PROGRESS IN PEDIATRICS

RESUME ON INFECTIOUS DISEASES *

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The chief general advances made in contagious diseases in the past few years are the wider use of the so-called aseptic technic with the handling of cases, based on the notions of Grancher, and a tendency to attempt active immunization as a means of either preventing these diseases or forestalling their manifestation in a severe form.

HOSPITAL CARE

The newer view of the hospital care of patients with contagious diseases admits as possible and desirable their maintenance in all cases in the same building or even in the same ward with general nursing. Its success seems to depend almost entirely on the conscientiousness with which doctors and nurses carry out the few simple technical precautions, which are in fact almost identical with those observed in the surgical operating room.

The article by Richardson¹ gives a brief résumé of work previously done, especially in English hospitals, with description of hospital and technic used. Three per cent. cross infections is reported as the average. Similar hospitals in this country are in operation at the University of Michigan,² in Evanston,³ and in Chicago.⁴

One of the others under construction is to be at Iowa City. An attempt was made to introduce this system in the new children clinic of Vienna,⁵ and over 10 per cent. of cross infections were reported, the high figure being due no doubt to the well-known inferiority of continental nurses. Connell⁶ describes the Monsall Hospital, Manchester, where this same method is being used. There have been as yet no official reports from the newer hospitals, although at Ann Arbor the percentage of cross infections during the

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* From the Department of Pediatrics, University of Michigan, Ann Arbor.

1. Richardson, D. L.: Jour. Am. Med. Assn., 1913, lxi, 1882.

2. Tr. Clin. Soc. Univ. Mich., 1913-1914, v, 90.

3. Sturm, M. J.: Mod. Hosp., iii, 3.

4. Durand Hospital.

5. Von Pirquet, C.: Ztschr. f. Kinderh., 1912, v, 213.

6. Connell, W. T.: Canad. Med. Assn. Jour., May, 1912, xli, 594.

first year was about 2. Phillips⁷ urges the early isolation of all patients with mild or severe cases. In a series of 900 patients taken care of by the aseptic method there were but two cross infections.

Disinfection after contagious diseases has been discontinued in New York for four years. Chapin⁸ shows that, in the instances of diphtheria and scarlet fever, recurrences have not increased in number, being 1.53 per cent. after 1908 and 1.48 per cent. before in scarlet fever, and 1.75 per cent. after 1908 and 1.71 per cent. before in diphtheria. Bedding disinfection is also dispensed with.

CHICKENPOX

Greeley⁹ describes what he believes to be the etiologic agent of chickenpox, smallpox, and vaccinia. This is a sporothrix which corresponds to the *cytorrhycles variolae* (Councilman). It passes through the Berkefeld filter No. 5 and does not grow on artificial media. Mycelial growth is said to be obtainable.

Kling¹⁰ is the first to have successfully inoculated against varicella. He took the contents of the vesicle of a case at the height of the disease and injected it intradermally in fifty-eight patients, avoiding when possible the drawing of blood. On the eighth day one, usually more, small, red papules appeared. These suggested the lesions seen in cowpox. After a day or so a small, raised, red zone developed about these papules, from which vesicles appeared, which dried up in three or four days, the scab of which did not disappear for two or three weeks. The material from this vesicle could be used for inoculating other nonimmune individuals. Occasional rise of temperature was reported, but rarely illness or general rash. It is interesting to note that in several patients previously inoculated with cowpox vaccine a positive result was obtained, further evidence of the nonidentity of the two viruses. Of the patients inoculated, none developed chickenpox, although they had been exposed. Handrick¹¹ attempted to repeat this work, using the percutaneous method, with negative results. Tieche¹² describes a simple method of differentiating between chickenpox and variola, which depends on the fact that the intradermal inoculation of material from the smallpox lesion will give a positive reaction in the immunized individual, that is to say, vaccinated, whereas no reaction is obtained with the content of the varicella vesicle. By heating the suspected material for five minutes at

7. Phillips, C. H.: Brit. Med. Jour., 1912, No. 2694, p. 357.

8. Chapin: Medical Officer, 1913, ix, 218.

9. Greeley, H.: Med. Rec., New York, 1914, lxxxvi, 204.

10. Kling, C. A.: Berl. klin. Wchnschr., 1913, I, 2083.

11. Handrich, E.: Monatschr. f. Kinderh., 1914, xiii, 242.

12. Tieche: Cor.-Bl. f. schweiz. Aerzte, 1913, xliii, 735, 779; Ibid., 1914, xlv, 1121.

80 F. an earlier reaction was obtained. These tests were done by the experimenter on himself.

Besides these articles several clinical reports may be quoted. For example, Heim¹³ tells of a family in which the mother had herpes zoster. Some weeks after this both children had measles with zoster-like arrangement of the lesions. Lereboullet and Moricand¹⁴ report a case of varicella contracted at birth from the mother, the disease appearing fourteen days after birth. Lentz¹⁵ tells of an instance of indirect transmission in which the child apparently infected its two sisters and mother with the disease and later itself became infected from these patients, thus carrying the disease without infecting itself. Three cases of acute appendicitis occurring during the course of measles are reported by Perier.¹⁶ Storrie¹⁷ has encountered two cases of hemorrhagic and gangrenous varicella. Krause¹⁸ reports cases of varicella in adults, which he believes to be very rare. The diagnosis was verified by the method of Tieche. Lilienthal¹⁹ reports six cases of varicella in adults, diagnosed as syphilis.

EPIDEMIC PAROTITIS

Little work of importance is reported on this subject. Feiling²⁰ studied the blood and spinal fluid in forty cases. He noted a slight absolute and relative increase of the white corpuscles and an early increase of the lymphocytes. In one case orchitis and leukopenia, with relative increase of polymorphonuclears, were found. The spinal fluid was studied when meningeal symptoms, such as vomiting, amblyopia, drowsiness and loss of patellar reflexes, were present. The fluid was found to be colorless and slightly turbid, with 2,500 white blood cells per cubic millimeter, of which 96 per cent. were mononuclears. Barach²¹ studied the blood and found a leukopenia of 5,000 to 600 cells at the outset of the disease and over 48,000 at the height. With the subsiding of the parotid tumor the leukocytes tend to increase. He says that the lymphocytes are increased in number while the polymorphonuclears become fewer. The eosinophils disappear, to return later in greater number than normal. Friedjung²² reports a case of recurrence of mumps in a 15-month-old baby after an interval of slightly over four months.

13. Heim, P.: Berl. klin. Wchnschr., 1912, xlix, 2349.

14. Lereboullet, P., and Moricand, I.: Arch. de méd. d. enfants, 1914, xvii, 288.

15. Lentz, O.: Deutsch. med. Wchnschr., 1913, xxxix, 1148.

16. Perier, E.: Ann. de med. et chir. inf., 1914, xviii, 7.

17. Storrie, H. C.: Brit. Jour. Child. Dis., 1914, xi, 62.

18. Krause, P.: Deutsch. med. Wchnschr., 1913, xxxix, 881.

19. Lilienthal, L.: Deutsch. med. Wchnschr., 1913, xxxix, 1247.

20. Feiling, A.: Lancet, London, 1913, No. 4689, p. 71.

21. Barach, J. H.: Arch. Int. Med., 1914, xii, 791.

22. Friedjung, J. K.: Jahrb. f. Kinderh., 1913, lxxvii, 197.

The investigation of mumps in England by H. M. Gordon²³ shows that the highest mortality occurs in patients under 5 years and especially under 1 year. Gordon²⁴ also gives the pathologic findings in four fatal cases of mumps, the patients being from 2 to 4 years of age, death coming early, with a clinical picture of meningoencephalitis. The lumbar fluid showed increased pressure, with lymphocytosis. The salivary glands were clinically negative, but on histologic examination they showed a marked interstitial inflammation in the perivascular and excretory duct region. On Berkefeld filtration the material obtained from some of these cases seemed capable of producing meningitis and parotitis in monkeys. Acker²⁵ reports two cases complicated with meningitis. Dracinski and Mehlmann²⁶ have seen three cases of pancreatitis complicating mumps. The onset was with fever and headache and the patient presented severe symptoms of collapse, epigastric pain, vomiting, Cheyne-Stokes breathing, delirium, loss of patellar reflexes and acetonuria. Two cases of oöphoritis are reported by Brooks.²⁷ In one of these an abscess formed requiring incision. In the other both breasts atrophied. Conception did not take place in either case within the five years the patients were under observation.

MEASLES

Epidemiology and Prophylaxis.—Rohmer²⁸ analyzed a hospital epidemic and concluded that in the average case measles is infectious for at least seven days, that is, during the period of invasion and exanthem, but not during desquamation. The patients were all confined to their beds and the disease consequently carried from one to the other by the nurses or by utensils. Raffie²⁹ shows quite conclusively that school closure when measles appears is the most effectual method of controlling the disease. Thus, of 4,470 children, 2,180 were susceptible. There were 618 cases of measles before school closed and only 140 within fourteen days after closing, while but seventy-five new infections developed during the third week. Cohn³⁰ is of the same opinion, urging that all who have not had the disease be excluded at least fourteen days. Craster,³¹ in an interesting study of measles among immigrant children, showed that most cases appeared in June. The largest complication average a case mortality occurred in infant. The

23. Gordon, H. M.: Jour. Am. Med. Assn., 1914, lxiii, 414.

24. Gordon, H. M.: Lancet, London, 1913, clxxxv, 275.

25. Acker, G. N.: AM. JOUR. DIS. CHILD., 1914, vi, 399.

26. Dracinski, N., and Mehlmann, J.: Deutsch. med. Wchnschr., 1914, xl, 1566.

27. Brooks, H.: Jour. Am. Med. Assn., 1913, ix, 359.

28. Rohmer, P.: Jahrb. f. Kinderh., 1912, lxxv, 78.

29. Raffie, A. B.: Lancet, London, 1912, clxxxi, 294.

30. Cohn, M.: Ztschr. f. Schulgsndhtpf., 1914, pp. 654, 723.

31. Craster, C. V.: AM. JOUR. DIS. CHILD., 1914, vi, 122.

seasonal prevalence of complication was greatest in winter (December), with the case mortality highest in January. Otitis was the most frequent complication.

Corney³² describes an epidemic of measles in an island of the South Sea, which was like the classic outbreak in the Faroe Islands. Of the nearly 2,000 inhabitants one fourth died, the death rate between the years up to 5 and between 20 and 25 years being greatest. Of the fatal sequelae bronchopneumonia, phthisis and ileocolitis were prominent. Mery and Malhene³³ emphasized the fact that this disease has the greatest mortality in asylums and in foundlings' homes. For example, the total mortality in the institutions of France studied was 11 per cent. of the inmates. If the deaths from measles had been excluded, the mortality would have been 5 per cent. Kilbourne³⁴ reports 600 cases of measles occurring among adults in the Columbus barracks. The mortality was 5 per cent. This figure should be compared with the report of Crum,³⁵ who shows the mortality in patients over 20 years to be 0.3 per cent.; the mortality in patients from 1 to 4 years is 1 per cent., while in those under 1 year of age it is 3.5 per cent. The lowest mortality is found between the years of 5 and 9, when 0.2 per cent. is given. The lowest mortality thus occurs in patients infected between the ages of 5 and 19 years. These figures should guide us in quarantine and prophylaxis.

Pathology.—The loss of allergy occurring during measles is shown in several new ways by recent investigations. Thus Koch³⁶ shows strikingly the relationship that the various stages of measles bear to the loss of the power to react against infection. In the days immediately before and after the appearance of the exanthem, most purulent and secreting processes temporarily cease, for example, the fistula of the cold abscess, the reaction of meningitis, and the cavity of empyema. During the period of the rash there is a failure to react to tuberculin and vaccine, serum rashes and psoriasis. In the week following the exanthem there is the well-known increased tendency to purulent processes and their spread, together with the liability to thrombosis, embolism, necrosis and gangrene. Neumark³⁷ reports a case of a 3-year-old child, who developed the rash of measles four days after being vaccinated. The first typical vesiculation was not noted until eleven days after scarification, a delay of about four or five days. The reaction was normal from that time on.

