred in almost 100% of children. Maternal antibody gives protection for the first 6 months of life. In temperate areas there is a natural epidemic cycle every 2-3 years, less obvious in the tropics. With live attenuated vaccine, the condition is potentially completely controllable by immunization The WHO has set the objective of eradicating measles by the year 2010 as part of its expanded programmer of immunization. Incomplete vaccination of only 70-80% of the population may lead to outbreaks in older children and adults, in whom complications are more frequent. This necessitates to repeat mass immunization campaigns or second dosing of vaccine in an older age group. Natural illness produces life-long immunity [2].

Measles is a serious disease in the malnourished, vitamin-deficient or immuno compromised. Mortality clustering at the extremes of age is 1:1000 in developed countries, compared to up to 1:4 in developing countries. Death usually results from bacterial super infection such as pneumonia, diarrheal disease or cancrum oris [3].

Measles occurs worldwide; control efforts have substantially altered the global distribution [4].

Measles incidence has decreased substantially in regions where vaccination has been instituted; measles in the developing world has been attributed to low vaccination rates [5].

In developed countries during the prevaccine era, ≥90 percent of children acquired measles by age 15 years [6-8]. Following implementation of routine childhood vaccination at age 12 to 15 months, the age of peak measles incidence during epidemics in the United States shifted to six months of age. This is approximately the time at which transplacentally acquired maternal antibodies are no longer present if the mother has vaccine-induced immunity [9-11].

It is a notifiable disease in Iraq. This means that, by law, cases are required to be reported to a health officer or local government authority. WHO, Iraqi MOH. but in Iraq after march 2003 violence of occupied, and boots of terrorism, displacement and internal migration led to interrupted and delayed in Iraqi immunization program and this led to incomplete vaccination of about 50-70% of population which may lead to outbreak in older children.

In our study we analyzed the measles' patients who admitted to Al-Yarmouk Teaching Hospital in Baghdad during the outbreak of measles' in 2010-2011 according to history, clinical presentation, complication of measles and search for history of immunization and the difference in clinical course between immunized and non immunized patients and study the effect of vitamin A in different doses on natural history of disease.

The study was conducted aiming to identify the relationship between history of immunization against measles and the natural history of disease and to study the relationship between different doses of vitamin A and natural course of measles disease.

Patient and Methods

This cross-sectional study was conducted in Al-Yarmok Teaching Hospital. The study included 632 patients (318 males) & (314 females) their age 15-42 years whose admitted to this hospital in a period between October 2010 to April 2011 all of them diagnosed as measles disease according to clinical manifestation and conformed by ELISA for detected antibody (IgM ,IgG) against measles. The patients are divided into two groups according history of immunization (475 immunized &157 no immunized).as shown in table 1.

Table (1): The measles patients admitted in Al Yarmok Teaching Hospital between October 2010 to April 2011 according to immunization status.

History of immunization	No	%	Male		Female	
			No	%	No	%
Immunized	475	75.1	222	35.1	253	40.0
Non immunized	157	24.9	96	15.1	61	9.7
Total	632		318		314	

Patients was also subdivided into three groups according to the management of disease with using vitamin A , first group treated without vitamin A (242 patient),and second group with 400 I u vitamin A (219 patient),while third group treated with 800 IU vitamin A (171 patient) to evaluate the effect of vitamin A on the course of the disease.

The study proposal was approved by ethical committee at the faculty of medicine, Al Mustansiriya University and Ethical Committee of Al-Yarmouk Teaching Hospital.

Results

The study showed all patients who were infected with measles after more than 10 years of last immunization. Despite high community vaccination coverage, measles outbreaks can occur among under or non-vaccinated children [12,13].

There are various types of clinical presentation of measles, Classical measles infection in immunocompetent patients or Modified measles in patients with preexisting, but incompletely protective, anti-measles antibody, or severe measles, or complicated measles including secondary infection, giant cell pneumonia, and measles inclusion body encephalitis. [14].

