months earlier. She was found to have a raised but unchanging titre of complement-fixing antibodies to mumps virus particle antigen in her two specimens of sera (the titres of Sendai complement-fixing antibodies showed a rise from 1/16 to 1/64, but the corresponding titres of mumps complement-fixing antibodies were 1/32 and 1/32).

In the 23 cases reported here evidence of Sendai infection was found in retrospect and no specimens of throat washings or swabs were available for isolation tests. The failure, so far, to isolate a virus only stresses the importance of obtaining suitable specimens for attempted virus isolation from cases of suspected influenza.

Summary and Conclusion

During 1956 the 872 suitably paired sera from cases of respiratory illness sent to this laboratory for investigation were examined for evidence of complement-fixing antibodies to Sendai virus.

Twenty-three cases of respiratory illness have been described in which a fourfold or greater rise in titre of complement-fixing antibodies to Sendai virus was found.

The illnesses varied from a mild influenza-like malady to a severe pneumonia; cough and laryngeal symptoms were often prominent. Cases were found in both sexes and among all age groups.

Evidence of an antigenic relationship between mumps and Sendai antigens was found. This was illustrated in a proportion of patients suffering from mumps who showed a rise in complement-fixing antibodies to both Sendai and mumps virus particle antigens.

Only one case in the present series gave a rising titre of complement-fixing antibodies to both Sendai and mumps virus particle antigen. The possible cause of this is discussed.

The C.F.T. for Sendai virus infection appears to be reliable, and a diagnosis can be readily made by serological means in cases of respiratory illness. Cross-reactions did not occur with other virus antigens used during the routine investigation of sera for respiratory illness.

Sendai virus or a related virus should be considered as a possible cause of respiratory disease, especially during the winter months.

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REFERENCES

- Chanock, R. M. (1956). *J. exp. Med.*, **104**, 555.
 Fukumi, H., Nishikawa, F., and Kitayama, T. (1954). *Jap. J. med. Sci. Biol.*, **7**, 345.
 Jensen, K. E., Minuse, E., and Ackermann, W. W. (1955). *J. Immunol.*, **75**, 71.
 Kuroya, M., Ishida, N., and Shiratori, T. (1953). *Yokohama med. Bull.*, **4**, 217.
 Sano, T., Niitsu, I., Nakagawa, I., and Ando, T. (1953). *Ibid.*, **4**, 199.
 White, G. B. B., Gardner, P. S., Hope-Simpson, R. E. (1957). *British Medical Journal*, **1**, 381.

NEWBORN PNEUMONITIS VIRUS (TYPE SENDAI)

EVIDENCE OF INFECTION IN SOUTH-WEST SCOTLAND

BY

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The newborn pneumonitis virus (N.P.V.) (type Sendai) was isolated by Kuroya *et al.* (1953) from the lungs of newborn infants who died during an outbreak of pneumonitis in the wards of the department of paediatrics of the Tohoku University, Japan. The virus was cultured by intranasal inoculation of mice and was subsequently adapted to the allantoic cavity of the embryonated egg. Isolations of N.P.V. were reported about the same time by Misao (personal communication to Kuroya *et al.*) and Ohashi (personal communication to Kuroya *et al.*), from an epidemic of A prime influenza; later Matsuzawa *et al.* (1954) found antibody to the virus in healthy adults in various parts of Japan.

In the U.S.A. Jensen *et al.* (1955) found antibody to N.P.V. by haemagglutination inhibition tests in about 40% of paired sera from a variety of illnesses. These authors observed the highest levels of antibody in the under 18 age group, and in serum from more than 559 varied illnesses they found eight instances of what they considered a significant rise in antibody titre to N.P.V. In only two patients were they able to correlate rising titres of antibody with a clinical illness: one patient was diagnosed as a case of atypical pneumonia; the other case as a mild respiratory illness.

This paper presents evidence for the existence in south-west Scotland of an antigenic stimulus producing antibodies to N.P.V. Antibody was discovered on routine screening of paired serum specimens. Fourfold rising titres were observed in nine instances by complement-fixation tests; clinical details of these are summarized. No attempts were made to isolate the virus.