32. Corney, B. G.: *Brit. Jour. Child. Dis.*, 1913, x, 252.

33. Mery, H., and Malhene: *Bull. Soc. de pédiat. de Paris*, 1913, xv, 1.

34. Kilbourne, E. D.: *Mil. Surgeon*, 1912, xxxi, 294.

35. Crum, F. S.: *Am. Pub. Health*, 1914, iv, 289.

36. Koch, H.: *Ztschr. f. Kinderh.*, 1914, xi, 267.

Tunncliffe³⁸ has found a distinct diminution of phagocytic activity of the leukocytes for streptococci, staphylococci and tubercle bacilli, during the period of the leukopenia, with the return to normal of the blood the phagocytic index also tended to increase. In cases of monkeys inoculated with the blood of measles patients a similar phenomenon is observed. Moltschanow³⁹ shows that the loss of tuberculin sensitiveness is independent of the fever and complications, but is in close association with the rash. Lucas and Prizer⁴⁰ and Nicolle and Conseil⁴¹ verify the work of Hektoen and of Anderson and Goldberger by injecting the blood of measles patients intracerebrally and intraperitoneally.

The incubation period was found to be six days, the Koplik spots appearing on the average of four days later. The virus was transmitted from one ape to the second and from the second to the third. They assume that the virus is in the blood within twenty-four hours after the buccal spots appear and thirty-six hours after the beginning of the skin eruption. A leukopenia is found in the preeruptive stage. The latter observers also find the virus in the blood nine days after inoculation. C. von Pirquet⁴² applies his theory of incubation to this disease. He assumes that the infecting micro-organisms enter the body and during incubation there is developed the so-called *ergin*, which has the character of an antibody. This takes part in the digestion of the invading micro-organisms, with the result that there is formed a toxic product, or apotoxin, which in turn produces the fever, enanthem, and exanthem. The quick death of the virus explains the definite and rapid ending of the disease. He believes also that the process of agglutination plays a part in the formation of the rash. Just why the apotoxin should appear first, and possibly in the greatest quantity, in the tissues of the head is not clearly explained. It seems necessary, however, that the tissues must be saturated with a certain amount of this substance and that, therefore, the regions with the richest blood supply receive the greatest amount of the antibody and so show the rash first.

Remembering the work of Pfeiffer on the toxicity of the urine in anaphylaxis, Aron and Sommerfeld⁴³ examined the urine in a series of cases of measles, intravenously injecting from 1 to 2 c.c. into a

38. Tunncliffe, R.: *Am. Jour. Infect. Dis.*, 1912, xi, 474.

39. Moltschanow, B.: *Russk. Vrach.*, 1911, No. 43; abstr., *Jahrb. f. Kinderh.*, 1912, lxxi, 619.

40. Lucas and Prizer: *Jour. Med. Research*, April, 1912, xxvi, 181.

41. Nicolle, C., and Conseil, E.: *Paris Letter, Jour. Am. Med. Assn.*, 1912, lviii, 289.

42. Von Pirquet, C.: *Ztschr. f. Kinderh.*, 1913, vi, 1.

43. Aron, H., and Sommerfeld, P.: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 1733.

guinea-pig. While from 2 to 4 c.c. normal urine were well borne, 2 c.c. were stated to have been sufficient to produce quick death, with the symptoms of anaphylaxis. The substance is thermostable and dialyzable. There seems to be no relationship with the period of exanthem. The duration of excretion of the poison varies in different individuals. These investigators had negative results with the urine of patients with typhoid fever, pertussis, scarlet fever and diphtheria. The urine derived from a patient with serum exanthem and fourth disease gave positive results. Mautner⁴⁴ comes to a different conclusion, in that while the urine of measles patients was toxic, the same property was found in specimens voided by those infected with diphtheria, peritonitis, scarlet fever, valvular heart disease and arthritis.

Koch⁴⁵ describes a prodromal rash occurring in one fourth of his cases. This consisted in brownish-red, macular, illly defined spots, fleeting in character. They appeared chiefly on the face at the time or immediately after Koplik spots are seen. A further aid in the early diagnosis of measles comes from Grumann.⁴⁶ On both tonsils he found punctate and linear whitish swellings of about 3 mm. in length in the neighborhood of the lacunar depressions; these might also be seen on the more prominent follicular eminences. They seemed to appear either coincidentally with the Koplik spots or they might be present alone when the Koplik spots were absent, tending to precede the eruption by one or two days. He suggests that they may be superficial infiltrations or necroses. Lucas,⁴⁷ studying the blood in measles, found that the change in the differential picture took place about a week before the appearance of the characteristic symptoms. This consisted in the replacement of the normal relative mononuclears by a polynuclear increase. Some disintegrated cells were found, which, while not specific, when taken with the above transformation were of importance in epidemics, enabling earlier isolation without waiting for the appearance of the Koplik spots. Lutz⁴⁸ gives the necropsy findings in twenty-two cases of measles in which thrombus formation was encountered. Of these, six cases involved chiefly the pulmonary artery, while in two cases portal veins were partly obstructed.

Epidemiology and Mortality.—Feibelmann⁴⁹ reports two cases in which measles occurred a second time in the same individual. In one

44. Mautner, H. L.: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 1815.

45. Koch, H.: *Ztschr. f. Kinderh.*, 1913, ix, 1.

46. Grumann, M.: *München. med. Wchnschr.*, 1914, lx, 132.

47. Lucas, W. P.: *AM. JOUR. DIS. CHILD.*, 1914, vii, 149.

48. Lutz: *Berl. klin. Wchnschr.*, 1913, l, 1566.

49. Feibelmann: *Arch. f. Kinderh.*, 1911, lvii, 50.

of these it was impossible to determine whether the disease was to be recorded as a recurrence or a second infection. Koplik spots were found in each instance. Only five such cases are reported in the literature. On the other hand, Friedjung⁵⁰ reports three persons who, though definitely exposed, did not contract the disease, the patients now being 17, 19 and 19 years of age, respectively. It is possible that this is one of the rare cases of natural immunity. The striking influence of good hygienic surroundings on mortality is shown in the report of Maier.⁵¹ Since the contagious patients have been moved into new quarters, the mortality from measles has been halved.

Complications and Sequelae.—Weill and Gardere⁵² found an infectious erythema occurring in eight severe cases, of which four of the patients died. This erythema appeared at symmetrical points, distributed on the extremities, the trunk and abdomen not being involved except occasionally where the rash tended to become general. This was associated with ulceration in the mouth, in the cheek and in the pharynx, where Hutinel believes that secondary invaders found portals of entry. The mucous membrane lesions, however, were not necessarily present. There may be a succession of eruptions which are independent of the severity of the mucous membrane lesions or the severity of the disease. Clinical symptoms of the secondary infection may precede the rash. Griscom⁵³ found double choked disk occurring in a patient in the third week of the disease. Complete recovery took place. Morgenstern and Gruber⁵⁴ found multiple infarcts of the skin in a poorly nourished, rickety infant 1 year old. Multiple necrotic areas on the outer and lower side of the thigh below the gluteal fold were the chief lesions. Death occurred on the fifth day following the appearance of the rash. Delcourt⁵⁵ found two cases of subcutaneous emphysema as a complication of bronchopneumonia. This he interprets as being due to perforation of adherent lung. Ligabue⁵⁶ reports a case of subphrenic abscess following measles. Fischl⁵⁷ saw a case in which a hemorrhagic diathesis appeared following the disease with resulting enormous subcutaneous hemorrhages. Pertussis was also present. Galop⁵⁸ adds to the cases of gangrene of the limbs. Bronchopneumonia and enterocolitis were also present.

50. Friedjung, J. V.: Wien. med. Wchnschr., 1914, p. 939.

51. Maier, L.: München. med. Wchnschr., 1913, lx, 636.

52. Weill, E., and Gardere, C.: Rev. de méd., 1913, xxxiii, 545.

53. Griscom, M.: Ann. Ophth., 1912, xxi, 42.

54. Morgenstern and Gruber: Ztschr. f. Kinderh., 1914, xii, 100.

55. Delcourt: La Patholog. Infantile, 1914, xi, No. 1.

56. Ligabue, P.: Policlinico, Rome, xxi, No. 7.

57. Fischl: München. med. Wchnschr., 1912, lix, 621.

58. Galop, M.: Arch. de méd. d. enfants, 1914, xvii, 49.

Just before the appearance of the complications the popliteal pulse could not be felt, while the femoral pulse was still present.

Treatment.—Temporary interest was aroused by a rather extravagant statement of Milne,⁵⁹ who said that if as soon as possible after the outbreak of the rash pure eucalyptus oil were rubbed over the body of the patient twice a day and the tonsils swabbed every two hours with a solution of 10 per cent. phenol in oil for the first twenty-four hours, isolation became unnecessary and complications and secondary infections were prevented and disinfection rendered needless. Even the eating utensils were not sterilized. Elgart⁶⁰ repeated this and found that while it did not do all that its author predicted, it did seem to produce a diminished mortality. It is not uninteresting to find that he did not use phenol, finding that 50 per cent. lime water was as efficient and that he did not rub the body with the eucalyptus. Connolly⁶¹ also believes that he has had help from this method, in that in comparative groups the mortality was but 5 per cent. among severe cases, whereas it was 11 per cent. in a similar group untreated. Marfan⁶² shows that salvarsan given to a child as treatment for syphilis did not protect it against measles. This treatment has been more used in cases of scarlet fever, where further reference will be made to it.

GERMAN MEASLES

Outside of studies in hematology little of importance has been reported. Schwaer⁶³ finds a slight increase in the white cells with the mononuclears relatively greater in number. A leukopenia is not characteristic, as stated by many. The eosinophils, which disappear in measles at the height of the disease, are said to be constantly present in this disease. Hamburger⁶⁴ denies the report that he saw the eosinophils increase at the height of measles eruption. Saito⁶⁵ was fortunate enough to see an epidemic of 105 cases, including seventeen adults and six infants. The incubation period seemed to vary from fifteen days to twenty-three days. In only thirteen cases was the temperature over 100 F. The rash was of the characteristic papular type with anemic margins. Glandular enlargement was constant. The white blood count varied between 6,000 and 12,000 cells. Saito, in contrast with Schwaer, found the polynuclear cells relatively increased. Eosinophilia at the period of the fading rash was common, one case

59. Milne, R.: *Lancet*, London, 1911, p. 1070.

60. Elgart, J.: *Med. Klin.*, 1913, ix, 1251.

61. Connolly, D. L.: *Practitioner*, London, 1912, lxxxix, 664.

62. Marfan, A. B.: *Paris Letter*, *Jour. Am. Med. Assn.*, 1912, lviii, 1387.

63. Schwaer: *München. med. Wchnschr.*, 1913, ix, 1203.

64. Hamburger, F.: *München. med. Wchnschr.*, 1913, ix, 2120.

65. Saito, H.: *Ztschr. f. Kinderh.*, 1914, x, 54.

of 42 per cent. being noted. No loss of susceptibility to tuberculin was made out as in cases of measles.

WHOOPING COUGH

Statistics and Epidemiology.—Emphasis has again, in the past few years, been laid on the high mortality from whooping cough. Morse⁶⁶ shows that while it causes the smallest number of deaths, 11.4 per 100,000, of the four important contagious diseases, still the percentage of mortality is very high and more attention should be paid to prophylaxis and isolation. Rucker⁶⁷ comments on the recent public health reports which state that 10,000 children a year are sacrificed to this disease. Pisek⁶⁸ finds the mortality in New York City to be over 10 per cent. of reported cases. According to his figures many of these died of tuberculosis. He urges special hospitals for the detention of such patients. An objection to the institutional care of such patients on the basis of the influence of proximity and the resulting suggestion is raised by Galisch.⁶⁹

Experimental Work and Diagnosis.—Inaba⁷⁰ was able microscopically as well as culturally to demonstrate the Bordet-Gengou organism in 90 per cent. of his cases. A not uninteresting part of this report is the statement that the influenza bacillus differs from the organism of whooping cough in its cultural characteristics. The author finds that the whooping cough bacillus has more resistance and does not seem to have the same tendency to pleomorphism that the influenza bacillus has. He recognizes defibrinated goat's blood agar as the best medium for the cultivation of the bacteria. Manicatide⁷¹ finds an organism which he denominates bacillus Z as the etiologic agent of whooping cough. This organism resembles the organism of influenza. He finds that the serum of both goats and sheep can be used for treatment and prophylaxis. The work surely needs further confirmation.