All patients who were infected with measles had history of fever (632 patientss -100%) and defeveranse with appearance of rash(632 patients 100%), nausea (517 patients81%), vomiting(427patients 67,5%), conjunctivitis (607 patients 96%) ,abdominal pain (310patients 49%), diarrhea12%), cough(598 patients 94.6%), productive cough (416 patients 65.8%, dry), kopliks spot(629 patients 99.5%), death 3patients 0.4%). and this result is compatible with other studies of measles in other world (table2).

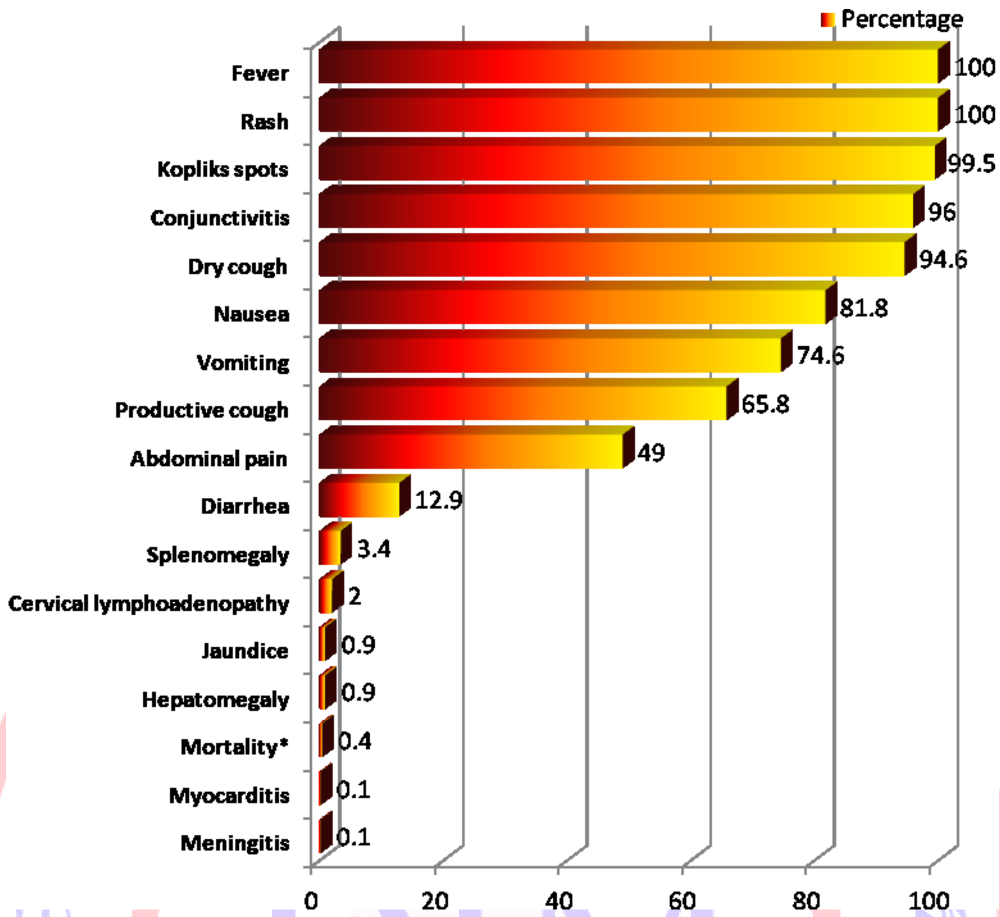

Figure (1): The clinical symptoms & signs of measles whose admitted in Al-Yarmok teaching hospital (October 2010-april 2011) (*2 females in second & third trimester & one diabetic male with sever pneumonia).

All patients presented with prodromal phase which is defined by the appearance of symptoms which typically include fever, malaise, and anorexia, followed by conjunctivitis, coryza, and cough. The severity of conjunctivitis is variable and may also be accompanied by lacrimation or photophobia [15].

The respiratory symptoms are due to mucosal inflammation from viral infection of epithelial cells. Fever is typically present; the pattern may be variable. Various fever patterns have been described; fever as high as 40ºC can occur. The prodrome usually lasts for two to three days but may persist for as long as eight days [16].

