NECROPSY FINDINGS IN A CASE OF Q FEVER IN BRITAIN

BY

J. W. WHITTICK, M.B., Ch.B., B.Sc.

(From the Department of Pathology, Royal Cancer Hospital,
London)

[WITH SPECIAL PLATE]

Q fever, first described by Derrick (1937) in Australia, was recognized clinically in Great Britain by Harman in 1949 and confirmed serologically by MacCallum *et al.* (1949), who also isolated rickettsiae from one of his cases. Three of Harman's patients had become infected, presumably by inhalation, at the necropsy they performed on a man who died from pneumonia. That *Rickettsia burneti* was the cause of this pneumonia was not suspected until later. Histological examination has since shown the presence of *Rickettsia* bodies not only in the consolidated lungs, as mentioned in Harman's paper, but also in other lesions. In earlier reported fatal cases of Q fever—and these are very few—rickettsiae have not been demonstrated in the tissues.

As the disease is now known to occur in this country, a fuller description of the pathological findings seems necessary.

Clinical History

A tailor aged 78 was admitted for investigation of dysphagia of five weeks' duration. After nearly three weeks in hospital he suddenly became febrile and later developed signs of pneumonia and auricular fibrillation. Despite treatment with sulphonamides and penicillin he became comatose and died 11 days after the onset. No cutaneous rash appeared during his illness.

During radiography of the pharynx, a few days after admission, it had been noted that there was some spilling of barium into the trachea and bronchi. None was seen in the lungs 11 days before death.

Necropsy Findings (24 hours after death).—**Lungs**.—The lower lobe of the right lung was enlarged and completely consolidated, its upper half being red and the lower grey. All other lobes were congested. The right pleural cavity was obliterated by diffuse fibrous adhesions; the left sac was normal. Mucosal congestion and some mucopurulent material were present in the trachea and main bronchi. **Brain**.—There was a group of three or four foci (largest 0.3 cm. in diameter) of softening in the putamen of the right lentiform nucleus, and another (0.5 cm. in diameter) in the basilar part of the upper pons on the left side. **Spleen**.—This was slightly enlarged, with a soft dark reddish-brown pulp. **Testis**.—A pale-brown discrete nodule, 0.3 cm. in diameter, was found in the mediastinum of the right testis. There were no significant changes in other organs.

Histology

Lung.—Sections from the red and grey areas of the diffusely consolidated right lower lobe showed differences due to stages in the pneumonic process. In the red area, consolidation was not uniform, the exudate within alveoli having a patchy distribution. Throughout there was intense congestion of blood vessels. Alveoli were filled with an eosinophil non-fibrillary coagulum in which were a few cells. These consisted of neutrophilic polymorphs and round cells in about equal numbers; red corpuscles were scanty, and were present at only a very few points. The round cells were of different types. A few were lymphocytes and plasma cells, but most were larger mononuclear macrophages which, owing to degenerative changes, varied in appearance from elements of about plasma-cell size with well-stained cytoplasm and dark nuclei to large pale cells with finely granular or vacuolated cytoplasm and vesicular, often peripheral, nuclei. The vacuolated appearance was striking, and was not due to the presence of lipid: the contents of the vacuoles failed to stain with Sudan III and were

not doubly refractile. The exudate within bronchioles was similar to that in the alveoli, though in and about some respiratory bronchioles there was a higher concentration of neutrophilic polymorphs. There was some oedema of interlobular connective tissues and of the walls of blood vessels within them.

In the basal zone of grey hepatization the pneumonic process was more uniform. Here there was little congestion. The alveolar walls were considerably thickened (Plate, Fig. 1), through infiltration by many macrophages and smaller numbers of lymphocytes, plasma cells, and neutrophils. In some there was also early fibroblastic proliferation. Scattered areas showed necrosis and breakdown of septa. Within the alveoli the exudate was cellular (Fig. 2) and consisted mainly of swollen degenerate macrophages with pale finely granular or vacuolated cytoplasm. Red corpuscles were more numerous and often predominated within small groups of distended alveoli. Neutrophils were only slightly more plentiful than in the zone of red hepatization. Swollen, degenerate, roughly fusiform cells lining alveolar walls were peeling off to join the exudate. Bronchioles contained a cellular exudate of similar type, and their mucosae showed degenerative changes with necrosis and loss of epithelium. Oedema and round-cell infiltration had produced much widening of subpleural and interlobular connective tissues, and there was also oedematous thickening of the walls of the interlobular blood vessels. Sections which included the pleura showed a thick layer of fibrous tissue with a ragged outer surface where chronic adhesions had been broken down in removal of the lung.

At only two points in the many sections examined was there any barium. It was very small in amount, and there was no special or concentrated reaction about it. No bacteria could be found in Gram-stained sections.