Diagnosis of the cough from similar clinical stages is determined by several authors by means of the reaction of complement deviation. Delcourt⁷² finds it of special service. Friedlander and Wagner⁷³ use the fresh antigen, this being a seventy-two hour culture on ascitic agar. Fresh serum is also used. By this means they believe that they are able to diagnose the presence of the disease in its earlier stages, in

66. Morse, J. L.: Jour. Am. Med. Assn., 1913, lx, 1677.

67. Rucker: Jour. Am. Med. Assn., 1912, lix, 1882.

68. Pisek: New York Med. Jour., 1914, xcix, 970.

69. Galisch, A.: Med. Klin., 1912, viii, 488.

70. Inaba, I.: Ztschr. f. Kinderh., 1912, iv, 252.

71. Manicatide, M.: Ztschr. f. Kinderh., 1913, vii, 226.

72. Delcourt, A.: La Patholog. Infantile, 1912, ix, No. 1.

73. Friedlander, A., and Wagner, E. A.: Jour. Am. Med. Assn., 1914, lxii, 1008.

contradistinction to Bacher and Metchnikoff,⁷⁴ Bordet,⁷⁵ and Netter and Weill,⁷⁶ who were able, by employing the usual technic, to find a positive reaction only at the height of the disease or in convalescence. Thirty examinations on eighteen cases were positive in the paroxysmal stage; in three cases two positive results were found even in the catarrhal stage. Neurath⁷⁷ attempted to produce an intracutaneous specific allergic reaction with the endotoxin of the Bordet-Gengou bacillus. No reliable results were obtained. Both control and patient, with the exception of a few infants, were positive.

An interesting contribution to the pathologic anatomy of whooping cough was made by Mallory and Horner.⁷⁸ They found that the cilia of the epithelial cells lining the trachea, bronchi, and possibly the nose were, in the specimens examined, covered with a thick layer of minute bacilli, and believe that the location of the organism is apparently characteristic of the disease and that the action seems to be partly mechanical, producing inhibition of the ciliary movements and of the cellular secretions. The blood changes have again been studied by Schneider,⁷⁹ and they are in the main confirmatory of previous workers. His results may be summarized briefly by stating that there is a leukocytosis up to 80,000, the average being 27,000. The mononuclears are relatively increased during the first four weeks, 86 per cent. being the highest and 60 per cent. the average. No prognostic conclusions can be drawn from the blood picture.

Clinic and Complement.—That the notion regarding pertussis, supported by Czerny, who overemphasized the neurotic element, a stand which he has recently disavowed, should find some adherents is not surprising. Dobelli⁸⁰ took up this view and was vigorously combated by Feer.⁸¹ Feer admits the psychic element, but believes that it is possible that Czerny was deceived by pertussis-like cough of tuberculosis or that occasionally following pneumonia. The association of pertussis and spasmophilia has been the subject of several communications. Wernstedt⁸² tells of an epidemic in which the patients showed increased irritability of the nerves, but no evidence of the presence of specific organisms. Erlanger⁸³ denies a necessary association between the two conditions.

74. Bacher and Metchnikoff: *Centralbl. f. Bakteriöl., Orig.*, 1912, lxi, 218.

75. Bordet: *Centralbl. f. Bakteriöl., Orig.*, 1912, lxxvi, 236.

76. Netter and Weill: *Compt. rend. Soc. de biol.*, 1913, lxxiv, 236.

77. Neurath, R.: *Med. Klin.*, Berlin, 1914, x, 1619.

78. Mallory, F. B., and Horner, A. C.: *Jour. Med. Research*, 1912, xxvii, 115.

79. Schneider: *München. med. Wchnschr.*, 1914, lxi, 303.

80. Dobelli, E.: *Cor.-Bl. f. schweiz. Aerzte*, 1912, Nos. 4 and 23.

81. Feer, E.: *Cor.-Bl. f. schweiz. Aerzte*, 1912, No. 6.

82. Wernstedt, W.: *Hygiea*, Stockholm, September, 1912; abstr., *München. med. Wchnschr.*, 1912, lix, 605.

83. Erlanger, B.: *Monatschr. f. Kinderh.*, xii, No. 8.

A number of interesting complications and sequelae are again reported. Roedelius⁸⁴ has seen a case of optic atrophy, the seventh on record. He believes this to be due to neural infections as well as to the mechanical influences. Sylvester⁸⁵ reports eight patients with cerebral complications, of whom seven died. In two, micro-organisms were demonstrated in the spinal fluid. Weigert⁸⁶ saw a meningocele develop in an infant after three weeks of coughing. Later, as the fontanels grew smaller, the tumor disappeared. No permanent injury of the brain was demonstrable. Two months following a severe pertussis polydipsia developed in an 8-year-old patient of von Starch.⁸⁷ The diabetes mellitus which was diagnosed was of slight severity.

Vaccine Treatment.—The vaccine treatment of whooping cough has been quite frequently reported. Ladd⁸⁸ reports eight patients, of whom three were infants. From 40,000,000 to 50,000,000 bacteria were given. The average duration of the disease was eight weeks. The author draws no definite conclusions as to the beneficial results produced, but feels that the severity of the paroxysms was diminished. Zahorsky⁸⁹ reports favorably of his experience. He attributes to the vaccine a certain immunizing power. Nicolle and Connor⁹⁰ treated 104 patients and saw fifty-seven cured, thirty-eight improved, while twenty-five were uninfluenced. Bamberger⁹¹ had six cases in which he gave 21,000,000 bacteria every day for from five to fifteen days. This author believes that both the symptoms and severity of the disease were abated and that fewer complications were noted. According to Wilson,⁹² whenever a systemic reaction was produced by the vaccine an improvement followed. In his twenty-three cases he used a total of 60,000,000 to 80,000,000 bacteria and felt that a distinct benefit was produced. Sill⁹³ has a series in which the patients' ages range from six months to three years. In the patients earliest seen the improvement was the most marked. Individual doses of from 2,000,000 to 6,000,000 were given, but improvement was frequently not seen until three injections had been given. In one case he gave a total of 220,000,000 bacteria, at the rate of 40,000,000 every second day. Two exposed patients had weekly injections of 20,000,000 bacteria and did not contract the disease. Scott⁹⁴ also was satisfied with the vaccine

84. Roedelius, E.: Arch. f. Kinderh., 1913, lxii, 161.

85. Sylvester, P. H.: Boston Med. and Surg. Jour., 1914, clxx, 406.

86. Weigert, R.: Monatschr. f. Kinderh., 1914, xiii, 139.

87. Von Starch, W.: München. med. Wchnschr., 1912, lix, 1317.

88. Ladd, M.: Arch. Pediat., 1912, xxix, 581.

89. Zahorsky, J.: Interstate Med. Jour., 1912, xix, 844.

90. Nicolle and Connor: Compt. rend. Acad. d. sc., 1913, No. 24, p. 1849.

91. Bamberger, A.: AM. JOUR. DIS. CHILD., 1913, v, 33.

92. Wilson, S. M.: New York Med. Jour., 1913, xcvi, 823.

93. Sill, E. M.: AM. JOUR. DIS. CHILD., 1913, v, 379.

94. Scott, G. D.: New York Med. Jour., xcvi, 176.

treatment, in that a distinct ameliorating influence on the symptoms was found. Luttinger⁹⁵ used the vaccine in severe cases in which medicine was of no avail, and in ten of these cases was able to diminish the severity of the paroxysms as well as to shorten the duration of the disease. He believes that he was successful in immunizing against the disease one exposed patient by the use of 50,000,000 bacteria. He prefers the subcutaneous injection. His highest total dose was 150,000,000. One of the most interesting contributions to our knowledge of the use of vaccines comes from Hess,⁹⁶ who describes his experience in an orphan asylum of 357 inmates, the patients varying in age from a few days to 6 years. The vaccine was used by him chiefly for prophylactic purposes, although it was also used in treatment. Of 240 patients who were vaccinated with from 100,000,000 to 2,000,000,000 bacteria, twenty, or 8.3 per cent., developed the disease. Of eighty who were definitely exposed, or, to put it in its most unfavorable light, of 130 who were not vaccinated, fifty-nine, or 22 per cent., developed the disease. If the degree of exposure in the two groups of cases was at all comparable, the results are surely most striking. This observer has less favorable statements to make as to the therapeutic efficiency of the vaccine, in that he did not even observe a distinctly beneficial influence on the symptoms. Hartshorn and Moeller⁹⁷ found that a certain number of patients improve with commercial vaccine, others did not. They urge the continuation of its use only when a quick and distinct benefit is found. Graham⁹⁸ sums up his experiences by stating that about three fourths of the patients are symptomatically benefited. He also ascribes a certain prophylactic value to the vaccine.

It seems probable that any conclusions as to the efficiency of the vaccine treatment of pertussis must be guarded. Knowing the numerous remedies suggested in the past, enthusiastically acclaimed and as quickly dropped from our armamentarium, one wonders whether the vaccine will have the same fate. The reports seem to show, with few exceptions, an influence on the symptoms. Whether this benefit is in the eyes of the observer or is a real one only the future can tell. The further use of the vaccine seems, however, to be definitely indicated. Patients should be treated early and vigorously, but this treatment should be discontinued if beneficial effects are not obtained. While vaccine therapy is still in the experimental stage, still more is this true with regard to the use of the vaccine as a prophylactic. No

95. Luttinger, P.: *Med. Rec.*, New York, 1913, lxxxiv, 1125.

96. Hess, A. F.: *Jour. Am. Med. Assn.*, 1914, lxiii, 1007.

97. Hartshorn, W. M., and Moeller, H. N.: *Arch. Pediat.*, 1914, xxxi, 587.

98. Graham: *Arch. Pediat.*, 1914, xxxi, 578.

harmful results have been reported, however, and there seems no reason why further investigations should not be carried out.

Miscellaneous Treatment.—Popper⁹⁹ urges suggestive treatment with the faradic treatment in the later stages of the disease. Ochsenius¹⁰⁰ favors local treatment of the pharynx with 2 per cent. silver nitrate. This also has a psychic effect. Rusca¹⁰¹ reports an interesting case in which a little patient with pertussis was operated on for a complicating appendicitis. The pain produced by coughing made the child exert its will to control the paroxysms. This emphasizes the psychic element of the disease.

DIPHTHERIA

Statistics and Epidemiology.—The great interest shown in diphtheria in recent years is due undoubtedly to the fact that although we have an effective means of diagnosis and treatment, still the morbidity rate and mortality has not tended to show so great a diminution as might be expected. Abel,¹⁰² speaking of conditions in Germany from 1892 to 1898, shows that the total number of deaths from diphtheria in one year is greater than those from scarlet fever. The city mortality is higher than that of the country. He urges more intensive and more systematic cultures in order to control this condition. Braun¹⁰³ also emphasizes this fact in regard to the city of Berlin. Von Drigalski¹⁰⁴ shows that by systematic culturing and isolation it was possible to rid a population of nearly 200,000 of much of its diphtheria. In this connection reference should be made to the excellent treatise by von Behring¹⁰⁵ on the subject of the control of contagious diseases. Seligman and Schloss¹⁰⁶ describe in detail their carefully controlled attempts to weed out diphtheria in several schools and institutions. Throughout the report they emphasize the necessity of systematic culturing, as well as the desirability of routine cultures, before patients are admitted. The significance of snuffles in infants is also recognized, although they fail to give sufficient mention to this same symptom in older children. Details relating their experiences with treatment, etc., are given.