This study shows the shortness duration of prodrome stage in patients who were previously vaccinated or under vaccinated (table 3).

Table (3): The duration of fever and the prodrome history according to immunization state.

Duration	**Total**		**Immunized**		**Non immunized**	
	No	**%**	**No**	**%**	**No**	**%**
2nd Day	198	31.1	182	38.0	16	10.1
3id	105	16.7	62	13.0	43	27.4
4th	177	28.0	118	24.8	59	37.6
5th	152	24.0	113	23.8	39	24.9
Total	**632**		**475**		**157**	

Clinical improvement typically ensues within 48 hours of the appearance of the rash. After three to four days, the rash darkens to a brownish color and begins to fade, followed by fine desquamation. The rash usually lasts six to seven days.

There are some variation in clinical course of disease in patients who were previously immunized and treated with 800 I u of vitamin A for 21 days, there was a rapid improvement and less complication and less mortality as shown in(table 4,5) and fig 1,2.

The study shows the role of previous history of immunization to rapid desquamation and fading of rash than non immunized, and there was no significant difference between male and female in clinical course of disease.

The use of vitamin A in treated patients who were infected with measles show the rapid fading of rash and decrease incidences of complications. There was significant improvement in use 800 I u of vitamin A regarding use of 400 I u as show in table (4,5) and fig 1,2.

Table (4): The Course & duration of appearance rash & fading according to immunization history of patient of measles whose admitted in Alyarmouk teaching hospital(October 2010-april 2012).

Course	Total	immunized	Non immunized
5th day	92	92	No
6th day	87	74	13
7th day	105	63	42
8th day	168	145	23
9th day	87	59	28
10th day	93	42	51

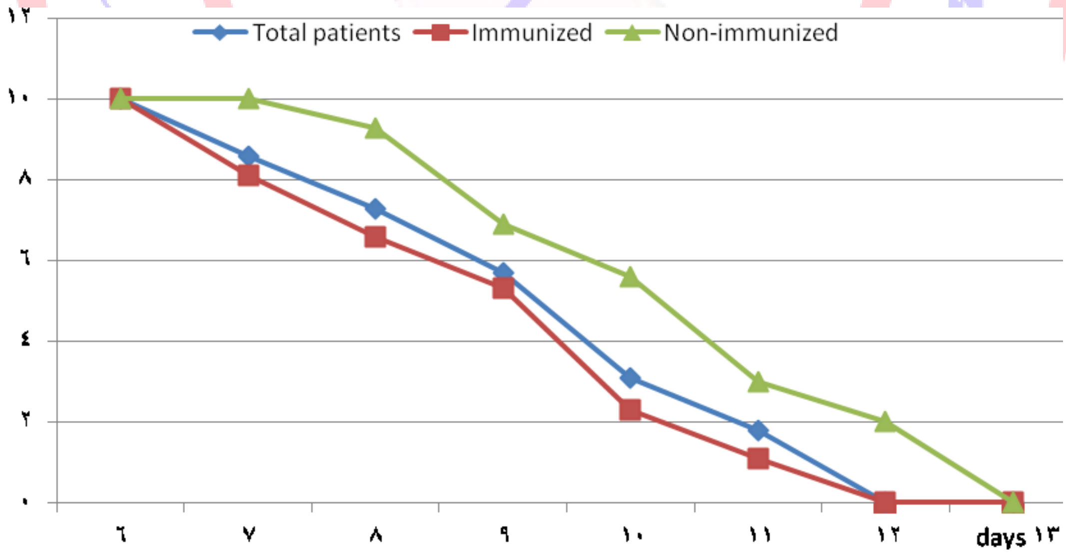

Figure (2): The Course & duration of appearance rash & fading according to immunization history of patient of measles whose admitted in Alyrmok teaching hospital(October 2010-april 2012)(1-total patients,2-patients had history of immunization,3-patients non immunized).