Methods

The population investigated and the techniques used have been described briefly in a previous paper (Grist, Somerville, and Carson, 1957). During the winter seasons of 1955 and 1956 the sera were drawn from three sources: paired sera were obtained from 175 adults admitted to the pneumonia wards of Ruchill Hospital, Glasgow; 97 pairs were obtained from infants admitted to the infant pneumonia wards of the same hospital; and 172 serum pairs were provided from cases of upper respiratory illness by general practitioners participating in the scheme for detection of influenza in the community during the course of influenza vaccine trials by the Medical Research Council (1955). In every instance the interval between collection of the serum samples in a pair was more than 7 and usually between 10 and 14 days.

The Sendai strain of N.P.V. was supplied by the World Influenza Centre of the World Health Organization. This virus was passed by the allantoic route in embryonated eggs at the eleventh day of incubation. Allantoic fluids were harvested and pooled 72 hours after incubation with 0.1 ml. of 1/1000 dilution of virus. After titration in "chess-board" experiments the pooled allantoic fluid was used at an

optimal dilution as an antigen in complement-fixation (C.F.) and haemagglutination-inhibition (H.I.) tests. Positive and negative control ferret sera were supplied by the Virus Laboratory of the School of Public Health, University of Michigan.

The C.F. and H.I. techniques employed have both been described by Grist (1955). A small-volume C.F. test with a 90-minute fixation period at 37° C. was used with all adult sera, but infant sera were tested by a small-volume cold-overnight test in view of the relative insensitivity of short fixation with infant sera reported by Grist (1957). In H.I. tests identical techniques were used with adult and infant sera, but owing to shortage of serum C.F. tests only were performed in some instances.

Tests for virus-neutralizing antibody were not performed because of shortage of serum.

Results

The results of C.F. tests on paired sera, using N.P.V. as antigen, are shown in Table I. Failure to fix complement at a dilution of 1/8 or less was observed in 88% of sera, and a small proportion from each group was found to be anti-complementary. Complement fixation at 1/16 or 1/32 and twofold rise or fall in titre were observed in 12 cases, but only fourfold rises were regarded as positive evidence of the relevant antigenic experience. A fourfold rise in titre was found in nine instances—three in the adult pneu-

TABLE I.—Distribution of Antibody Titres to Newborn Pneumonitis Virus by Complement Fixation

Category of Cases	Total Cases	C.F. Antibody Titres of Serum Pairs							
		A.C.*	<8	8	16	32	Rising ×2	Falling	Rising ×4
Adult pneumonia	175	8	154	6	—	1	2	1	3
Infant "	97	10	87	—	—	—	—	—	—
"Influenza" ..	172	13	130	15	4	—	3	1	6

* Anticomplementary.

TABLE II.—Distribution of Antibody Titres to Newborn Pneumonitis Virus by Haemagglutination Inhibition

Category of Cases	Total Cases	H.I. Antibody Titres of Serum Pairs							
		<8	8	16	32	64	128	Rising ×2	Falling
Adult pneumonia	162	112	19	11	12	1	1	3	—
Infant pneumonia	58	24	13	16	4	—	—	—	1
"Influenza" ..	161	95	37	14	8	2	—	4	—

TABLE III.—Serological Results in 9 Cases Showing Fourfold Rise in Complement-fixation Titre with Newborn Pneumonitis Virus Antigen

Case No.	Date of Onset	Age and Sex	Diagnosis	Day of Disease—Serum Specimens	C.F. Titres			H.I. Titres	
					N.P.V.	Flu. A	Flu. B	N.P.V.	Flu. C
F2	3/12/54	38 F	"Influenza" ..	5 22	<8 16	N.T. <8	N.T. <8	N.T. 8	16
F32	1/1/55	35 M	"	5 21	<8 32	<8 8	N.T. <8	<8 16	16
F38	8/1/55	47 M	"	5 14	<8 16	N.T. <8	N.T. <8	8 8	<8 <8
F136	3/1/56	52 F	"	1 15	<8 32	8 16	<8 <8	16 16	64 64
F141	8/1/56	42 M	"	1 25 47	8 8 32	N.T. <8 N.T.	N.T. <8 N.T.	16 32 64	N.T. N.T. N.T.
F147	13/1/56	36 F	Pneumonia ..	1 10	<8 16	N.T. <8	N.T. <8	32 32	64 64
R293	17/11/54	69 M	Bronchopneumonia ..	5 15	<8 32	N.T. <8	N.T. <8	<8 16	16 16
R496	24/1/56	75 M	Pneumonia ..	4 14 21 28 42	<10 >160 >160 160 160	N.T. <8 N.T. N.T. N.T.	N.T. <8 N.T. N.T. N.T.	8 128 N.T. N.T. 40	16 16 N.T. N.T. N.T.
R574	26/3/56	65 F	Pneumonia + congestive cardiac failure	22 32	<8 128	N.T. <8	N.T. <8	<8 128	64 64