Teague¹⁰⁷ reports some experiments done to show how far droplet infection plays a part in the spread of the disease. He found that in

99. Popper, E.: Med. Klin., 1913, No. 26.

100. Ochsenius: Therap. d. Gegenw., 1913, liv, 502.

101. Rusca, F.: Cor.-Bl. f. schweiz. Aerzte, 1914, No. 19.

102. Abel, R.: Centralbl. f. Bakteriöl., 1912, lxiv, 229.

103. Braun, W.: Deutsch. med. Wchnschr., 1912, xxxix, 255.

104. Von Drigalski: Berl. klin. Wchnschr., 1912, xlix, 1792.

105. Von Behring: Einführung in die Lehre von der Bekämpfung der Infektionskrankheiten.

106. Seligman, E., and Schloss, E.: Ztschr. f. Kinderh., 1912, iv, 451.

107. Teague, O.: Jour. Infect. Dis., 1913, xii, 398.

talking or coughing only small numbers of droplets are emitted and these but a few inches from the mouth, thus forcing the conclusion that contact infection direct or indirect, is, as in other contagious diseases, the chief method of propagation. That one attack of diphtheria does not confer a lasting immunity is shown by Montefusco,¹⁰⁸ who saw a patient with three clinical attacks in eight months. Reiche¹⁰⁹ writes of his experience in a recent severe diphtheria epidemic in Hamburg, in which he encountered 344 patients who had previously had diphtheria. Of these, 119 had never received antitoxin.

Carriers and Contacts.—Von Hoff¹¹⁰ concludes that in a large number of cases diphtheria bacilli will persist up to five months after the disappearance of the clinical symptoms, even though the cultures are negative. After this they tend to diminish. Brückner¹¹¹ and others bring out a most interesting fact, namely, that at certain times of the year at Dresden it seems that the percentage of bacillus carriers undergoes an enormous but not to be explained increase, up to 48 per cent. of examined cases. These cultures are found in a large number of children who are not clinically ill. It is not stated, however, whether this increase is connected with the increase of the number of clinical cases of diphtheria and whether these patients are not really contacts. This brings up, of course, the well-known difficulty of determining the significance of the culture morphologically positive. Van Biemsdyk¹¹² found among thirty-three children, nineteen of whom had just had diphtheria, organisms resembling Klebs-Loeffler bacillus in twenty-four instances. Of these, but two were virulent. In a region free from diphtheria for ten years, in 50 per cent. of children examined the same organisms were found. His criteria of virulence were the formation of acid and agglutination in a dilution of at least 1 to 500. Riebold¹¹³ saw an epidemic produced in a children's colony by a carrier. Delyannis¹¹⁴ also emphasizes the importance of isolation and treatment of carriers. In three villages endemic diphtheria was not controlled until the carriers had been recognized. Arms and Whitney¹¹⁵ also emphasize the rôle of contact in the spread of diphtheria.

Pathologic Anatomy and Physiology.—Abramow¹¹⁶ studied the hypophysis in experimental diphtheria and believes that there is an early hyperstimulation and hypersecretion with resulting exhaustion.

108. Montefusco, A.: Gazz. d. osp., March 16, 1913, xxxiv, No. 32.

109. Reiche, F.: Med. Klin., 1913, ix, 1668.

110. Von Hoff, G.: Monatschr. f. Kinderh., 1914, xiii, 133.

111. Brückner: Abstr., München. med. Wchnschr., 1913, ix, 554, 609.

112. Van Biemsdyk, J. M.: Nederl. Tijdschr. v. Geneesk., 1914, p. 1066.

113. Riebold, G.: München. med. Wchnschr., 1914, lxi, 923.

114. Delyannis, K.: Wien. klin. Wchnschr., 1913, xxvi, 1389.

115. Arms and Whitney: Am. Jour. Pub. Health, 1912, No. 10, 799.

116. Abramow, S.: Virchows Arch. f. path. Anat., 1914, ccxiv, 408.

It is interesting to note, however, that the first changes appear in the adrenal. The author, however, does not definitely state that there is an interrelation between these two glands. Kreutsfeldt and Koch¹¹⁷ also find the pars intermedia of the hypophysis markedly affected, there being in guinea-pigs a diminution in size with granular cystic degeneration. Wildebrand¹¹⁸ examined the hypophysis in fatal cases of diphtheria in children and finds again distinct degenerative changes in the pars intermedia. He emphasizes the therapeutic value of pituitrin in these severe cases of diphtheria. Moltschanoff¹¹⁹ again emphasizes the marked change in the adrenal glands and sees in this pathology the justification for the great potency of epinephrin in cardiac collapse.

Involvement of the heart in diphtheria is commented on by Rohmer.¹²⁰ In two cases, although heart block was demonstrated by the electrocardiogram at autopsy, the His bundle was found to be relatively unaffected. Tanaka,¹²¹ however, finds a uniform diffuse degeneration of the auriculoventricular bundle, although in one case of severe arrhythmia this muscle filament showed no change. Several other communications have appeared on this subject. Wilson¹²² in his résumé refers to the chief of these.

While it has been commonly assumed that the vasomotor center is greatly affected and is believed to be the cause of the circulatory collapse in diphtheria intoxication, Porter and Pratt¹²³ in their animal experiments have been unable to find evidence to bear out this statement. The earlier views have been probably due to faulty interpretation of experiments. This is one other fact which tends to indicate that suprarenal failure plays an almost sole part in this condition. The finer mechanism of this is shown by McCallum¹²⁴ in the isolated heart of an animal, with an artificial circulation containing diphtheria toxin. He shows that if there is sufficient pressure in the coronary artery, the heart will still beat for hours. Leede¹²⁵ examined the blood in fatal cases during an epidemic of unusual severity. Out of 256 cases he found the streptococcus in 205, the pneumococcus in twenty-three, the Klebs-Loeffler bacillus in nine, and the latter in conjunction with streptococcus in four. Liedke and Volckel,¹²⁶ however, in seven

117. Kreutsfeldt, G., and Koch, R.: *Virchows Arch. f. path. Anat.*, 1913, ccxiii, 123.

118. Willebrand: *Zentralbl. f. d. ges. inn. Med. u. d. Grenzgeb.*, 1912, iii, 132.

119. Moltschanoff, W.: *Jahrb. f. Kinderh.*, 1912, Supplement 200.

120. Rohmer, P.: *Jahrb. f. Kinderh.*, 1912, lxxvi, p. 391.

121. Tanaka: *Virchows Arch. f. path. Anat.*, 1912, ccvii, 113.

122. Wilson, F. N.: *AM. JOUR. DIS. CHILD.*, 1915, x, 376.

123. Porter, W. T., and Pratt, J. H.: *Am. Jour. Physiol.*, 1914, xxxiii, 431.

124. McCallum, W. G.: *Am. Jour. Med. Sc.*, 1914, cxlvii, 37.

125. Leede, W. H.: *Ztschr. f. klin. Med.*, 1913, lxxvii, 297.

126. Liedke and Volckel: *Deutsch. med. Wchnschr.*, 1914, xl, 594.

fatal cases, found diphtheria bacilli in the heart, lungs, spleen, kidneys and in the bone marrow. Reye,¹²⁷ in sixty-seven cases, found bacteria in the lungs fifty-six times. Of these, the diphtheria bacillus was in pure culture but six times; twenty-seven times it was associated with streptococci and in twenty-three cases with other micro-organisms.

Bacteriology.—Unending attempts are being made to simplify the interpretations of the laboratory findings in diphtheria and to bring them into harmony with the clinic. The fact that the mere morphology gives no positive information and the fact that not only in the culture but also in the throat the organisms of diphtheria tend to undergo involution, though apparently retaining the power to again become virulent, make the problem almost hopelessly difficult. Thiele and Embleton¹²⁸ report that they have been able to transmute a characteristic Hoffman diphtheroid into a virulent organism with the typical morphology of the diphtheria bacillus, capable of producing pathologic changes in a guinea-pig. The significance of this is at once apparent. If verified, it would indicate that the involution types of organisms found in the respiratory tract of the patient so many months after the disappearance of clinical symptoms are still capable of producing infection. The opposite has been accomplished by Römer.¹²⁹ He transforms the virulent into an avirulent modification by passage through guinea-pigs. Meunier still adheres to the commonly accepted views that the polar body organisms and the barred and solid types are the only ones to be feared. Baerthlein¹³¹ found that in progressive cultures the diphtheria bacilli lost their virulence, and with this is associated a change in the form and appearance of the colony produced. Kolmer,¹³² from a large series of cultures, concludes that only the granular type, using the classification of Westbrooke, are virulent. The barred types are of doubtful significance, while the small forms may be excluded, unless small polar granules are found, when they are to be regarded as positive. Kolmer,¹³³ using the complement fixation reaction as a basis for classifying the diphtheria-like bacilli, shows that all of them are related and that the true Hoffmann bacillus is probably an example of mutation.

There is no relation between the occurrence or degree of complement fixation and the antitoxin strength of the immune serums. This again brings up the fact, commonly overlooked, that not only is there

127. Reye, E.: München. med. Wchnschr., Oct. 29, 1912, lix, 2383.

128. Thiele and Embleton: Ztschr. f. Immunitätsforsch. u. exper. Therap., 1913, xix, 643, 666.

129. Römer, P. H.: Berl. klin. Wchnschr., 1914, li, 503.

131. Baerthlein, K.: Berl. klin. Wchnschr., 1913, l, No. 22.

132. Kolmer, J. A.: Jour. Infect. Dis., 1912, xi, 56.

133. Kolmer, J. A.: Jour. Infect. Dis., 1912, xi, 44.

an antitoxic, but also an antibacterial, immunity developed. Menard,¹³⁴ cultivating diphtheria bacilli on serum in contact with antitoxin, found them unaffected; they seemed, however, to lose their power of producing toxin. Lavari¹³⁵ in this connection has been able to find by means of the complement fixation test that there is an antibacterial amboceptor to be found in antitoxin. No conclusions are drawn as to its significance. Townsend¹³⁶ reports the finding of virulent pseudodiphtheria bacilli in the urinary tract. Kolmer¹³⁷ in forty cases made 100 cultures from the penis, and finds diphtheroid bacilli which, however, he states to be avirulent.

Cultural Methods.—Conradi and Troch¹³⁸ describe a new medium for elective culture of diphtheria bacilli. This consists in ordinary beef serum in which is incorporated a small percentage of sodium tellurate and of calcium malate. The diphtheria bacilli are first grown on ordinary Loeffler's serum for three hours and are then transferred to plates of the new mixture. The diphtheria bacilli colonies are supposed to reduce the tellurate, a black colony resulting. Other micro-organisms are stated not to do this. Calcium malate is supposed, moreover, to retard the growth of these other organisms. Several investigators have used this plan and their reports are far from enthusiastic. Hanau¹³⁹ sees no proportionate advantage over the older method. Klunker¹⁴⁰ is of the same opinion. Schurmann and Hajos,¹⁴¹ however, used the Conradi-Troch plates and omitted the simple serum altogether. They found a larger number of positive cultures as well as a simplification of the picking out of colonies. Wagner¹⁴² found no more positive results, but found it easier to locate the organisms. Markl and Pollak¹⁴³ speak well of this new medium.

Another improvement is suggested by von Drigalski and Bierast.¹⁴⁴ They add 3 per cent. sterile ox bile to Loeffler's glucose bouillon serum. Voelckel,¹⁴⁵ Schulz,¹⁴⁶ and Grundman¹⁴⁷ are not favorably impressed with their experiences. Conradi¹⁴⁸ has an ingenious technic for sepa-

134. Menard, P.: Presse méd., 1913, xxi, 636.

135. Lavari: Ann. d. Ist. Maragliano p. la cura d. tuberc., 1913, vii, No. 2.

136. Townsend, W. W.: Jour. Am. Med. Assn., 1913, lxi, 1605.

137. Kolmer, J. A.: Arch. Pediat., 1912, xxix, 94.

138. Conradi and Troch: München. med. Wchnschr., 1912, lix, 1652.

139. Hanau: Centralbl. f. Bakteriöl., 1913, lxxii, 245.

140. Klunker: München. med. Wchnschr., 1913, lx, 1025.

141. Schurmann, W., and Hajos, E.: Deutsch. med. Wchnschr., 1913, xxxix, 786.

142. Wagner, G.: München. med. Wchnschr., 1913, lx, 457.

143. Markl and Pollak: Wien. klin. Wchnschr., 1913, xxvi, 1617.

144. Von Drigalski, W., and Bierast: Deutsch. med. Wchnschr., 1913, xxxix, 1327.

145. Voelckel, E.: München. med. Wchnschr., 1913, lx, 883.

146. Schulz, F. C. R.: Deutsch. med. Wchnschr., 1913, xxxix, 2195.

147. Grundmann: Berl. klin. Wchnschr., 1913, l, 2287.

148. Conradi, P.: München. med. Wchnschr., 1913, lx, 1073.

rating the diphtheria bacilli from other micro-organisms, based on the fact that if a mixed culture be shaken up in a test tube containing salt solution and oil, the diphtheria bacilli will be taken up by the oil, whereas the rest of the organisms go into the salt solution. Cotton swabs surrounded by filter paper and moistened with ligroin are dipped into the oil later, the oil passing through the paper into the cotton and the bacteria remaining on the filter paper. Af Heurlin¹⁴⁹ attempts to differentiate by cultural methods the true and the false diphtheria bacilli. This is based on the capacity which the true diphtheria bacilli have of developing without oxygen. Consequently, in deep stabs into alkaline phenolphthalein glucose agar, the true bacilli will be toward the bottom. On blood glucose phenolphthalein agar it is found that pseudodiphtheria bacilli do not produce hemolysis.

