

GERMAN MEASLES (RUBELLA): AN EXPERIMENTAL STUDY *

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Investigations as to the nature of German measles are totally lacking. This is probably due to the fact that this disease is mild and so rarely encountered in hospital wards. The only opportunity afforded for a systematic study from a laboratory standpoint is the occurrence of an epidemic in an institution where children are housed in large numbers. An occasion of this kind—an epidemic attacking fifty or more children in an infant asylum—led to the present investigation, which includes a bacteriological study of the blood, inoculations of blood into monkeys with the object of producing the disease, and a cellular examination of the blood during the period of incubation of the disease.

In four instances the blood was obtained for bacteriological examination. In three of the cases the rash had been present for less than twenty-four hours, and in the fourth for about thirty-six hours; in two the temperature of the child was above the average, that is to say, between 102 and 103 F. So that it may be said that I was able to obtain the blood in severe cases as well as at the very onset of the disease. The latter circumstance would appear of particular importance when we remember that the virus of measles has been found with regularity only in the early period following the stage of exanthem. Numerous cultures made on mediums containing serum and hemoglobin showed no growth whatsoever. Other cultures were made by Dr. Zingher, whom I wish to thank in this connection, according to the method developed by Noguchi for the cultivation of the spirochete of syphilis; the medium contains two parts of salt-free agar, one part of ascitic fluid, fresh kidney tissue, and is covered with liquid petrolatum to insure anaerobic conditions. It was not found possible to obtain any growth from the inoculation of the blood in our cases. The tubes were incubated for some weeks.

An attempt was made to produce this disease in monkeys. Four *Macacus rhesus* monkeys were inoculated with blood obtained from four different cases. In two instances the blood was from the same source as that used for purposes of cultivation. In all cases the rash had existed less than twenty-four hours; in most the temperature was high when the blood was withdrawn. Following is a summary of the protocols:

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CASE 1.—Feb. 7, 1913. Child which developed rash during the night; temperature normal.

Three c.c. of citrated blood inoculated intraperitoneally into Monkey 1. The temperature was followed for four weeks. Although it frequently rose to 103 or over, there was no sudden rise or fall.

CASE 2.—March 3, 1913. Rash seen on child for first time this morning; temperature 101 F.

Five c.c. of blood obtained from right jugular vein, and inoculated intraperitoneally a few hours later into Monkey 2. The course of the temperature is shown in the accompanying chart. It will be noticed that there is a definite rise occurring on the nineteenth day after inoculation and lasting for about forty-eight hours.

CASE 3.—March 6, 1913. Child with rash for past twelve hours; temperature 101 F.

Four c.c. inoculated intraperitoneally into Monkey 3. For three weeks temperature varied between 101.1 and 102.3 F. No rash.

CASE 4.—March 8, 1913. Temperature of patient 101.3 F. when blood was withdrawn. Rash had existed about twelve hours.

Eight c.c. of blood inoculated intraperitoneally into Monkey 4; cultures also taken. For the next three weeks the temperature ranged between 101.3 and 103 F. No exanthem.

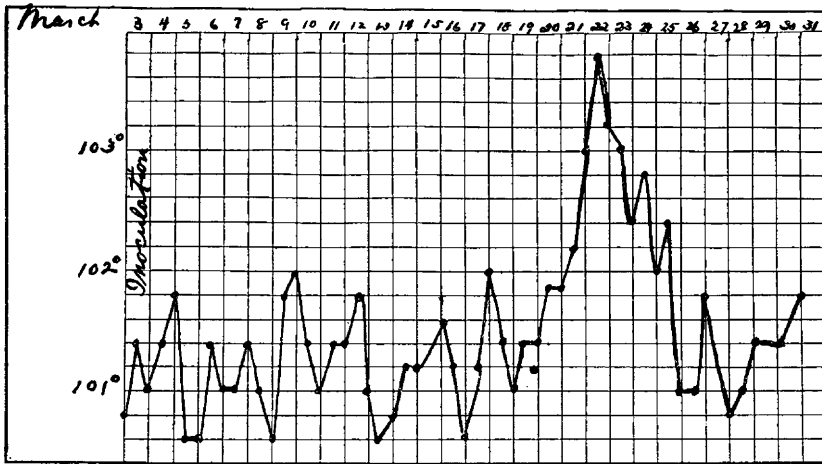


Chart of temperature of monkey (Case 2) inoculated with blood from early case of rubella.