Table (5) group of patients of measles according sex & immunity status & treatment with vitamin A in different dose (400 Iu -80 I u for 21 days) whose admitted in Alyarmouk Teaching Hospital(October 2010-april 2012).

Table (5): The patient of measles according sex & immunity status & treatment with vitamin A in different doses (400 Iu -80 I u for 21 days) whose admitted in Alyarmouk Teaching Hospital(October 2010-april 2012).

Use of Vit. A	Total	Males	Females	Immunized	Non-Immunized
Without Vit. A	242(38.3%)	128(40.3%)	114(36.3)	210(44.2%)	32(20.4%)
Vit. A 400i u	219(34.7)	137(43.1)	82(26.1)	157(33.1%)	62(39.5%)
Vit. A 800 iu	171(27.1)	53(16.7)	118(37.6)	108(22.8%)	63(40.1%)

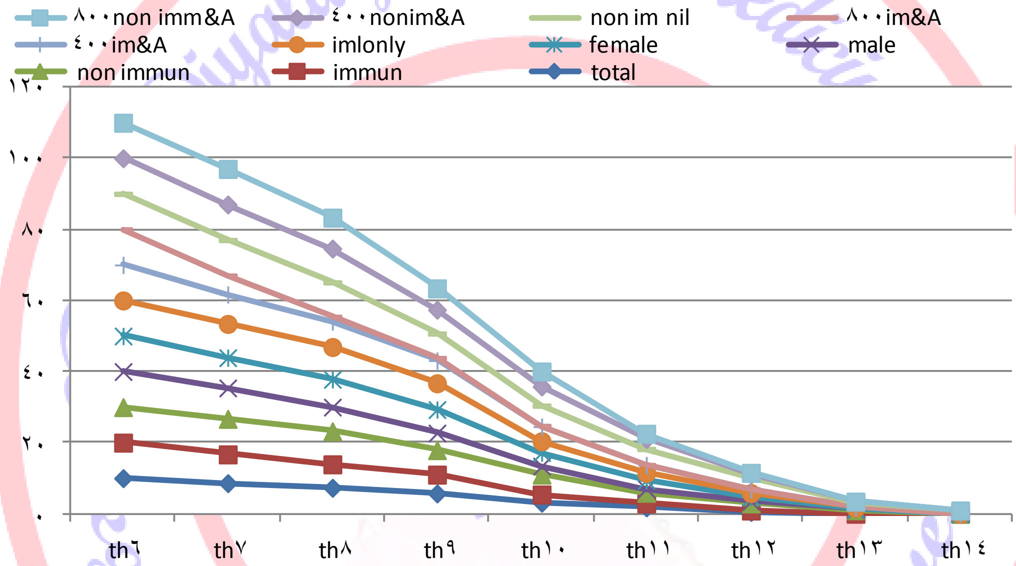

Figure (3): The group of patients of measles according to the(sex, immunized states & treatment with vitamin A in different dose (400 I u-80 I u for 21 days) and course of fading rash whose admitted in Alyarmouk Teaching Hospital(October 2010-april 2012).

The complication of measles common in non immunized patient and in pregnant women and immuno compromised patient such as diabetic patient in this study, there were three patients died and all were non immunized and one of them had history of diabetes and one she was pregnant and all admitted to hospital in late stage as show in table -6- and this finding agrees with other studies.

Higher measles complication rates have been observed in developing countries [17-18].

Complication rates associated with measles infection are variable. In the 1990 United States outbreak, the following complication rates were observed [19]:

Overall complication rate — 22.7 percent
Diarrhea — 9.4 percent
Otitis media — 6.6 percent Pneumonia — 6.5 percent Encephalitis — 0.1 percent
Death — 0.3 percent

And this results in comparison with our study from view point of complication as shown in table 6 the pneumonia and diarrhea were more in the Alyarmouk Hospital and the mortality is the same as in USA outbreak (table 6).

Table (6): show the complication of measles according to the immunization status of patient whose admitted in Alyarmouk teaching hospital (October 2010-april 2011).