Immunology.—Interesting steps in advance are found in the introduction of the intradermal application of diphtheria toxin for clinical purposes by Schick and a like clinical application by von Behring of a suggestion made first by Theobald Smith, namely, that mixtures of toxin and antitoxin be used to actively immunize against diphtheria. The first full communication of Schick¹⁵⁰ has to do with the application of the so-called Römer test and the first observations were done with the blood serum of a diphtheria patient to determine the toxin content.

In another communication he¹⁵¹ finds that local hypersensitization does not result, even though the tests be frequently repeated. He also used this method¹⁵² as a means of determining the amount of diphtheria antitoxin necessary to neutralize circulating toxin and found that by giving as little as 500 units per kilogram of body weight (250 units per pound) in 91 per cent. of all cases the toxin reaction could be prevented. In other words, this amount of antitoxin was sufficient to neutralize not only the circulating toxin, but also that amount in addition which was introduced for the test. No retroactive power of the serum could be made out—another confirmation of the importance of early treatment. Prophylactic injections were given only to those patients who had a positive toxin test. He¹⁵³ suggests that if the intracutaneous tests are negative, there are sufficient protective bodies in the patient's serum, and he also concludes that there is an immunity in these cases. As to whether the diphtheria bacillus might not gain a hold in the mucous membrane in spite of this immunity is not discussed. The strength of

149. Af Heurlin, M.: München. med. Wehnschr., 1914, lxi, 703.

150. Schick, B., and Michiels, J.: Ztschr. f. Kinderh., 1912, v, 255.

151. Schick, B.: Centralbl. f. Bakteriöl., 1912, lxvi, 121.

152. Schick, B.: Wien. klin. Wehnschr., 1914, xxvii, 1966.

153. Schick, B.: München. med. Wehnschr., 1913, lx, 2608.

the toxin suggested for this test is such that 0.1 c.c. is equivalent to $\frac{1}{50}$ of the lethal dose for a guinea-pig which weighs about 250 gm.

Park, Zingher and Serota¹⁵⁴ have tried out this reaction in 700 cases of scarlet fever. Fifty-seven per cent. (400 cases) gave negative reaction and developed no diphtheria, although the patients did become carriers. Using this reaction, they also found that the intravenous administration of serum was more effective than the subcutaneous or intramuscular. Kleinschmidt¹⁵⁵ found that of eighteen infants, sixteen showed no antitoxin in the blood. The two patients in whom antitoxin was found were in an institution where they may have been exposed. Of sixteen infants who were bacillus carriers, antitoxin was found in the blood of ten, as much as 2.5 units per cubic centimeter being determined. Otto¹⁵⁶ found that the percentage of antitoxin in adults is greater in those who are frequently exposed to diphtheria, as in a hospital. Carriers and excretors of the bacilli also showed a high content. An acute infection gives only a moderate immunity, whereas a chronic infection is necessary for this purpose. Larval infections, without symptoms, are especially potent. Schütz¹⁵⁷ also in a series of cases finds that the Schick test gives a definite clue as to the susceptibility of the patients. Hahn¹⁵⁸ also, using the method of Römer, shows that attendants in diphtheria wards and others frequently exposed have the highest antitoxin content of the blood. Kassowitz and Gröer¹⁵⁹ show that the immunity of the new-born, which exists in 80 to 90 per cent. of all cases, depends on the antitoxin derived from the mother's blood. Beyer¹⁶⁰ found that antitoxin was found in the blood of every patient who had been injected, from one-half to four-fifths of the total quantity being present. On the fifth and the sixth days from one-fifth to three-tenths were still present. In from two to three weeks only from five- to six-hundredths could be demonstrated. In certain instances a larger amount was found than would be theoretically expected. Harriehausen and Wirth¹⁶¹ found toxin in the blood of patients with diphtheria, using the Römer method. Less than 0.1 c.c. of serum was sufficient to produce necrosis and, indeed, in one fatal case 0.04 c.c. caused a very severe necrosis in twelve hours. In ten cases of postdiphtheritic paralysis toxin was found five times.

Theobald Smith in 1903 found that a mixture of diphtheria toxin and antitoxin, in which the former was in slight excess, caused a pro-

154. Park, Zingher, and Serota: *Arch. Pediat.*, 1914, xxxi, 481.

155. Kleinschmidt, H.: *Jahrb. f. Kinderh.*, 1913, lxxviii, 442.

156. Otto, R.: *Deutsch. med. Wchnschr.*, 1914, xl, 542.

157. Schütz: *München. med. Wchnschr.*, 1913, lx, 2608.

158. Hahn: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 1366.

159. Kassowitz and Gröer: *Abstr., Jahrb. f. Kinderh.*, 1913, lxxviii, 609.

160. Beyer, W.: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 2353.

161. Harriehausen and Wirth: *Ztschr. f. Kinderh.*, 1913, vii, 132.

duction of a large amount of antitoxin in the blood without producing serious symptoms and suggested then that this method might be used to advantage in children. Von Behring¹⁶² was the first to apply this on a large scale and sent out mixtures for use, determining that the observations should be made with the greatest exactness possible by means of regular examination of the content of the blood of the children immunized. His program is a model of thoroughness. He states in his first communication that the presence of 0.1 of a unit per cubic centimeter of blood was sufficient to protect individuals during an epidemic; with the injection of 100 units into a child the antitoxin disappears in 20 days after reaching 0.025 per c.c. If a homologous serum is used, the passive immunization endures a considerably longer time. He notes that the assumption of the permanent binding of toxin and antitoxin in vitro is a false one and also that the proportion of toxin and antitoxin which will produce symptoms varies with the different species. The human animal is not sensitive at birth, but becomes so after it has been exposed to infections, bacillus carriers, for example, being especially sensitive and producing antitoxin easily. He made a further observation, which requires confirmation, however, that those treated with this new mixture, which will hereafter be referred to as T. A., did not harbor the diphtheria bacilli even though exposed. The experimental work, which is best seen in the original, as, for example, in the article by Viereck,¹⁶³ contains many interesting observations. He shows among other things that the adult is 100 times more sensitive, per kilogram of body weight, than is an infant. Zangemeister¹⁶⁴ also finds this lack of susceptibility in the new-born and in those not infected. The method of administration is described by Schreiber.¹⁶⁵ About 0.1 c.c. of the mixtures, of which there are several, is used at intervals of from three to five days and is given as often as three times. Its effect is noted in from twenty-three to twenty-five days. The lowest serum content produced per cubic centimeter was 0.75, the highest 1, although by repeated injections (four to seven), as much as from 10 to 75 units per cubic centimeter was obtained. The author maintains that there must be from 0.04 to 0.1 per cubic centimeter for effective protection. He found four failures in twenty-one cases.

Kleinschmidt and Viereck¹⁶⁶ prefer the intracutaneous rather than the subcutaneous method of administration. Not only is there heightened immunizing power, but there is an added advantage in that the susceptibility of the individual is indicated by the reaction following the

162. Von Behring: *Deutsch. med. Wchnschr.*, 1913, xxxix, 873.

163. Viereck: *Deutsch. med. Wchnschr.*, 1913, xxxix, 978.

164. Zangemeister, W.: *Deutsch. med. Wchnschr.*, 1913, xxxix, 977.

165. Schreiber, E.: *Deutsch. med. Wchnschr.*, 1913, xxxix, 928.

166. Kleinschmidt and Viereck: *Deutsch. med. Wchnschr.*, 1913, xxxix, 1977.

injection. For example, there may be no more than simple redness produced in some cases, while in others a more general reaction, with fever, malaise, headache and swelling of the lymph glands follows. If the second injection produces a local reaction with distinct redness and swelling, they expect to find about 0.5 units of antitoxin produced per cubic centimeter of blood. Kissling¹⁶⁷ immunized 310 children by this method and of the 111 children who received two prophylactic injections, none contracted diphtheria. Of the 119 who received but one, eight developed the disease. Von Behring and Hagemann¹⁶⁸ also used the intracutaneous method, using 0.1 c.c. of total solution, but they were not of the opinion that the degree of local reaction was an indication of the amount of antitoxin formed. Bauer¹⁶⁹ was unable to free ten carriers of their bacilli by this method. Park, Zingher and Serota¹⁷⁰ used the Schick test to determine whether the active immunization was indicated and found that two thirds did not require it. They determined that the active immunity might not develop until late and when produced lasted from one to two years. Kohn and Sommers¹⁷¹ used this method in five epidemics, 633 cases in all being immunized. They also used the intracutaneous method. Of these patients only two developed the disease and that in a mild form.

Schrieber¹⁷² reports a total of 700 patients treated, of whom but twelve developed diphtheria. Blacher¹⁷³ has analyzed the various types of gallop rhythm. His most important conclusion is that an increase in peripheral resistance is one of the causes, so that it is not necessarily an index of the myocardial change. He assumes that the heart in diphtheria is very sensitive to all stimuli—nervous, mechanical, etc.

Diagnosis and Clinical Findings.—That there may be some difficulty in the diagnosis of diphtheria is shown in the communication of Charlier,¹⁷⁴ who states that phlegmonous angina and malignant diphtheria are almost indistinguishable and if the possibility of the latter disease is not borne in mind and no cultures taken, unsuitable treatment may be instituted. The association of Vincent's angina and diphtheria, or the presence of diphtheria bacilli in cases which are clinically Vincent's angina, is described by Reiche.¹⁷⁵ The author, however, does not discuss the question of serum therapy. Weill¹⁷⁶ summarizes the vari-

167. Kissling: *Deutsch. med. Wchnschr.*, 1913, xxxix, 2500.

168. Von Behring and Hagemann: *Berl. klin. Wchnschr.*, 1914, li, 917.

169. Bauer, J.: *Deutsch. med. Wchnschr.*, 1914, xl, 582.

170. Park, Zingher and Serota: *Jour. Am. Med. Assn.*, 1914, lxiii, 859.

171. Kohn and Sommers: *Deutsch. med. Wchnschr.*, 1914, xl, 13.

172. Schreiber: *Therap. d. Gegenw.*, 1914, lv, 98.

173. Blacher, W.: *Jahrb. f. Kinderh.*, 1914, lxxix.

174. Charlier, G.: *Hygiea*, Stockholm, lxxv, No. 6; abstr., *Jour. Am. Med. Assn.*, 1913, lxi, 1084.

175. Reiche, F.: *Med. Klin.*, 1914, x, 1381.

176. Weill, E.: *Patholog. Infantile*, 1913, x, 101.

ous faucial manifestations of diphtheria and emphasizes especially the perforating, ulcerating, anginal form, which is of a very severe character and which has a tendency to form ulcers in the soft palate, in the gums and other portions of the buccal mucous membrane. Various secondary invaders are found on culture. Lind¹⁷⁷ emphasizes the fact that pharyngeal diphtheria may run a mild course without membrane formation, the diagnosis not being made unless cultures are taken. He fails to state whether or not nasal diphtheria, so commonly associated with this type of infection, was present.

The need of emphasizing the significance and frequency of nasal diphtheria is shown in numerous articles. Moss¹⁷⁸ calls attention to it from the point of view that it is a neglected source of infection in the public schools. Conradi¹⁷⁹ describes the prevalence of nasal diphtheria in infants with nutritional disturbances and shows that serum therapy is without effect. Von Bokay¹⁸⁰ reports two cases of diphtheria of the gums in infants in whom the initial infection was in the nasal tract.