It will be seen that in each instance from 3 to 8 c.c. of blood was inoculated intraperitoneally. In no case did the rash develop. In view of the fact, however, that this appears so rarely and faintly in experimental measles, it was hardly anticipated that we would succeed in producing a rash experimentally in rubella. Our attention, therefore, was closely directed to the course of the temperature. In only one instance was there a rise in temperature, following a considerable period of incubation (see chart). In the others there was no such rise. In view of the fact that the temperature of monkeys is somewhat unstable, too great significance should not be accorded this rise of temperature. In general,

it may be stated that there is danger in placing too great reliance on a rise of temperature as the sole criterion of the production of a disease in monkeys. If the rise is sudden and the period of incubation carefully controlled, however, this method of study is of value.

Although there have been no cultures whatsoever made of the blood in German measles and no inoculation experiments on monkeys, there have been, as might be supposed, some previous investigations as to the number and type of leukocytes in this disease. Hildebrandt and Thomas¹ found a leukopenia at the onset of the exanthem, and an increase of the lymphocytes, as well as an increase in the large Türk cells. Michaels,² as the result of an investigation of eighty cases of rubella, also found a leukopenia in the majority of cases. These studies, however, were carried out after the rash had appeared; and the only study which has taken cognizance of the blood in the earlier stages of the disease was one by Plantenga.³ Our investigation concerned itself entirely with the blood during the incubation period. This was very easily carried out in the institution; for as soon as rubella developed, blood-smears were taken daily from the healthy children in the ward and were laid aside for examination in the event of some of these children developing the disease. In this way, in numerous instances, consecutive blood examinations were carried out before and up to the appearance of the rash. The following data show the results of these examinations, which were kindly carried out for me by Dr. Jerome Zuckerman:

1. H. B., 2 years old. Exanthem May 2.						
Per Cent. of	April 28	April 29	April 30	May 2		
Polyn.	55	66	53	50		
Lymph.	20	22	35	35		
L. mono.	11	5	8	10		
Eosinoph.	3	4	4	4		
Basoph.	1	3	0	1		
2. L. S., 3½ years old. Exanthem May 2.						
Per Cent. of	April 28	April 29	April 30	May 2		
Polyn.	59	51	54	41		
Lymph.	28	33	36	45		
L. Mono.	5	9	9	9		
Eosinoph.	8	7	1	4		
Basoph.	1		
3. S. S., 5 years old. Exanthem May 2.						
Per Cent. of	April 28	April 29	April 30	May 2	May 12	
Polyn.	49	46	50	31	50	
Lymph.	35	39	40	55	34	
L. Mono. ...	7	5	4	5	8	
Eosinoph. ..	5	10	5	6	4	
Basoph.	4	0	1	3	4	

1. Hildebrandt and Thomas: *Ztschr. f. klin. Med.*, 1906, lix, 444.

2. Michaels, M.: *Arch. Pediat.*, 1908, xxv, 598.

3. Plantenga: *Arch. de méd. d. enf.*, 1903, vi, No. 3.

4. M. G., 2 years old. Exanthem	June 14.			
Per Cent. of	June 11	June 13	June 14	June 19
Polyn.	43	33	34	53
Lymph.	46	57	56	42
L. Mono.	7	7	7	5
Eosinoph.	4	3	3	
5. G. S., 2 years od. Exanthem	June 19.			
Per Cent. of	June 14	June 18	June 19	
Polyn.	40	34	29	
Lymph.	51	62	63	
L. Mono.	8	1	7	
Eosinoph.	3	1	
6. R. K., 2½ years old. Exanthem	June 19.			
Per Cent. of	June 14	June 18	June 19	
Polyn.	52	35	45	
Lymph.	45	59	51	
L. Mono.	3	6	4	
7. W. S., 2 years old. Exanthem	June 19.			
Per Cent. of	June 14	June 18	June 19	
Polyn.	54	46	45	
Lymph.	41	52	54	
Eosinoph.	5	2	1	

It is evident that *in almost all cases of German measles there was a definite increase in the lymphocytes even preceding the appearance of the exanthem.*

It would seem that this premonitory lymphocytosis might be of value to institutions in heralding the fact that infection has taken place, and in facilitating the segregation of infected from non-infected children, and thus, perhaps, in limiting the spread of an epidemic. That there is a lymphocytosis at the time of the appearance of the rash may also serve to differentiate rubella from scarlet fever, a disease with which it is sometime confounded, but which is associated with an increase of polynuclear cells in its early stage.

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