N.T. = Not tested.

monia and six in the "influenza" group. For comparison the results of H.I. tests are shown in Table II. In this series 78% failed to inhibit haemagglutination at a serum dilution of 1/8 or less, but this proportion is raised to 95% if a dilution of 1/32 or less, as is customary with the influenza viruses, is used as the index of negativity. Only four cases were found with a fourfold rise in titre by H.I., and these also showed a similar rise by C.F. tests. A falling titre by H.I. in the case of one infant was not reflected in the C.F. test.

The main findings in the nine cases which showed a fourfold rise in titre by one or other test are shown in Table III. In contrast to the experience of Japanese investigators all cases in this series were adult. The description "influenza" in the diagnosis column denotes an influenza-like illness of varying severity in a patient drawn from the general-practitioner "influenza" group in Tables I and II. The other cases belong to the group of adult pneumonias.

In general, antibody reacting with N.P.V. appeared between the 5th and 10th days of illness, and the titre increased until the end of the second or third week. Thereafter the level decreased slowly during the third and subsequent weeks.

The appearance of antibody was delayed in two cases—F141 and R574. In these an initial febrile illness was complicated later by acute respiratory symptoms, which in turn were followed by rising titres of antibody reacting with N.P.V. One case (R 496) developed a rising antibody titre to influenza during the course of his stay in hospital at a time when the antibody titre to N.P.V. was at its highest level. The influenzal antibody response followed a clinical relapse during the convalescent phase of his initial illness. Apart from this case no other evidence of infection with influenza viruses was found in the nine patients under discussion.

Clinical Aspects of Infection with N.P.V.

All patients suffered from an acute respiratory illness which differed in severity from case to case but which presented no distinguishing pattern. All were diagnosed clinically as suffering from either pneumonia or influenza during winter months when both pneumonia and influenza were prevalent. The main features of the illness in each group are summarized in Table IV.

The cases of patients who were admitted to hospital with a diagnosis of pneumonia may be briefly described.

Case R293.—A man aged 69, whose illness began on November 17, 1954, was admitted to hospital five days after the onset of febrile illness. The presenting symptoms were headache, pleural pain, cough, and breathlessness. On admission there was minimal sacral oedema with slight overfilling of neck veins. Chest examination revealed coarse moist sounds at all areas despite

TABLE IV.—*Summary of Two Types of Case Showing Antibody Reacting with Newborn Pneumonitis Virus*

	Influenzal	Pneumonic
No. of cases	5	4
Age (average)	43 years	61 years
Sex	M—3; F—2	M—2; F—2
Duration (average) ..	3 weeks	6 weeks
Previous history ..	Normal	1 normal; 1 congestive cardiac failure; 2 chronic bronchitis
Onset abrupt with ..	Headache; myalgia; fever—not over 101° F. (38.3° C.); malaise	Headache. Fever±. Malaise
Followed by	Nasal catarrh; pharyngitis; cough	Signs of pneumonia with or without congestive cardiac failure
Physical findings ..	Few	Lobar or bronchopneumonia with or without congestive cardiac failure
Treatment	Antipyretic therapy	Penicillin
Result	Satisfactory	Satisfactory

absence of dullness or diminution of air entry. W.B.C. was 20,600 per c.mm. X-ray examination revealed patchy consolidation in lower lobe of right lung, and a normal heart shadow. Treatment with crystalline penicillin removed fever in 24 hours, and thereafter improvement was rapid despite the development of a few crepitations at the left lung base following an attack of tachycardia on the 12th day of illness. X-ray examination showed chest clear at 15 days. This patient was reputed to have had a coronary thrombosis three years previously which was followed by an episode of congestive cardiac failure, but electrocardiograms during the course of the present illness revealed only "left heart strain and myocardial disease." During the first ten days in hospital antibody reacting with N.P.V. increased from less than 1/8 to 1/32 by C.F. and from less than 1/8 to 1/16 by H.I. tests.