Complication of measles	Total	immunized	Non immunized
Diarrhea	82(12.9%)	27(5.9%)	55(35%)
Otitis media	43(6.8%)	3(0.6%)	40(25.4%)
Pneumonia	116(18.3%)	33(5%)	83(52%)
Encephalitis	3(0.4%)	-	3(1.9%)
Mortality	3(0.4%)	-	3(1.9%)
Total	632	457	157

The winter in Iraq is season of outbreak of measles and its the season of school study , January and February are most months of outbreak in the Iraq and Baghdad as shown in table -6.

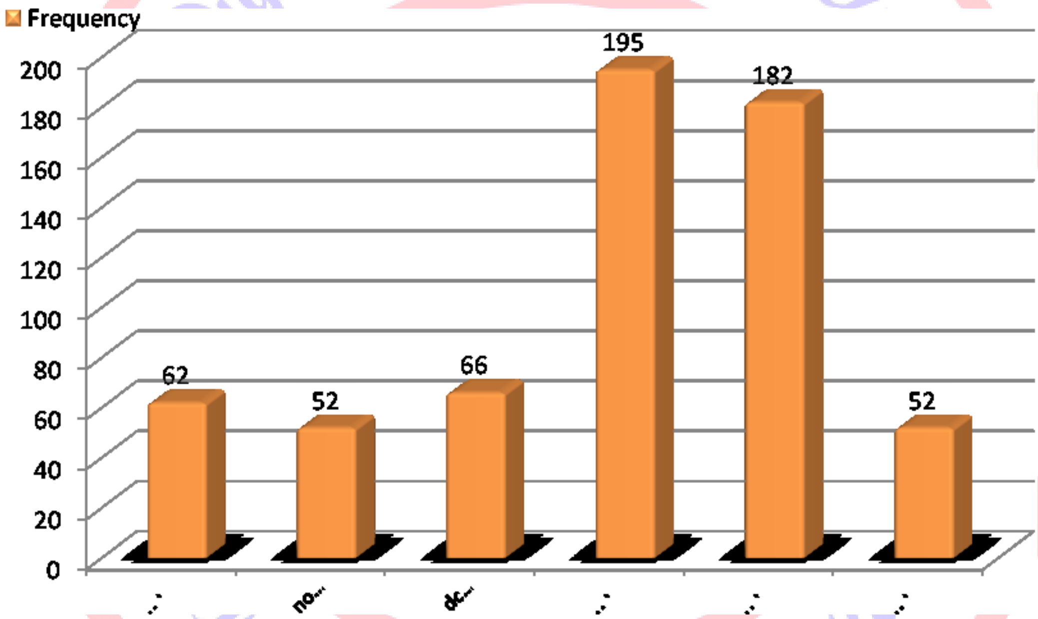

Figure (4): The presentation of patient of measles whose admitted in Al-Yarmok Teaching Hospital (October 2010-april 2012) according to the month of outbreak

All ages were susceptible to the infection with measles, but more ages were in childhood and youth as show in table -7

Table (7): The presentation of patient of measles who were admitted in Al-Yarmouk Teaching Hospital (October 2010-april 2012) according to the age of presentation.

Age	Total	Male	Female
11-20 years	164(30.0%)	40(12.6%)	124(39.5%)
21-30 years	347(55.0%)	208(64.8%)	139(44.3%)
31-40 years	115(18.2%)	67(21.0%)	48(15.3%)
41-50 years	6(0.8%)	3(0.9%)	3(0.9%)
Total	632	318	314

In this study the outbreaks in adult age group is more in age between 21-30 years old as shown in table -8

Discussion

All patients presented with prodromal phase which is defined by the appearance of symptoms which typically include fever, malaise, and anorexia, followed by conjunctivitis, coryza, and cough. The severity of conjunctivitis is variable and may also be accompanied by lacrimation or photophobia [20].

The respiratory symptoms are due to mucosal inflammation from viral infection of epithelial cells. Fever is typically present; the pattern may be variable. Various fever patterns have been described; fever as high as 40ºC can occur. The prodrome usually lasts for two to three days but may persist for as long as eight days [21].