Forbes and Newsholme¹⁸¹ discuss the possible association of membranous rhinitis and diphtheria. For therapy they prefer an autogenous vaccine composed of streptococci and Klebs-Loeffler bacilli. They did not use serum. David¹⁸² assumes that he has seen a case of acute primary diphtheritic pneumonia. A secondary rise in temperature following the crisis led to death. At necropsy tracheal diphtheria was made out and the diphtheria bacilli cultivated in almost pure culture from the lungs. Tylecote¹⁸³ reports a case of diphtheria of the stomach with fatal outcome. Cargin¹⁸⁴ reports a case of membranous enteritis, diphtheritic membranes being passed during the ten days of the illness. Pollak¹⁸⁵ observed a case of diphtheritic sepsis following an infection which resulted from the piercing of the ears in an infant. Kleinschmidt¹⁸⁶ is able to corroborate the statement of Bingel that the intracutaneous injection of toxin produces a very great response in the formation of antitoxin. In the case of anal diphtheria Blühdorn¹⁸⁷ reports epidemics in which the cases were of unusual severity, so that from 20,000 to 30,000 units of antitoxin were insufficient to prevent postdiphtheritic palsies.

177. Lind, S. C.: *Jour. Am. Med. Assn.*, 1913, ix, 1412.

178. Moss, E.: *New Orleans Med. and Surg. Jour.*, 1913, lxxv, 703.

179. Conradi, E.: *München. med. Wchnschr.*, 1913, ix, 512.

180. Von Bokay, Z.: *Ztschr. f. Kinderh.*, 1914, xi, 191.

181. Forbes and Newsholme: *Lancet*, London, 1912, No. 4614, p. 292.

182. David, O.: *München. med. Wchnschr.*, 1913, ix, 2431.

183. Tylecote, F. E.: *Brit. Jour. Child. Dis.*, 1913, x, 211.

184. Cargin, H. M.: *Lancet*, London, 1913, No. 175, p. 23.

185. Pollak, R.: *Wien. klin. Wchnschr.*, xxvi, 1306.

186. Kleinschmidt: *München. med. Wchnschr.*, 1913, ix, 1477.

187. Blühdorn, K.: *München. med. Wchnschr.*, 1912, lix, 1266.

Diphtheria bacilli in the urine are found by numerous observers. Koch¹⁸⁸ took 111 samples from twenty-six patients and found characteristic virulent micro-organisms four times in the urine of two patients. They were found, however, only in the early stages in severe cases in which the patients died with symptoms of cardiovascular failure. Conradi and Bierast¹⁸⁹ found in 155 cases that fifty-four excreted diphtheria bacilli. Beyer¹⁹⁰ also has high positive results, finding them even in cases where the patients harbor the bacilli in the tonsils. Freifeld¹⁹¹ reports a case of secondary cystitis in which the diphtheria bacilli were present for many months, treatment being without effect.

Complications.—Benesi¹⁹² describes three types of diphtheritic otitis; (a) primary diphtheria of the ear; (b) secondary diphtheria of the ear; (c) diphtheritic otitis associated with general infection. Jervis¹⁹³ reports a case of pulmonary abscess. Beyer¹⁹⁴ saw a case of fetid diphtheritic bronchitis with recovery. Schmidt¹⁹⁵ saw a case of bronchiectasis in which diphtheria bacilli were present in the sputum for two years. Stewart¹⁹⁶ reports a case of pulmonary embolism in which the initial attack, which was mild, became rapidly severe. Leede¹⁹⁷ describes four cases of postdiphtheritic hemiplegia. Reiche¹⁹⁸ shows that in eight cases of meningitis the infecting microorganism was never the diphtheria bacillus, being either the meningococcus, *B. Coli*, streptococcus, pneumococcus or staphylococcus. Dynkin¹⁹⁹ describes the necropsy findings in a case of cerebral involvement with aphasia, in which widespread softening was noted. Wolff²⁰⁰ saw a case of postdiphtheritic facial palsy following nasal diphtheria. According to Schuster,²⁰¹ certain strains of diphtheria bacilli may excrete a neurotropic toxin. Thus, three members of the family suffered with postdiphtheritic paralysis.

Therapy.—The intravenous therapy first suggested by von Behring in 1901 has been extensively practiced of late years, but little critical work has appeared with regard to its possible clinical advantage. Beyer²⁰² tried it in twenty-six cases and obtained the impression that

188. Koch, R.: Deutsch. med. Wchnschr., 1912, xxxviii, 2358.

189. Conradi and Bierast: Deutsch. med. Wchnschr., 1912, xxxviii, 1580.

190. Beyer, W.: München. med. Wchnschr., 1913, ix, 240.

191. Freifeld, E.: Berl. klin. Wchnschr., 1913, i, 1761.

192. Benesi, O.: Wien. klin. Wchnschr., 1912, xxv, 1385.

193. Jervis, J. J.: Brit. med. Jour., 1914, i, No. 2781, p. 859.

194. Beyer: München. med. Wchnschr., 1913, lxi, 25.

195. Schmidt: Berl. klin. Wchnschr., 1912, xlix, 2090.

196. Stewart, D.: Lancet, London, 1912, No. 4622, p. 866.

197. Leede, W. H.: Ztschr. f. Kinderh., 1913, viii, 88.

198. Reiche, F.: Ztschr. f. Kinderh., 1914, xi, 452.

199. Dynkin, A. L.: Jahrb. f. Kinderh., 1913, lxxviii, Supplement 267.

200. Wolff, S.: Jahrb. f. Kinderh., lxxvii, No. 2.

201. Schuster, P.: Neurol. Centralbl., 1914.

202. Beyer, W.: München. med. Wchnschr., 1913, ix, 1867.

the membrane disappeared more quickly when a subcutaneous injection was practiced, although its advantage was slight. Alber,²⁰³ on the other hand, is of the opinion that striking results were achieved in thirty-two very severe cases, in which the intravenous administration of serum was combined with intramuscular injections. Of these patients, but two died, even though it was necessary to do five tracheotomies. Fever dropped strikingly in two days at most, and the membrane seemed to come off more quickly. Only one case of serum rash followed. There were, however, eight cases of paralysis of the soft palate, but no general neuromyopathy. Park²⁰⁴ covers the subject of antitoxin administration and considers it from several aspects. Conclusions drawn from his animal experiments verify the observations of other observers; as, for example, the fact that a heterologous serum disappears from the circulation more rapidly than does a homologous serum. When given subcutaneously the maximum antitoxin content of the blood is not achieved until after forty-eight hours, although it lasts from two to three days. He feels that it is better to give one large dose than several small ones. Intravenous administration of serum is indicated in severe cases, 5,000 units in this way being equivalent to 20,000 subcutaneously. Woody²⁰⁵ discusses the effect of very large doses of antitoxin on the basis of mortality statistics. The following figures taken from hospital cases are as valuable as data of this kind can be:

Year	Cases	Deaths	Per Cent.	Dosage
1908.....	1426	127	8.55	Very small
1909.....	2153	144	6.69	Large
1910.....	1870	120	6.42	Larger than 1909
1911.....	1895	130	6.86	Smaller than 1909-1910
1912.....	1676	101	6.02	Larger doses

Nemmsers²⁰⁶ urges the use of the Besredka method of giving antitoxin and shows that the danger even with repeated antitoxin administration is very slight. Schibayama²⁰⁷ tried to avoid anaphylactic phenomena by the rectal administration of antitoxin, but he found that it did not give an appreciable passive immunity. The account of several experiences with the intralumbar administration of serum have appeared. Porak,²⁰⁸ in a case of severe postdiphtheritic paralysis, gave seven such treatments in as many days, with satisfactory results. Kleinschmidt,²⁰⁹ on the basis of laboratory experiments as to the firmness of union between toxin and brain tissue and the power of antitoxin to

203. Alber, K.: *Jahrb. f. Kinderh.*, 1914, lxxx, 312.

204. Park, W. H.: *Boston Med. and Surg. Jour.*, 1913, clxvii, 73.

205. Woody, S. G.: *Jour. Am. Med. Assn.*, 1914, lxiii, 861.

206. Nemmsers, M.: *Deutsch. med. Wchnschr.*, 1913, xxxix, 740.

207. Schibayama, C.: *Deutsch. med. Wchnschr.*, 1913, xxxix, 738.

208. Porak: *Bull. Soc. de pédiat. de Paris*, 1912, p. 314.

209. Kleinschmidt, H.: *Jahrb. f. Kinderh.*, 1912, lxxvi, 179.

separate such mixtures, urges this method of treatment, even though the experiments are disputed by Beyer.²¹⁰ Bingel²¹¹ interprets the vomiting which occurs in malignant diphtheria five or more days after the onset of the disease (when the local signs in the throat are moderate) as being of cerebral origin. He also gave the serum by injection into the lumbar space. Symptomatic improvement was noted, but the high mortality was not diminished. Weintraud also urges this form of treatment.

Krause and Becher²¹³ emphasize the fact that the curative action of diphtheria antitoxin does not depend necessarily upon its strength in vitro. There seems to be a variation of the avidity of different antitoxins for toxin.

The use of vaccine or bacterial substances in the treatment has been attempted with varying results. This method has been used chiefly in the case of carriers or in low grades of infections. Hewlett and Nankivell²¹⁴ used the method of McFadyen, which consists in the grinding, in the presence of intense cold, of the washed diphtheria bacilli and then passing the material through a Berkefeld filter. Results in active cases are not greater than by the method of serum administration. It is interesting to note that one patient was cured only after a necrotic turbinate in the nose had been removed.

Treatment of Carriers.—Petruschky found success in the treatment of carriers by vaccine made from bacilli killed by chloroform and washed free of toxin. Meyer²¹⁶ also had good results, especially in the treatment of nasal diphtheria in infants. Weil²¹⁷ reports the results in fifteen cases, in only six of which were they satisfactory. In these, however, the cultures remained permanently negative. He advises the use of large doses, up to 200,000,000.

It seems to me scarcely necessary to quote completely the literature which has appeared dealing with the "overriding" treatment of diphtheria carriers with staphylococcus cultures (Schiötz). Bissell²¹⁸ calls attention to some studies that he has made, unfortunately not published in full, which tend to show that the use of the staphylococcus spray may deceive the observer. This investigator finds that the "overriding" does not produce extermination of the bacilli in the fauces, but that in

210. Beyer, W.: *Jahrb. f. Kinderh.*, 1913, lxxvii, 65.

211. Bingel, C.: *Deutsch. Arch. f. klin. Med.*, 1911, civ, 370.

213. Krause and Becher: *Deutsch. med. Wchnschr.*, 1913, xxxix, 1081.

214. Hewlett and Nankivell: *Lancet*, London, 1912, No. 4638, p. 143.

216. Meyer, F.: *Ztschr. f. Kinderh.*, 1912, ii, 575.

217. Weil, A. L.: *Laryngoscope*, 1914, xxiv, 804.

218. Bissell, W. G.: *Jour. Am. Med. Assn.*, 1913, lxi, 1393.

the cultures taken the staphylococci tend to overgrow the diphtheria bacilli in the serum tube. De Witt²¹⁹ shows that there is no inherent antagonism between the diphtheria bacillus and the staphylococcus in culture. In animal experiments she also found that, as compared with the controls, in 40 per cent. of the cases the bacilli were gotten rid of more readily by this method, whereas, in 60 per cent. the result was the same. Many of the clinical articles which have appeared on this subject give only a small number of cases, without the careful control suggested as above. Rolleston²²⁰ found that there was nothing accomplished from this treatment in nasal cases. Lorenz and Ravenel²²¹ show, for example, that in one case in their series the patient became a carrier in three months after this treatment and that the reinfection was again "cured" by the use of spray. They also show that in several instances the cultures, which were negative, again became positive. Alden²²² comments on the different by-effects, such as fever, sore throat and edema of the face. He was satisfied with two negative cultures taken two days following the treatment. Ten Broeck²²³ uses the thallophytic fungus, *Achlya mascaris*, as a spray.