Brain.—In the foci of cerebral and pontine softening the tissues showed both perivascular and more widespread loosening of texture with occasional small perivascular haemorrhages (Fig. 4). Some of the capillary vessels showed swelling of their endothelium and a few contained thrombi. No perivascular cellular exudate was present in the affected areas, but there was slight marginal increase of neuroglial cells, and these, with Giemsa staining, contained many cytoplasmic granules. Some of the granules were coarse and irregular in shape and were probably degenerative products, the result of clasmotodendrosis, but others were morphologically, and in their grouping, rickettsiae. Support for their identification as rickettsiae was provided by the presence of similar bodies in the cytoplasm of some capillary endothelial cells as well as extracellularly in the damaged areas. The same problem has arisen in typhus, and the criteria applied by Wolbach *et al.* (1922), similar to those given here, appear to be valid. The nervous lesions were probably at a very early stage of development.

Spleen.—The Malpighian bodies were very small, and the pulp was distended with red corpuscles and mononuclear macrophages which had abundant pale granular or finely vacuolated cytoplasm: many were undergoing necrosis. Smaller numbers of lymphocytes and neutrophils were also present.

Testis.—In the mediastinum was a single discrete focus of compactly grouped large macrophages with dark nuclei and granular cytoplasm of polyhedral or indefinite outline (Fig. 3). Capillary blood vessels, accompanied by fibroblasts, were scattered through the nodule, which at its centre showed degenerative changes and loosening of texture. Thrombi were present in small neighbouring veins.

Kidneys.—Apart from cloudy swelling of tubular epithelium, occasional small cortical foci of round-cell infiltration, and ischaemic fibrosis of a few glomeruli, there was nothing of note.

There were no significant changes in other organs, though the liver and pituitary were not available for examination.

Distribution of Rickettsiae

The methods of Giemsa (Wolbach's modification), Casteñeda, Macchiavello, and Goodpasture (Goodpasture and Burnett, 1919) were applied to sections. The first and the last (slightly modified) gave the best results and demonstrated great numbers

of both coccoid and bacillary forms of rickettsiae in the lesions of lung, spleen, testis, and brain, where they were both intracellular and extracellular in position (Fig. 5). Macrophages in the first three sites were the chief elements parasitized; while, in the brain, neuroglial cells contained the organisms. In the kidneys smaller numbers were found within tubular epithelium, lying free in the lumen, and also within cells of the intertubular connective tissues.

(Professor A. W. Downie, Liverpool University, has kindly examined sections from the lung, and agrees that the numerous small bodies in the exudate have the morphological and staining characteristics of rickettsiae.)

Discussion

Q fever is rarely fatal. There seem to have been only six other recorded cases—two in Australia (Queensland Ann. Rpt Hlth and Med. Services, 1936–7 and 1938–9) and four in America (Lillie *et al.*, 1941; Irons and Hooper, 1947; Brown *et al.*, 1948). In two of these (Irons and Hooper) necropsy was not made. In all but one case (Queensland Ann. Rpt Hlth and Med. Services, 1936–7) death was due to a diffuse pneumonia of lobar or greater extent with histological features (Lillie *et al.*, 1941; Perrin, 1949) similar to those described here. In its gross appearance the consolidated lung simulates pneumococcal lobar pneumonia, but histologically is quite unlike it, and in its mononuclear exudate and other features resembles psittacosis and other virus pneumonias (Binford and Hauser, 1944). In the two cases in which histological examination was made rickettsiae could not be found.

Changes in the nervous system have not previously been observed in Q fever, nor is there any description of testicular lesions, though both Irons and Hooper (1947) and Gsell (1948), in clinical accounts, report the occurrence of orchitis, and Wegmann (1949) describes the development of symptoms of encephalitis in a patient recovering from Q fever pneumonia.

Splenic enlargement of the "toxic" type described here has been present in other cases.

Summary

A description is given of the pathological changes in the first fatal case of Q fever reported in this country. The patient, a man of 78, died of pneumonia after an acute febrile illness lasting 11 days. All who took part in the necropsy became infected, probably by inhalation.

Numerous rickettsiae were found in the pneumonic exudate, which was predominantly of mononuclear cell type, in lesions of brain, testis, and spleen, and also in the kidneys. This is the first recorded occasion on which they have been demonstrated in human tissues.

I am very grateful to Dr. R. A. Willis for advice, to Dr. A. C. Christie, who performed the necropsy, to Mr. C. G. Chadwin for his expert histological technique, and to Mr. L. A. Cowles for the photomicrographs.