All patients included In this study were presented with prodromal symptom (fever 100%, rash100%, dry cough96,5%, Kopliks spots 99,5%) but shortness the prodromal course and fading of rash in previous immunized or incomplete immunization patient.s

The study shows the role of previous history of immunization to rapid desquamation and fading of rash than non immunized, and there was no significant difference between male and female in clinical course of disease.

The study showed all patients who were infected with measles after more than 10 years of last immunization. The role of previous immunization decrease morbidity mortality and modified the course of disease to sub acute presentation.

As shown in United State from 1989 to 1991, a major resurgence occurred, affecting primarily unvaccinated preschoolers. This measles resurgence resulted in 55,000 cases and 130 deaths [7]. And prompted the recommendation that a second dose of measles vaccine be given to preschoolers in a mass vaccination campaign that led to the effective elimination in the United States of endemic transmission of the measles virus [22,8].

From January to June 2008, 131 cases of measles were reported to the CDC [23,11]. Although 90% of those 131 cases were associated with importation of the virus to the United States from overseas, 91% of those affected were unvaccinated or had unknown or undocumented vaccination status. At least 47% of the 131 measles infections were in school-aged children whose parents chose not to have them vaccinated [24,11].

There are some significant variation in clinical course of disease in patients who were previously immunized and treated with 800 I u of vitamin A for 21 days, there was a rapid improvement and less complication and less mortality as shown in(table 4,5) and fig 1,2.

The use of vitamin A in treated patients who were infected with measles (regarding immunized or non-immunized) show the rapid fading of rash and decrease incidences of complications. There was significant improvement in use 800 I u of vitamin A regarding use of 400 I u. And the improvement rapid in previous immunized and use of 800 I u vitamin A in modifiable course of disease and decrease mortality and morbidity.

The complication of measles common in non immunized patient and in pregnant women and immuno compromised patient such as diabetic patient in this study, there were three patients died and all were non immunized and one of them had history of diabetes and one she was pregnant and all admitted to hospital in late stage as show in table -6- and this finding agree with other studies.

Unvaccinated males and females are equally susceptible to infection by the measles virus. Excess mortality following acute measles has been observed among females at all ages, but it is most marked in adolescents and young adults. Excessive non–measles-related mortality has also been observed among female recipients of high-titer measles vaccines in Senegal, Guinea Bissau, and Haiti [25,18].

Although measles is historically a disease of childhood, infection can occur in unvaccinated or partially vaccinated individuals of any age or in those with compromised immunity.

In this study the outbreaks in adult age group of the 632 cases whose admitted to Alyarmouk Hospital in period between October 2010 –April 2011 is (30%)involved persons aged 11-20years,(55%) involved adults aged 21-30 years old ,(6%) involved adult older than 40 years old as shown in table -8

of the 66 cases of measles reported in the United States in 2005, 7 (10.6%) involved infants, 4 (6.1%) involved children aged 1-4 years, 33 (50%) involved persons aged 5-19 years, 7 (10.6%) involved adults aged 20-34 years, and 15 (22.7%) involved adults older than 35 years [26,10].

Among the 118 US patients reported to have measles between January 1 and May 20, 2011, age ranged from 3 months to 68 years [12]. More than half were younger than 20 years: 18 (15%) were younger than 12 months, 24 (20%) were 1-4 years old, 23 (19%) were 5-19 years old, and 53 (45%) were 20 years of age or older [27].

Conclusion

The role of immunization aganist measles is very important role to decrease out break and decrease mortality and morbidity of the disease, therefor must be re immunization aganist measles in booster dose in the 18th&30th years old ,and in premarital program in Iraq ,and planning a pregnancy programmer , she should make sure that she has a measles vaccination unless she has had the disease in the past ,all these roles to decrease the outbreak in pregnant women's to decrease mortality and morbidity. The use of vitamin A in treatment of measles patient to decrease mortality and morbidity of disease, and must be supplement to child and scholar in outbreak season of disease.

