to be concerned in the synthesis of fats from protein, and perhaps in tryptophan metabolism. Biologically active derivatives also include pyridoxal (concerned in tyrosine decarboxylation and possibly in biochemical transaminations) and pyridoxamine. Another derivative, pyridoxic acid, is described as a dietary factor for chicks. The need of man for pyridoxin has been questioned: symptoms of deficiency are, however, said to include cheilosis resembling that seen in deficiency of riboflavin. Pyridoxin has recently been used in the treatment of agranulocytosis.

Pantothenic acid (formerly called "chicken pellagra factor" or "filtrate factor") prevents a characteristic dermatitis in birds. It is needed also by dogs and pigs. Signs of deficiency in rats include growth failure, dermatitis, nose-bleeding, depilation about the nose, occurrence of a sticky exudate in the eyelids, and achromotrichia, together with adrenal lesions. It is also a growth factor for micro-organisms. Pantothenic acid is thought to be probably needed by humans, but its significance is still obscure.

Inositol is identical with bios I, needed for growth of yeast and other micro-organisms. An experimental deficiency in rats or mice is said to cause alopecia. Deficiency in man is unknown, but inositol may possibly be a "secondary nutrient"—that is, it may stimulate the intestinal microflora to synthesize other nutrients essential to the host.

Para-aminobenzoic acid (or "Paba") is a growth factor for various micro-organisms, and is said to prevent achromotrichia in some experimental species. It may be a "secondary nutrient" (see above) for man. Its special interest is that drugs of the sulphonamide type exert their bacteriostatic action by "blocking" the bacterium's supply of Paba. Conversely, Paba can negative the bacteriostatic action of the sulpha-drugs. Recent work suggests that large doses of Paba itself may exert an anti-infective action in animals in some circumstances.

"Q" FEVER

A SEROLOGICAL INVESTIGATION OF A GROUP OF CASES PREVIOUSLY REPORTED AS PRIMARY ATYPICAL PNEUMONIA

BY

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Derrick (1937) first described "Q" fever in Australia, and the causative agent was isolated by injection of the blood and urine into guinea-pigs. Burnet and Freeman (1937) showed that the infective agent was a rickettsia, which was subsequently named *Rickettsia burneti*. In the winter of 1944 an epidemic of so-called primary atypical pneumonia occurred among New Zealand troops in the Cassino area (Adams and Porteous, personal communication). Later in 1944 Turner (1945) recorded a similar epidemic of 280 cases from the Naples area. During the same year an outbreak of primary atypical pneumonia occurred among German troops in Greece, and was referred to by them as the "Balkan gripe." Dr. Caminopetros, at the Pasteur Institute in Greece, was able to establish the infection in guinea-pigs by injection of blood taken from cases in the early stages of the infection. Subsequently, blood taken from these guinea-pigs was investigated at the laboratories of the Commission on Acute Respiratory Diseases at Fort

Bragg, North Carolina (1946), and *R. burneti* was isolated. In the winter of 1945 an epidemic of "atypical pneumonia" occurred among New Zealand and British troops in the Naples and Caserta area. Similar epidemics arose among British and American troops in the Mediterranean theatre of operations. Detailed studies of some of these epidemics have recently been reported by Robbins and Rustigian (1946). In a British parachute regiment, probably infected in Athens before being transferred to Italy, serological tests later established the diagnosis of "Q" fever. Four epidemics among U.S. troops in Northern Italy were fully investigated. *R. burneti* was isolated from the blood of some of these cases, and by serological tests it was demonstrated that 75% of the cases of "atypical pneumonia" in the same area were in fact cases of "Q" fever.

In May, 1945, an epidemic of "atypical pneumonia" occurred in mid-Atlantic amongst a group of airmen who had recently been stationed at Grottaglie Air Base in Southern Italy, in the Taranto area. These were fully investigated when the airmen arrived at Camp Patrick Henry, Virginia (Feinstein *et al.*, 1946). Epidemiological and aetiological studies were made, and it was demonstrated that the infective agent was the "Balkan gripe" strain of *R. burneti* (Commission on Acute Respiratory Diseases, 1946).

Clinically the epidemic of so-called primary atypical pneumonia recorded by Adams *et al.* (1946) was very similar to the cases recorded by Robbins and Rustigian (1946) and by Feinstein *et al.* (1946), in which the aetiological agent was established as *R. burneti*. On this account it was decided to attempt to establish the infective agent in the New Zealand Hospital cases.

Clinical Features

For complete clinical details of the cases readers are referred to the original report of Adams *et al.* (1946). The main clinical features may be summarized for the sake of completeness.

The epidemic occurred between February and April, 1945, and during this period 511 cases were reported in the Naples-Caserta area, 161 of which were treated at the 2nd N.Z. General Hospital. Of these, 50 consecutive cases were studied in detail clinically and by serial pathological and radiological investigations.

In brief, the clinical picture was as follows. In most cases there was a prodromal period of about six days. The actual onset was abrupt in 96%, and severe headache, malaise, lassitude, and anorexia were the most constant symptoms. Pyrexia from the onset averaged 8.6 days, was over 103° F. (39.4° C.) in 70% of cases, and defervescence was by lysis in 86%. The pulse followed the temperature, though it showed a tendency to a relative bradycardia. The respiratory rate was little affected. Cough was present in 94%, but was not an outstanding feature; it occurred about the fifth day. Sputum was scanty and in 28% contained blood. Chest pains occurred in 46% of the cases, and in 26% of these a pleural rub was detected.