The fact that the diphtheria bacilli in carriers localize themselves either in the crypts of the tonsils or in the nasal tissues is being recognized more and more as a basis on which efficient treatment of these troublesome cases must be founded. Reference has been made to the work of Hewlett and Nankivell,²¹⁴ wherein mention is made of the necessity of removing a necrotic turbinate. Albert,²²⁴ after reviewing the methods, suggests that the crypts be cleaned out and treated with a strong antiseptic solution. Greene²²⁵ removes the tonsils and adenoids in bacillus carriers, preceding the operation with prophylactic doses of serum. Dreyfus,²²⁶ while reporting but one case, brings out a very valuable point. The patient described suffered with polyneuritis, chiefly sensory in character. The infection took place in June, the neuritis developing the month after. At the time of operation the antitoxin content of the blood was 0.10 unit per cubic centimeter. In spite of this, 2,000 units were given as an added precaution. The tonsils were found to contain pus, and the presence of diphtheria bacilli was easily demonstrated. Immediate improvement was noted and a complete recovery obtained after removal of the tonsils.

219. De Witt: Jour. Infect. Dis., 1912, x, 24.

220. Rolleston, J. D.: Brit. Jour. Child. Dis., 1913, x, 298.

221. Lorenz and Ravenel: Jour. Am. Med. Assn., 1912, lix, 690.

222. Alden, A. M.: Jour. Am. Med. Assn., 1913, lxix, 1876.

223. Ten Broeck, L. L.: Med. Rec., New York, 1914, lxxxv, 49.

224. Albert: Am. Pub. Health Jour., 1913, lxi, 1027.

225. Greene, J. B.: Boston Med. and Surg. Jour., 1913, clxviii, 912.

226. Dreyfus: Med. Klin., 1914, x, 970.

SCARLET FEVER

Epidemiology.—Striking advance has been made in recent years in the study of scarlet fever. As to the nature of the disease, Von Szontagh²²⁷ reviews his earlier experiences and statements and emphasizes his notion, without bringing out definite experimental evidence, that scarlet fever differs from tonsillitis only in the fact that it indicated a peculiar reaction on the part of the body to the infecting micro-organism. The circumstantial evidence which he relies on to bear out his very firm conviction is found in the frequency of the so-called idiopathic origin of cases without epidemic, the great variability of the rash, the variation in infectiousness, and the long infectivity of the purulent discharges from the nose and ears. He shows, for example, that the frequency of scarlet fever during the year in Budapest tends to remain at a more constant level throughout the year, than is the case in other diseases, such as measles, in which distinct seasonal variations are found.

The question of the existence of scarlet fever in Japan is discussed in a communication,²²⁸ and while it is not distinctly proved that scarlet fever does not exist, it seems quite certain that the disease is one of very great rarity or, if present, occurs in a form which is either different from the type we are accustomed to see, or is very difficult to recognize. The method of transmission by books is discussed by Nesbit.²²⁹ During an epidemic it seemed quite probable that the books from the public library played no part in the spreading of the disease. Fleas are blamed in the London letter²³⁰ for the transmission of scarlet fever. These parasites in London multiply during late summer and autumn, but are not so prolific in winter. The curve of the incidence of scarlet fever parallels this exactly.

The question of a familial predisposition to scarlet fever and especially to the complicating nephritis is a subject of discussion between Mathies²³¹ and Bode.²³² Using the statistical method, the former concludes that there is no distinctly peculiar familial disposition, stating that members of the same family need not have the same type of the disease and that there may often be several different streptococci complications in such a group. The latter, using the same method, finds just the reverse. Urszinji²³³ believes that in time of epidemics children should be subjected to routine throat gargles with an antiseptic solution.

227. Von Szontagh: *Jahrb. f. Kinderh.*, 1912, lxxvi, pp. 1 and 654.

228. *Jour. Am. Med. Assn.*, 1913, lix, 669.

229. Nesbit, O. B.: *Jour. Am. Med. Assn.*, 1912, lix, 1526.

230. London Letter: *Jour. Am. Med. Assn.*, 1914, lxii, 1183.

231. Mathies: *Jahrb. f. Kinderh.*, 1913, lxxviii, Supplement, 116.

232. Bode, P.: *Jahrb. f. Kinderh.*, 1914, lxxix, 438.

233. Urszinji, J.: *Pest. med.-chir. Presse*, 1913, p. 245.

Vaccine prophylaxis is urged by Watters,²³⁴ who uses the method of Gabritschewsky. Three injections of streptococcus vaccine were given at intervals of eight days to nurses who had not yet had scarlet fever. Of the fourteen not injected, five developed the disease; of the twenty-one injected, only one developed the disease. De Biehler,²³⁵ Krukowsky,²³⁶ and Czarkowsky,²³⁷ all used this method and found that of 128 cases only two developed the disease. Keifer and Ferry,²³⁸ in a rather small series also have a favorable impression of the value of this method of prophylaxis. Their vaccine contained both streptococcus and a so-called micrococcus "S." Several injections of about 200,000,000 organisms at intervals of from two to three days served to render efficient protection. Previous to the use of the vaccine a morbidity of 6 per cent. of those exposed was noted. None were affected while the vaccine was used, but the disease again appeared after ceasing to use it. Not only that, but the mortality and frequency of complications is asserted to have been diminished.

The return cases as a source of infection is discussed by Baginsky,²³⁹ after the matter had been brought up as a result of an English law suit. Sexton²⁴⁰ has observed sixteen return cases in three years and notes that they may occur even if there is no discharge from the eyes, the ears or the respiratory tract. They occur usually in the winter and are believed to be due to coryza developing. Wegmann²⁴¹ in thirty-two return cases found that eighteen were of the exudative type, and he believes that these children with their greater susceptibility to infections of the upper respiratory tract are more likely to harbor the infecting organisms. Higgins²⁴² believes that when the diphtheria bacillus has been present there is a greater tendency to a prolongation of the infectious stage beyond the ordinarily accepted period. An interesting instance of reinfection is reported by Jacobson.²⁴³ In a family of four all of whom had had scarlatina, which had been diagnosed by several physicians, the disease again developed.

Diagnosis.—The differentiation of scarlet fever from infectious erythema has long been known as being of the greatest difficulty. Any method which will be of assistance has been eagerly seized upon. Döhle²⁴⁴ reports further investigations dealing with leukocytic inclusion

234. Watters, W. H.: Jour. Am. Med. Assn., 1912, lxiii, 546.

235. De Biehler, M.: Arch. de méd. d. enfants, 1914, xvii, 193.

236. Krukowsky: Medycyna, 1914, xlix, 990.

237. Czarkowsky: Medycyna, 1914, xlix, 985.

238. Keifer, G. L., and Ferry, N. S.: Med. Rec., New York, 1914, lxxxv, 1846.

239. Baginsky, A.: Abstr., Jahrb. f. Kinderh., 1913, lxxvi, 473.

240. Sexton, L. A.: Arch. Pediat., 1913, xxx, 360.

241. Wegmann: Abstr., Jahrb. f. Kinderh., 1913, lxxviii, 474.

242. Higgins, T. S.: Brit. Jour. Child. Dis., 1912, x, 418.

243. Jacobson: Arch. de méd. d. enfants, 1914, xvii, No. 4.

244. Döhle: Centralbl. f. Bakteriöl., 1912, ??? 57.

bodies, which he described the year before. Kretschmer²⁴⁵ found these bodies in all early cases of scarlet fever, but found them also in diphtheria and septic diseases. Glomset²⁴⁶ found them often in health and obtained them artificially by shaking the blood. Schippers and de Lange²⁴⁷ found them in all cases of scarlet fever, but also in other diseases, especially of streptococcal origin. They produced them by injecting dogs with this micro-organism. Bongartz²⁴⁸ found them in typhoid, pneumonia and pertussis. Iskander Ahmed²⁴⁹ found them in German measles. Nicoll,²⁵⁰ however, missed them in this disease. Granger and Pale²⁵¹ missed them in the very severe cases of scarlet fever. They are not present in the so-called toxic rash. The value of these inclusion bodies in scarlet fever may be summed up by stating that they have only a negative diagnostic value; that is to say their absence speaks against a given rash being of scarlatinal origin. The Diazo reaction was suggested as a means of distinguishing between the serum rash and true scarlet fever. Woody and Kolmer²⁵² find that the Diazo reaction is as often positive in diphtheria as in scarlet fever and therefore is of no service. Schultz and Grote²⁵³ used the Abderhalden method, hoping to determine whether a ferment with a specific action upon the scarlatinal lymph glands existed. They found that the ferments obtained were not specific for such glands, but would digest lymph gland tissues in general.

An interesting diagnostic test has been put forward by Umber.²⁵⁴ Noting that urobilinogen appeared in the urine in many cases of scarlet fever, he suggested the use of an acid solution of paradimethylamido-benzaldehyde (Ehrlich's reagent) and found 96 per cent. positive results. Schelenz²⁵⁵ verifies these findings and shows a section of an acute interstitial hepatitis. He emphasizes the fact that the test is valid only when done on the freshly passed urine. Hesse²⁵⁶ also is of the opinion that the test is of value, and finds that it is necessarily coincident with the exanthem and that of course it can not be relied on alone for diagnosis. Gromski²⁵⁷ determined the presence of urobilinogen by means of the spectroscope. He found it to vary with the tem-

245. Kretschmer: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 2163.

246. Glomset, D. L.: *Jour. Infect. Dis.*, 1912, xi, 468.

247. Schippers and de Lange: *Nederl. Tijdschr. v. Geneesk.*, 1913, 544.

248. Bongartz, H.: *Berl. klin. Wchnschr.*, 1912, xlix, 2124.

249. Ahmed, Iskander: *Berl. klin. Wchnschr.*, 1912, xlix, 1232.

250. Nicoll: *Arch. Pediat.*, 1912, xxix, 350, 416; *Ibid.*, 1913, xxx, 346.

251. Granger and Pale: *Brit. Jour. Child. Dis.*, 1913, x, 9.

252. Woody and Kolmer: *Arch. Pediat.*, 1912, xxix, 12.

253. Schultz, W., and Grote, L. R.: *München. med. Wchnschr.*, 1913, lx, 2510.

254. Umber, F.: *Med. Klin.*, 1912, viii, 322.

255. Schelenz, C.: *Med. Klin.*, 1913, ix, 622.

256. Heese, O.: *Med. Klin.*, 1913, p. 294.

257. Gromski: *Abstr., Jahrb. f. Kinderh.*, 1914, lxxix, 383.

perature. Alimentary levulosuria could be produced by giving 40 to 60 gm. levulose. Jakobovicz²⁵⁸ found the Wassermann reaction positive in eighteen out of fifty-five cases. It did not become positive, however, until the end of the third week and occurred most often in the severe cases. Michael²⁵⁹ produced the so-called Rumpel-Lede phenomenon in 60 per cent. of healthy children by means of a blood pressure cuff, pressure of 60 mm. being applied for ten minutes. The spontaneous appearance of this phenomenon is discussed by Meyer,²⁶⁰ who found it in all cases of scarlet fever, and in some cases of measles, sore throat and pernicious anemia. It was not found in German measles or erythema multiforme. Kirsch²⁶¹ is of the opinion that the rash of scarlet fever is due to the action of the toxin upon the muscular element of the capillaries and that, in given cases, the damage may be of a more or less permanent character, leading to the so-called angioneuroses. In the disappearing scarlet fever eruption, he²⁶² finds at times that the tonus of the arteries and veins does not completely return to normal. During this period there are areas of pallor and also the appearance of persisting dilated capillaries. Hahn²⁶³ discusses surgical scarlatina and finds a more intense rash, but a milder course with rare complications, to be the rule. The enanthem is either absent or, if present, is very slight only. The point of entrance of the virus is the face or the mouth.