References

[1] Black, FL. Measles. In: Viral infections in humans: Epidemiology and control, Evans, AS, Kaslow, RA (Eds), Plenum Publishing, New York 1997. p.507.

[2] Davidson's principles and practice of medicine, 20th edition, 2006.p300.

[3] Davidson's principles and practice of medicine, 20th edition, 2006.p301.

[4]WHO-recommended surveillance standard of measles. http://www.who.int/immunization_monitoring/diseases/measles_surveillance/en/index.html (Accessed on November 08, 2010).

[5] Muscat M, Bang H, Wohlfahrt J, *et al.* Measles in Europe: an epidemiological assessment. Lancet 2009; 373:383.

[6] Global measles mortality reduction and regional elimination: a status report. J Infect Dis 2003; 187(Suppl 1):S1.

[7] Parker AA, Staggs W, Dayan GH, et al. Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. N Engl J Med 2006; 355:447.

[8] Markowitz, LE, Katz, SL. Vaccines, Plotkin, SA, Mortimer, EA (Eds), WB Saunders, Philadelphia 1994. p.229.

[9] Arya LS, Taana I, Tahiri C, et al. Spectrum of complications of measles in Afghanistan: a study of 784 cases. J Trop Med Hyg 1987; 90:117.

[10] Papania M, Baughman AL, Lee S, et al. Increased susceptibility to measles in infants in the United States. Pediatrics 1999; 104:e59.

[11] Maldonado YA, Lawrence EC, DeHovitz R, et al. Early loss of passive measles antibody in infants of mothers with vaccine-induced immunity. Pediatrics 1995; 96:447.

[12] Markowitz LE, Albrecht P, Rhodes P, et al. Changing levels of measles antibody titers in women and children in the United States: impact on response to vaccination. Kaiser Permanente Measles Vaccine Trial Team. Pediatrics 1996; 97:53.

[13] Beckford AP, Kaschula RO, Stephen C. Factors associated with fatal cases of measles. A retrospective autopsy study. S Afr Med J 1985; 68:858.

[14] Clements, CJ, Cutts, FT. The epidemiology of measles: Thirty years of vaccination. In: Measles Virus, ter Meulen, V, Billeter, MA (Eds), Springer Verlag, Germany 1995. p.13.

[15] Hauspie RC, Pagezy H. Longitudinal study of growth of African babies: an analysis of seasonal variations in the average growth rate and the effects of infectious diseases on individual and average growth patterns. Acta Paediatr Scand Suppl 1989; 350:37.

[16] Schaumberg DA, O'Connor J, Semba RD. Risk factors for xerophthalmia in the Republic of Kiribati. Eur J Clin Nutr 1996; 50:761.

[17] Kagame K, Schwab L. Childhood blindness: dateline Africa. Ophthalmic Surg 1989; 20:128.

[18] CHRISTENSEN PE, SCHMIDT H, BANG HO, *et al*. An epidemic of measles in southern Greenland, 1951; measles in virgin soil. III. Measles and tuberculosis. Acta Med Scand 1953; 144:450.

[19] Centers for Disease Control (CDC). Measles--United States, 1990. MMWR Morb Mortal Wkly Rep 1991; 40:369.

[20] 20-cecil textbook of medicine 23th edition.2006: page 372.

[21] Muscat M, Bang H, Wohlfahrt J, *et al*. Measles in Europe: an epidemiological assessment. Lancet 2009; 373:383.

[22] Orenstein WA, Papania MJ, Wharton ME. Measles elimination in the United States. J Infect Dis 2004; 189 Suppl 1:S1.

[23] Centers for Disease Control and Prevention (CDC). Epidemiology of measles--United States, 2001-2003. MMWR Morb Mortal Wkly Rep 2004; 53:713.

[24] Centers for Disease Control and Prevention (CDC). Measles outbreak in a boarding school--Pennsylvania, 2003. MMWR Morb Mortal Wkly Rep 2004; 53:306.

[25] Parker AA, Staggs W, Dayan GH, *et al.* Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. N Engl J Med 2006; 355:447.