Case R496.—A man aged 75, whose illness began on January 24, 1956, had a history of chronic bronchitis for many years. On admission to hospital three days after the onset of acute exacerbation of bronchitis, he was cyanosed and orthopnoeic and producing large amounts of grey sputum. Auscultation revealed marked bronchospasm with some scattered adventitious sounds. X-ray examination showed patchy consolidation and a normal heart shadow. W.B.C. was 8,000 per c.mm. Treatment with crystalline penicillin and aminophylline produced clinical improvement in three days, but relapse occurred 15 days after admission to hospital with exacerbation of symptoms, fever, and malaise. A second course of treatment with penicillin and aminophylline again produced improvement, and the subsequent recovery was uneventful. Antibody reacting with N.P.V. increased from less than 1/10 to more than 1/160 by C.F. tests between the 4th and 14th days of illness. During the same time a rise in titre from 1/8 to 1/128 occurred by H.I. A specimen obtained at the 42nd day of illness still revealed a C.F. antibody titre of 1/160, although the H.I. titre had fallen to 1/40. Titration of this specimen for antibody to influenza A in parallel with the serum specimen obtained at the 14th day revealed that during this time antibody to influenza A had increased by C.F. tests from less than 1/8 to 1/160. The pooled specimen resulting from serum obtained at the 21st and 28th days of illness, when tested for antibody to influenza A, revealed a C.F. titre of 1/80, and it was therefore concluded that, while the initial illness had produced the rise in titre of antibody reacting with N.P.V., the clinical relapse, occurring at the height of the antibody response to the first agent, had produced antibody to influenza A.

Case R574.—A woman aged 65, whose illness began on March 26, 1956, was admitted to hospital with severe dyspnoea of sudden onset 21 days after a mild influenza-like illness. She was afebrile on admission, but overfilling of neck veins and cyanosis were present. Chest examination revealed inspiratory and expiratory rhonchi and crepitations at all areas. W.B.C. was 12,800 per c.mm. X-ray examination showed cardiac enlargement with bilateral extensive pulmonary congestion, consistent with cardiac failure. A temperature of 101° F. (38.3° C.) which developed 24 hours after admission to hospital was controlled in 72 hours by crystalline penicillin although no pathogenic bacteria were isolated in culture. An E.C.G. revealed myocardial damage. Treatment with penicillin continued for 10 days, and aminophylline was administered frequently during the first few days, after which the patient was digitalized. Subsequent recovery was uneventful. During the first ten days following admission to hospital antibody reacting with N.P.V. increased from less than 1/8 to 1/128 by both C.F. and H.I. tests.

The cases classified as "influenza" were with one exception treated at home by general practitioners and were mild

febrile infections of the upper respiratory tract. Three were female and three male, and the ages ranged from 35 to 52 years. The illness lasted between two and eight weeks and none was fatal. In five cases the onset was abrupt, with headache, myalgia, fever, and malaise rapidly followed by nasal catarrh and pharyngitis. The temperature did not exceed 101° F. (38.3° C.) and quickly settled. An irritable cough developed in two cases. All five had few physical findings within the chest, and none had an x-ray examination. The condition resolved with mild antipyretic therapy.

The sixth patient had a prolonged illness. A basal pneumonia which was treated with penicillin was slow to resolve at first and x-ray examination revealed consolidation of the right middle and lower lung lobes. The patient was detained in hospital, and resolution occurred spontaneously over five weeks.

Discussion

The present studies reveal the presence of a hitherto unrecognized antigenic stimulus in the adult population of south-west Scotland. This is capable of producing antibody reacting with N.P.V. The number of reports in the world literature of infection with this agent is small, and the pattern of illness attributable to it has not been clearly defined. However, all reports are in agreement that the severe illness and high fatality rate in newborn infants originally reported by Kuroya *et al.* (1953) are not seen when the adult is infected. Volunteer experiments in adults by Kuroya *et al.* (1953) suggested that the illness was mild and febrile, affecting the upper respiratory tract and clinically resembling influenza. Collateral confirmatory evidence was supplied by Misao and by Ohashi (personal communications to Kuroya *et al.*) when they isolated viruses antigenically similar to N.V.P. from adults during an influenza epidemic in Japan. One of two adult cases described briefly by Jensen *et al.* (1955) suffered from a mild respiratory illness at a time when influenza B was prevalent, and the second case was described clinically as suffering from an atypical pneumonia.