Physical Signs.—Severe toxæmia was a feature of some, and one-third showed generalized rhonchi on admission, but the most characteristic sign was a localized patch of sticky persistent crepitations, which were heard on an average on the sixth day from the onset of the acute symptoms. Usually there was enlargement of glands, and the spleen was palpable in 36% of cases. Scanty small pink macules fading on pressure were observed on the chest, back, and flanks in the early stages in 34% of cases.

Laboratory Investigations.—The results of serial pathological investigations can be summarized in brief. The white cell count revealed a slight polymorphonuclear

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response followed by a slight depression, which was maximal at the end of the first week. Thereafter there was a rise of polymorphs and lymphocytes, reaching a peak at the 16th to 18th day. Differential counts showed a slight relative lymphocytosis after the initial period. The blood sedimentation rate was elevated for two to three weeks. Cephalin-cholesterol flocculation was insignificant early in the disease but increased rapidly after convalescence had been established in the second week, thereafter falling slowly. Using horse cells, a significant positive heterophil antibody reaction was found in 36% of the cases at some stage of the disease. All but three, which were weakly positive, gave negative tests for cold agglutinins at all stages.

Radiological Investigations.—Postero-anterior and lateral studies were made in all cases. The characteristic findings were the localization of the lesion to one or more bronchopulmonary segments. The infiltration could be described as hazy mottled densities. These investigations also revealed the importance of the lateral studies for the demonstration of lesions situated beyond the heart shadow or in that portion of the lung situated behind the summit of the dome of the diaphragm. Complete radiological resolution in the majority occurred within six weeks of the onset.

Epidemiology

The possible route and sources of infection were examined in detail in some of the Northern Italian epidemics, and although no vectors such as ticks or fleas were incriminated it was found that the disease often made its appearance in units occupying farm billets and also where men were living in close proximity to animals such as cattle, rats, and pigeons. Various forms of insects were discovered in several of these billets, but it was thought that cases probably occurred by inhalation infection arising from the dust and droppings. The complete absence of insect-bites in any of the cases and the uniform picture of pulmonary involvement suggested that the route of infection was via the upper respiratory tract, such as probably occurred in the laboratory infection with the same agent (Robbins and Rustigian, 1946) and as is also seen in laboratory infections with other rickettsial diseases such as epidemic, murine, and scrub typhus. It was also found that many of the civilian population in the area where these cases occurred showed a high level of antibody to "Q" fever, which suggests that the infection was endemic in the local inhabitants.

In the New Zealand Hospital cases most of the patients came from a British infantry training depot where men were living in hutments and in which there was a rapid turnover of personnel. The staff of the hospital escaped lightly. A strict isolation technique was carried out in the wards until the temperature had been normal for a week or until productive cough had ceased. The regimental aid-post orderly, who treated men daily from the infantry training depot, and the hospital librarian, who visited the wards, both contracted the disease, but no case to our knowledge occurred among the nurses and orderlies who were attending the patients.

Serological Investigation

Of the 50 cases recorded by Adams *et al.* (1946), 47 were in United Kingdom troops; the remaining three occurred in New Zealand troops. As a test case, serum was taken from one of the latter and a glycerinated specimen was forwarded by air from New Zealand in 1946 to Dr. Norman Topping, Assistant Director of Health of the Division of Infectious Diseases of the National Institute of Health at Bethesda, Maryland. It was tested for complement fixation against antigen prepared from a strain of *R. burneti*

isolated in Italy. The serum was slightly anticomplementary, but in Dr. Topping's opinion the anticomplementary activity had no real significance when compared with the titres against the antigen (Table I).

TABLE I.—Complement-fixation Titre with Italian "Q" Fever Strain

	1 : 8	1 : 16	1 : 32	1 : 64	1 : 128	1 : 256
N.Z. test serum	4	4	4	4	3	Trace
Control serum	4	1	0	0	0	0

Subsequently one of us, with the assistance of the staff of A.M.D. 7 of the War Office, was able to collect sera from 21 of the 47 British cases. These were forwarded to Dr. Topping. Nineteen of them arrived safely and on test gave a positive complement-fixation reaction to the Italian strain of "Q" fever (Table II). It will be seen that in some the titres are low, but it has to be remembered that the initial infection occurred almost two years before the date of testing the sera.

TABLE II.—Result of Complement-fixation Test for "Q" Fever (Italian Strain)

No. of Serum	Titre	Result	No. of Serum	Titre	Result
1	1 : 64	+	13	1 : 32	+
2	1 : 32	+	14	1 : 32	+
5	1 : 32	+	15	1 : 64	+
6	1 : 16	+	16	1 : 64	+
7	1 : 8	+	17	1 : 4	+
8	1 : 4	+	18	1 : 32	+
9	1 : 64	+	19	1 : 16	+
10	1 : 16	+	20	1 : 32	+
11	1 : 8	+	21	0	—
12	1 : 16	+	22*	1 : 128	+

* Serum sent from New Zealand.

Professor S. P. Bedson kindly tested these sera for antibody to the virus of psittacosis. They were all uniformly negative.

Hence, out of 20 cases checked, 19 gave a positive complement-fixation reaction to the Italian strain of "Q" fever, and it is reasonable to assume that the infective agent of these cases of "primary atypical pneumonia" was the Italian strain of *R. burneti*.

Summary

An epidemic of "primary atypical pneumonia," previously recorded in the *British Medical Journal* as having occurred in the Naples-Caserta area in 1945, has been further investigated serologically, and 19 out of 20 sera tested gave a positive complement-fixation reaction to an Italian strain of "Q" fever two years after the initial infection. It is probable that the epidemic of so-called primary atypical pneumonia was in fact "Q" fever caused by an Italian strain of *R. burneti*.

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