Rolleston²⁶⁴ has studied the blood pressure in scarlet fever and finds it to be subnormal in 25 per cent. of the cases, varying with the extent and duration of the initial attack. It is little over normal in the first week, but the reading diminishes toward the end of the disease. A very moderate hypertension, which is never extreme or of long duration, is occasionally encountered during the time of kidney complications. It may be concluded, therefore, that the systematic blood pressure readings are of little diagnostic or prognostic significance in themselves. The pronounced hypotension met with in adrenal insufficiency of course calls for adrenal medication. Pancreatitis as a complication of scarlet fever has been seen by Goldie.²⁶⁵ In this series of four cases reported (one followed diphtheria) the pancreas was palpable. The symptoms were chiefly abdominal pain and tenderness, rigidity, tremor, jaundice, vomiting and general malaise. Tixier and

258. Jakobovicz, B.: *Jahrb. f. Kinderh.*, 1914, lxxix, 215.

259. Michael, M.: *Arch. Pediat.*, 1912, xxix, 298.

260. Meyer, O.: *Deutsch. med. Wchnschr.*, 1912, xxxviii, 2019.

261. Kirsch, O.: *Ztschr. f. Kinderh.*, 1912, iv, 92.

262. Kirsch, O.: *Wien. klin. Wchnschr.*, xxvi, 1848.

263. Hahn, H.: *Monatsch. f. Kinderh.*, 1913, xii, 233.

264. Rolleston, J. D.: *Brit. Jour. Child. Dis.*, 1912, ix, 444.

265. Goldie: *Lancet*, London, 1912, No. 183, p. 1285.

Troisier²⁶⁶ discuss the pathologic findings in the pancreas and the adrenal and call attention to the difficulty in definitely diagnosing the condition, pancreatitis, *intra vitam*; abdominal pain is a prominent symptom. In adrenal involvement abdominal or lumbar pain, cardiovascular collapse, and tachycardia are present.

Complications.—Several interesting complications are noted. Silberstein²⁶⁷ reports a very rare complication—symmetrical gangrene of the skin. McCririck²⁶⁸ reports a case of purpura fulminans developing nineteen days after the onset of the disease, with fatal termination. Stevenson²⁶⁹ has a case of purpura hemorrhagica. Eichhorst²⁷⁰ reports a case of complicating erythema nodosa. Riddell²⁷¹ reports a case of necrosis of the vertebra following scarlet fever. Gangrene of the sinus pyramidalis has been encountered by Hecker.²⁷² Edgerly²⁷³ discusses the joint complications in scarlet fever, with particular reference to the purulent form. The ear complications are discussed by Borden.²⁷⁴ The middle ear is involved in 94 per cent. of fatal cases; the mastoid, in 26 per cent. Holmgren²⁷⁵ does not find that the high mortality is necessarily associated with the percentage of otitis media. In his series only 33 per cent. of the patients in the fatal cases had otitis. After the second year the tendency to otitis diminished. This complication may develop without fever. He believes, however, that permanent perforations are present in 40 per cent. of all cases of otitis and that the hearing is affected in 73 per cent. The earlier the otitis develops the worse the prognosis, although the mastoid involvement tends to be associated more often with a late otitis. Children with adenoids have more serious results when the complication develops. He favors local treatment of the throat. The hospital at Stockholm has its own attending otologist for treatment of these patients.

Kalser and Lowy²⁷⁶ have studied the variations in blood serum concentration. An increase in concentration has been noted in most cases and, therefore, is of no value in predicting nephritis. Fishbein²⁷⁷ has used the functional test with phenolsulphonephthalein, but draws no definite conclusions as to the value in prognosis. Schridde²⁷⁸ studied

266. Tixier and Troisier: *Arch. de méd. d. enfants*, 1912, xv, 321.

267. Silberstein, L.: *Jahrb. f. Kinderh.*, 1912, lxxv, 350.

268. McCririck, R.: *Brit. Jour. Child. Dis.*, 1912, No. 110, p. 154.

269. Stevenson, E. C.: *West. Med. Rev.*, 1912, xvii, No. 3.

270. Eichhorst, H.: *Med. Klin.*, 1914, x, 1045.

271. Riddell, D. F.: *Glasgow Med. Jour.*, 1913, lxxviii, No. 6.

272. Hecker, T.: *St. Petersburg. Med. Ztschr.*, xxxvii, No. 18.

273. Edgerly, E. T.: *Jour. Iowa State Med. Soc.*, 1912, ii, No. 3.

274. Borden, C. R. C.: *Boston Med. and Surg. Jour.*, 1913, clxviii, 221.

275. Holmgren, G.: *Otolaryngologiska*, 1912; *abstr.*, *Jahrb. f. Kinderh.*, 1913, lxxviii, 485.

276. Kalser and Lowy: *Deutsch. Arch. f. klin. Med.*, 1914, cxvi, 82.

277. Fishbein, M.: *Jour. Am. Med. Assn.*, lxi, 1368.

278. Schridde, H.: *Beitr. z. path. Anat. u. z. allg. Path.*, 1912, lv, 345.

the pathology of the kidneys in scarlatina and found that the characteristic changes consist in an enormous heaping up of lymphocytes in the capillaries of the medulla. Later, plasma cells, eosinophils and mast cells are found. There are no polymorphonuclears and no streptococci.

Several attempts have been made to prevent nephritis by dietary treatment. De Biehler²⁷⁹ followed two groups of cases. In the first a milk diet was ordered, and but 2.4 per cent. developed nephritis, while among those given meat and mixed diet 5.3 per cent. showed this complication. Gerstley²⁸⁰ comes to the opposite conclusion in following 306 patients, of whom half were given milk and one half mixed diet with meat. Not only were there no bad results, but the anemia so frequently following scarlet fever was prevented in part. Brückner²⁸¹ in 241 cases is also convinced of the fact that the diet does not play a part in the development of the disease. Bell²⁸² makes an interesting attempt in accordance with the idea of Fisher to prevent nephritis, namely, the administration of water and alkali in addition to the usual bed and dietary treatment. He used potassium citrate and sodium bicarbonate in the first ten days of the disease. Of 388 cases, but 2 per cent. developed this complication. The effectiveness of this treatment can be gaged by referring to the article of de Biehler.²⁸³ Rosenfeld²⁸⁴ examined ninety-three patients who had had scarlet fever, of whom fifty-two showed albuminuria at the time of discharge from the hospital. No single severe chronic nephritis was found. Orthostatic albuminuria was found in eight cases and twenty-eight showed a simple albuminuria. Formed elements in small number were found in but six cases.

Therapy.—The finding of a positive Wassermann test in a certain number of cases of scarlet fever has induced some observers to attempt the use of salvarsan for therapeutic purposes. Klemperer and Woita²⁸⁵ administered this drug in sixty cases. The mortality was 8.3 per cent. Nephritis developed in 25 per cent. These figures speak for themselves. Glaser²⁸⁶ used the drug in forty-two cases and found it to be of beneficial influence only in severe throat conditions, and a critical fall in temperature was observed at times. It has no influence on complications or on toxic cases. Lenzmann²⁸⁷ treated forty-seven

279. De Biehler: *Arch. de méd. d. enfants*, 1912, xv, 759.

280. Gerstley, J. R.: *Monatsch. f. Kinderh.*, 1913, xii, 121.

281. Brückner: *Fortschr. d. Med.*, 1912, 1.

282. Bell, A. J.: *Am. Jour. Med. Sc.*, 1912, cxliv, 669.

283. De Biehler: *Arch. de méd. d. enfants*, 1912, xv, 579.

284. Rosenfeld, J.: *Ztschr. f. Kinderh.*, 1912, iv, 265.

285. Klemperer and Woita: *Therap. d. Gegenw.*, 1912, liii, 198.

286. Glaser: *Deutsch. med. Wchnschr.*, 1914, xl, 1760.

287. Lenzmann: *Therap. d. Gegenw.*, 1914, lv, 243.

patients having scarlet fever in a severe form with neosalvarsan, of whom but two died. This was given intramuscularly daily or every second day. The dosage was from 0.15 gm. to 0.3 gm. for children. The maximum dose in three days was never over 0.8 gm.

Reiss and Jungmann²⁸⁸ suggested the use of the serum of convalescents for treatment. The blood was obtained from scarlet fever patients during the third or fourth week. From 50 to 100 c.c. were given by intravenous injection in twelve cases with two failures, these being in a case of sepsis and in a case which turned out to be not scarlet fever. The ten cases were strikingly improved. The temperature fell within four hours, an average lowering of five degrees being attained. The pulse rate also became lower. It was most striking to see how delirious and toxic children would seem almost normal the morning after the injection. It had no effect, however, on secondary bacterial infections. Rowe²⁸⁹ found no difference between serum obtained from patients who had not had scarlet fever and serum from convalescents. He used from 40 to 50 c.c. intravenously and his results were in the main confirmatory of those cited above. Moog²⁹⁰ also found excellent results from human normal serum and believes that in the case of Moser's antistreptococcus serum the good effect obtained was due to the serum as such. Koch²⁹¹ reports twenty-two patients treated with convalescent serum by intravenous injections, 100 c.c. being used. Only bacterial complications were unaffected, while a beneficent influence on the disease was otherwise unmistakable. Barker,²⁹² apparently, independently of the above writers, used blood serum of immunes for the treatment in malignant septic cases. From 4 to 8 c.c. of the human serum hypodermically were given. No striking results were obtained. Prinzing²⁹³ noted that horse serum was not a satisfactory substitute for human serum. The critical fall in temperature did not follow its use and the symptoms were not so strikingly affected. Schultz²⁹⁴ found that the effect of human serum in scarlet fever was not due to the lipoid content, but with the non-treated serum, however, a critical fall in temperature could be produced. There are still some communications dealing with the use of the Moser serum. Schick²⁹⁵ found some improvement produced in toxic patients, while those in whom the bacteria themselves produce the symptoms were unaffected. He believes that the failures hitherto

288. Reiss and Jungmann: *Deutsch. Arch. f. klin. Med.*, 1912, cv, 70.

289. Rowe, C.: *Med. Klin.*, ix, 1978.

290. Moog: *Therap. Monatsh.*, 1914, p. 37.

291. Koch, R.: *München. med. Wchnschr.*, 1913, lx, 2611.

292. Barker, W. S.: *Arch. Pediat.*, 1914, xxxi, 599.

293. Prinzing, F.: *Med. Klin.*, 1914, x, 931.

294. Schultz, W.: *Deutsch. Arch. f. klin. Med.*, 1914, cxv, 627.

295. Schick, R.: *Therap. Monatsh.*, 1912, xxvi, 258.

reported may have been due to the small dosage or to a weak serum. Lewkowicz²⁹⁶ used an antistreptococcal serum in thirty cases, using twenty cases as controls. No effect was noted on the purely scarlatinal symptoms. The bacterial complications are not prevented, although they were surely improved. The Milne²⁹⁷ treatment referred to under measles is commented on by Kretschmer,²⁹⁷ who first calls attention to the fact that this method of treatment was first suggested by Curgenvén in 1890. Kretschmer finds that it has little protective prophylactic value and did not prevent complications. Koerber²⁹⁸ attempted to determine the efficiency of the Milne method by comparing the number of return cases, and he found there was no appreciable difference in the number. He is struck with the fact, however, that all complications in the eucalyptus series were less than in the controls. Only one half as many cases of nephritis developed in the treated series as in those nontreated. Schultze and Goldberger²⁹⁹ used the vaccine treatment as well as the Milne treatment. Their figures are rather suggestive in homes where better conditions might have been expected. Of 354 controls, a mortality of 3 per cent. was encountered, whereas among 128 patients in the slums who were subjected to this treatment the mortality was but 1.5 per cent. Complications were also less frequently observed in the treated patients.

Langauer,³⁰⁰ believing that the tonsils play an almost important rôle in scarlet fever, also believes in their local treatment. He used 10 per cent. hydrogen peroxid, 60 per cent. alcohol and 2 per cent. collargol in glycerin. When a membrane was present he removed this mechanically. Paoloantonio has found what seems to him a most efficient treatment for scarlatinal nephritis. In thirty cases the oral administration of from 10 to 20 drops of epinephrin (1 to 100) controlled the hematuria and edema and prevented the further development of the disease. Diuresis was increased and edema diminished.

296. Lewkowicz, X.: *Monatschr. f. Kinderh.*, 1912, x, 676.

297. Kretschmer, M.: *München. med. Wchnschr.*, 1912, lix, 1809.

298. Koerber: *München. med. Wchnschr.*, 1912, lix, 581.

299. Schultze and Goldberger: *Med. Rec.*, New York, 1914, lxxxv, 931.

300. Langauer, K.: *Pest. med.-chir. Presse*, 1913, p. 124.