The present investigation revealed infection with this agent during winter months when influenza viruses A and B were present, but influenzal antibody was only once associated with antibody reacting with N.P.V. The incidence of infection with influenza in the population under investigation has already been described (Grist *et al.*, 1957).

In addition our present experience confirms the mild influenza-like nature of the illness in the majority of cases, but adds the possibility of a more severe type affecting persons who have a previous history of chronic bronchitis or heart disease, and who fall within an older age group.

Summary

We examined 444 paired sera by complement-fixation test, and 381 of these pairs by haemagglutination-inhibition test for antibody reacting with newborn pneumonitis virus in the population of south-west Scotland. Evidence was found in adults for the existence of an agent which is capable of producing this antibody. Nine instances were detected of a fourfold rising titre by complement-fixation test, and clinical details recorded from these cases revealed that the infection presented either as a mild influenza-like illness or as pneumonia.

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ADDENDUM.—Since this paper was prepared for publication an outbreak of respiratory illness caused by infection with newborn pneumonitis virus in a hospital for the chronic

sick and infirm has been reported by Bruce White *et al.* (*British Medical Journal*, 1957, 1, 381). In this outbreak six patients developed rising titres of antibody, and the clinical illnesses resembled influenza.

REFERENCES

- Grist, N. R. (1955). *British Medical Journal*, 2, 994.
 — (1957). *Scot. med. J.*, in press.
 — Sommerville, R. G., and Carson, H. G. (1957). *British Medical Journal*, 1, 378.
 Jensen, K. E., Minuse, E., and Ackermann, W. W. (1955). *J. Immunol.*, 75, 71.
 Kuroya, M., Ishida, N., and Shiratori, T. (1953). *Yokohama med. Bull.*, 4, 217.
 Matsuzawa, M., Shiratori, T., and Kikuchi, H. (1954). Quoted by Jensen *et al.* (1955).
 Medical Research Council (1955). *British Medical Journal*, 2, 1139.

AGAMMAGLOBULINAEMIA WITH SPLENOMEGALY

BY

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Agammaglobulinaemia is a biochemical defect characterized by absence of serum gamma-globulin and is usually associated with deficiency of immunoglobulins, resulting in increased susceptibility to infection. The frequent recurrence of infection, which is the principal clinical feature of this condition, has been accentuated by the use of antibacterial drugs which have enabled these subjects to survive a succession of infections to which they might otherwise have succumbed.

Since agammaglobulinaemia associated with recurrent sepsis was first described by Bruton (1952) over 40 cases have been recorded. In these cases the symptoms and signs of the disorder have usually been those of recurrent infections. The purpose of this paper is to report two cases of agammaglobulinaemia in which enlargement of the spleen and liver and generalized enlargement of lymph nodes were also outstanding clinical features.

Case 1

The patient, a man of 33, had suffered from measles and pertussis in childhood, but apart from this had enjoyed good health until 1942, when at the age of 19 he had pneumonia. Enlarged lymph nodes were palpable in the neck and in both axillae, and the chest radiograph showed enlarged lymph nodes at the hilum of the right lung and shadows in the right lung. Respiratory symptoms recurred four months later and septic tonsils were removed. He remained in poor health and in the subsequent 14 years suffered numerous infections. In 1945 he had gingivitis, laryngitis, and pleurisy, and in 1946 seborrhoeic impetigo, herpes zoster, laryngitis, and pneumonia. In 1946 generalized enlargement of lymph nodes was present, enlarged nodes being palpable in the cervical, epitrochlear, axillary, and inguinal regions on both sides. In 1948 he had mumps and a respiratory infection, and in 1949 furunculosis and several respiratory infections.