REFERENCES

- Binford, C. H., and Hauser, G. H. (1944). *Publ. Hlth Rep., Wash.*, **59**, 1363.
 Brown, D. C., Knight, L. A., and Jellison, W. L. (1948). *Calif. Med.*, **69**, 200.
 Derrick, E. H. (1937). *Med. J. Aust.*, **2**, 281.
 Goodpasture, E. W., and Burnett, F. L. (1919). *Nav. med. Bull., Wash.*, **13**, 177.
 Gsell, O. (1948). *Schweiz. med. Wschr.*, **78**, 1.
 Harman, J. B. (1949). *Lancet*, **2**, 1028.
 Irons, J. V., and Hooper, J. M. (1947). *J. Amer. med. Ass.*, **133**, 815.
 Lillie, R. D., Perrin, T. L., and Armstrong, C. (1941). *Publ. Hlth Rep., Wash.*, **56**, 149.
 MacCallum, F. O., Marmion, B. P., and Stoker, M. G. P. (1949). *Lancet*, **2**, 1026.
 Perrin, T. L. (1949). *Arch. Path.*, **47**, 361.
 Queensland Ann. Rpt Hlth and Med. Services, 1936–7, p. 22, and 1938–9, p. 52.
 Wegmann, T. (1949). *Schweiz. med. Wschr.*, **79**, 690.
 Wolbach, S. B., Todd, J. L., and Palfrey, F. W. (1922). *The Etiology and Pathology of Typhus*, Cambridge, Mass.

PLACENTAL METASTASES IN MALIGNANT DISEASE COMPLICATED BY PREGNANCY WITH A REPORT OF TWO CASES

BY

S. BENDER, M.D., F.R.C.S.Ed., M.R.C.O.G.

(From the Department of Obstetrics and Gynaecology,
Liverpool University)

[WITH SPECIAL PLATE]

According to Willis (1934), "metastasis of maternal tumours to the products of gestation is very rare, the placenta is affected less rarely than the foetus, and foetal metastases probably always arise from placental deposits." This is borne out by the seven previously recorded cases which are summarized in Table I.

TABLE I

Author	Primary Growth	Placental Metastases	Foetal Metastases
Friedreich (1866) ..	Carcinoma of liver	Unknown	Present
Berghinz (1900) ..	Lymphosarcoma	"	"
Walz (1906) ..	Myxosarcoma of thigh	Present	Unknown
Markus (1910) ..	Malignant melanoma of ovary	"	Absent
Senge (1912) ..	Carcinoma of stomach	"	"
Weber <i>et al.</i> (1930) }	Malignant melanoma of thigh	"	Present
Holland (1949) }		"	"
Gray <i>et al.</i> (1939) ..	Carcinoma of adrenal cortex	"	Absent

On the question of how often maternal malignant disease which has metastasized elsewhere has failed to involve the products of gestation very little has been written, although Katsurada (1902) reported a case of malignant melanoma with widespread dissemination in a woman who died at term but in whose uterus and products of gestation no metastases were found. It is particularly surprising that no case has been reported of carcinoma cervicis with pregnancy in which the growth has involved the placenta by direct, vascular, or lymphatic spread. It might be because careful and thorough examination of the products has rarely been carried out in cases of maternal malignant disease. Thus Hinselmann (1925), in his critical review of the cases of Walz, Markus, Senge, and Friedreich, remarked with regard to the last-mentioned that the placenta, although macroscopically normal, "was not properly dissected out because at the time of delivery the importance of the case was not realized." The baby was subsequently found to have a metastatic growth in the left knee. Weber *et al.* (1930) were the first to record a case in which the neoplasia was demonstrated in all three—mother, placenta, and baby. This case has been discussed in further detail by Holland (1949).

During the past year six cases of maternal malignant disease in association with pregnancy have been encountered in this unit, and the findings are given in Table II. In the first of these cases the placenta and cord, which were macroscopically normal, were not examined microscopically, but in the remainder serial sections were studied. In addition, where the foetus was aborted or stillborn a post-mortem examination was carried out, with histological study of the organs.

In all cases of maternal malignant disease thorough histological study of the placenta should be a routine investigation. In this way the frequency of placental metastases might be more accurately estimated. Moreover, the prognosis for the mother may be revealed thereby; for if, in

J. W. WHITTICK: NECROPSY FINDINGS IN Q FEVER

FIG. 1.—Lung. Pneumonic consolidation with thickening of alveolar walls and perivascular tissues by round cells. ($\times 60$.)

FIG. 2.—Predominantly round-cell exudate in alveolus. ($\times 400$.)

FIG. 3.—Testis. Compact aggregation of macrophages forming nodule. ($\times 400$.)

FIG. 4.—Cerebrum. Margin of area of softening. ($\times 150$.)

FIG. 5.—(a) Extracellular rickettsiae in pulmonary alveolar exudate. (b) Intracytoplasmic rickettsiae in pulmonary alveolar exudate. (c) Rickettsiae in macrophage of testicular nodule. (d) Rickettsiae beside and in neuroglial cells. (All $\times 1,400$.)

B. F. BREARLEY and J. W. LAWS: CARCINOMA OF ISLETS OF LANGERHANS WITH HYPOGLYCAEMIA

FIG. 1.—Primary tumour. ($\times 150$.)

FIG. 2.—Secondary tumour in the liver. ($\times 150$.)