In 1950 he was admitted to hospital with pleurisy. A firm spleen was palpable 1 in. (2.5 cm.) below the left costal margin, and the liver was palpable 1 in. (2.5 cm.) below the right costal margin. Generalized enlargement of superficial lymph nodes similar to that found in 1946 was noted and the chest radiograph again revealed right hilar node enlargement. Penicillin was given and respiratory symptoms improved, but jaundice occurred later and lasted three weeks. At this time the level of serum globulin was normal and albumin was raised. Total protein was 8.8 g. per 100 ml. (albumin 6.1 g., globulin 2.7 g.). The thymol turbidity was 4 units (normal). The blood count was normal. Biopsy of an enlarged lymph node showed reactive hyperplasia but no other abnormality.

Between 1950 and 1954 he suffered six acute respiratory infections. In 1954 sarcoidosis was suspected because of respiratory symptoms, hilar node enlargement, lymphadenopathy, hepatosplenomegaly, and a negative Mantoux test. Another enlarged lymph node was removed and showed reactive hyperplasia but no evidence of sarcoidosis or any primary reticuloses. The total serum protein was 8 g. per 100 ml. (albumin 6.4 g., globulin 1.6 g.).

In November, 1955, he had measles for the second time. In December the zinc flocculation test was 5 units (normal). In February, 1956, he had pneumonia and was treated with tetracycline, but pneumonia recurred in May and he was again treated with tetracycline. In May the zinc flocculation test showed only 1.5 units, suggesting that the serum gamma-globulin was low. In June the total serum protein was 6 g. per 100 ml. (albumin 4.6 g., globulin 1.4 g.). In July he had another acute respiratory infection which responded to chlortetracycline.

On admission to hospital in July he was seen to be a lean man with a frequent dry cough. The spleen was palpable 8 cm. below the left costal margin and felt firm. The liver was palpable 6 cm. below the right costal margin. Moderately enlarged firm lymph nodes were palpable in the epitrochlear, axillary, and inguinal regions on both sides. Rales were heard at the bases of both lungs.

Investigations

Paper electrophoresis of serum revealed no detectable gamma-globulin. Total serum protein was 6.39 g. per 100 ml. Electrophoretic analysis on the Tiselius apparatus (Professor N. H. Martin) showed: albumin, 62.8% (4.01 g.); globulins—alpha-1 5.4% (0.34 g.), alpha-2 14.4% (0.94 g.), beta 17.5% (1.12 g.), gamma 0.0% (less than 100 mg. per 100 ml.). Gamma-globulin was present in negligible quantities as determined by immunological techniques—approximately 60 mg. per 100 ml. by both red-cell agglutination and precipitation diffusion methods. Zinc flocculation test, 1 unit; thymol turbidity test, 2 units.

Deficiency of circulating antibodies was demonstrated by the following investigations. His red blood cells were group A, but anti-B isoagglutinins were present in the serum in negligible quantities (titre 1 in 2). His serum failed to agglutinate suspensions of *Salm. typhi* or *Salm. paratyphi A* and *B* in spite of previous T.A.B. inoculation. Mumps complement fixation was negative in spite of a previous history of mumps. The antistreptolysin titre was less than 10 units per ml. The Schick and Dick skin tests were positive. No skin reaction occurred with 100 tuberculin units of P.P.D., or with *Candida albicans* antigen, which gives delayed-type reactions in 95% of healthy adults. The *C. albicans* complement-fixation test was negative.

Another axillary lymph node was removed. Examination of sections stained by haematoxylin and eosin showed diffuse hyperplasia of the reticulo-endothelial elements of the stroma of the node. The germinal follicles were numerous, with considerable variation in size, some follicles being large and hyperplastic. The axillary lymph node removed in 1954 had a similar appearance, and that removed in 1950 was also similar except that stromal hyperplasia was not so intense. Reticulin stains revealed well-marked follicular patterns. Examination of sections stained specially for plasma cells with Unna-Pappenheim methyl-green pyronine stain showed that in the node removed in 1956 transitional plasma cells (Fagraeus, 1948) were plentiful in the germinal follicles and along the sinuses. Mature plasma cells were very sparse, however, in contrast to normal nodes, where large numbers of mature plasma cells can usually be found in the sinuses. The appearance of the node removed in 1954 was similar.

The chest radiograph showed bilateral hilar lymph-node enlargement and shadows at the bases of both lungs.

The E.S.R. was persistently low even during infections (1–4 mm. per hour, Westergren). Red-cell and white-cell counts were normal. During infection normal neutrophil leucocytosis occurred.