gall-stones experimentally in animals by feeding with cholesterol until a hypercholesterinaemia occurs.

Another factor which appears to be associated with the formation of gall-stones is pregnancy, for gall-stones are undoubtedly common in multiparous women. This factor may act through the disturbance of cholesterol physiology which occurs in pregnancy, since hypercholesterinaemia is often present, and I have recently shown* that in rabbits the cholesterol content of the suprarenals is always greater in does than in bucks, but that during pregnancy the suprarenal cholesterol is depleted.

One other possibility may be considered. If the theory that bile salts are derived from cholesterol should prove correct, any interference with liver function might result in a diminished production of bile salts with a corresponding increase of cholesterol excreted in the bile, and a greater tendency for it to be deposited in the form of stones, either directly from the bile or through the wall of the gall-bladder. This would lay the onus of gall-stone formation on a primary defect in liver function.

To sum up, there seems little doubt from all these facts that the formation of gall-stones is to be attributed to some disturbance in cholesterol metabolism, but the evidence is not sufficient as yet to indicate decisively the nature of this disturbance.

ANAEMIAS.

In pernicious anaemia several authorities have recorded a hypocholesterinaemia, and this is not entirely dependent on the diminished number of red corpuscles—in fact, the blood cholesterol is less in the plasma than in the whole blood.

Pacini¹⁷ considered the low cholesterol values in pernicious anaemia to be a possible cause of the disease, on the ground that haemolysis of the red cells would take place more easily in the absence of the full protective powers of cholesterol. He claimed that inunction with lanoline, which contains a high percentage of cholesterol, was beneficial to the condition. The results, however, were not at all convincing, as the improvement may well have coincided with one of the periods of remission which are common in pernicious anaemia, and, further, the number of cases reported was too small to be of any significance. The majority of workers, however, agree with him in recording low values for the blood cholesterol in this disease. Similarly, in chlorosis and other types of anaemia hypocholesterinaemia is usually found.

In secondary anaemias there is some difference of opinion as to the cholesterol of the blood, some authors recording a hypocholesterinaemia, others no material change. In this connexion it may be noted that extensive haemorrhage, produced experimentally, results in a lipaemia, with its accompanying increase in blood cholesterol, so that it seems probable that the changes in blood cholesterol will vary with the severity of the anaemia and the manner and rapidity of its production. This problem is now being investigated by me. Reference must be made to the interesting work of MacAdam and Shiskin¹⁸ in relation to the anaemias. In addition to their confirmation of the findings of other workers on pernicious anaemia and secondary anaemias, these authors found that in acholuric familial jaundice and splenic anaemia there is a low cholesterol content of the blood, which gradually returns to normal after removal of the spleen. The explanation of this phenomenon is uncertain, but it is interesting to recall the property which the spleen possesses of removing excess of cholesterol from the blood. It is possible that in acholuric jaundice and splenic anaemia the spleen may have this property in an excessive degree, and keep the blood cholesterol at a low level, whilst on removal of the organ a return to normal cholesterol values would be expected.

Another group of cases deserves further investigation—namely, those conditions of splenomegaly which are associated with hypercholesterinaemia, as in the case recorded by Dyke.¹⁹ It is said that Gaucher's disease falls into this class, and various authors have claimed that the histological changes in the spleen characterizing Gaucher's

disease can be reproduced by intravenous injections of cholesterol. Others, however, have denied that the histological changes are similar, and further work is required on this problem. I have recently shown¹ that intravenous injections of cholesterol may increase the size of the spleen to twice or three times its normal size. It is thus easy to understand why the spleen becomes enlarged in conditions of hypercholesterinaemia.

The discussion of cholesterol changes in malignant disease, bacterial infections, and formation of local deposits of cholesterol have been omitted from this abstract:

REFERENCES.

- 1 Chamberlain (1928): *Journ. Physiol.*, lxxvi, No. 3, 17.
- 2 Klinkert (1915): *Berlin klin. Woch.*, l, 820.
- 3 Grigaut, Laroche, and Chauffard (1911): *L'Obstétrique* (Paris), iv, 481.
- 4 Epstein and Rothschild (1917): *Amer. Journ. Physiol.*, xlii, 585.
- 5 Maxwell (1927): *Quart. Journ. Med.*, xxi, 297.
- 6 Epstein and Laule (1922): *Arch. Int. Med.*, xxv, 553.
- 7 Gardner and Gainsborough (1928): *British Medical Journal*, November 24th, 955.
- 8 Gardner and Gainsborough (1927): *Biochem. Journ.*, xxi, 141.
- 9 Anitschkow and Chalazov (1914): *Centralbl. f. Path.*, xxiv, 1.
- 10 Scarff (1927): *Journ. Path. and Bact.*, xxx, 647.
- 11 Letulle, Labbé, and Heitz (1925): *Arch. des Mal. du Cœur*, v, 273.
- 12 Henes (1914): *Journ. Amer. Med. Assoc.*, lxiii, 146.
- 13 Howweather and Collinson (1926-27): *Brit. Journ. Surgery*, xiv, 583.
- 14 Campbell (1924-25): *Quart. Journ. Med.*, viii, 123.
- 15 Fox (1927-28): *Quart. Journ. Med.*, xxi, 107.
- 16 Blaisdell and Chandler: *Amer. Journ. Med. Sci.*, 174, 492.
- 17 Pacini (1918): *Amer. Med.*, xcii.
- 18 MacAdam and Shiskin (1923): *Quart. Journ. Med.*, No. 63, 193.
- 19 Dyke (1928): *Journ. Path. and Bact.*, xxxi, 173.

FURTHER OBSERVATIONS ON PNEUMOCOCCAL INFECTIONS.*

BY

C. H. WHITTLE, M.A., M.D.CAMB., M.R.C.P.LOND.,
CLINICAL PATHOLOGIST, ADDENBROOKE'S HOSPITAL, CAMBRIDGE.

PRIMARY lobar pneumonia and empyema occurring in previously healthy persons arise from infection with pneumococcal strains of high virulence only. Over 100 strains of pneumococci have now been collected, and the main conclusions reached last year^{1 2} have been confirmed.

The Pneumococcal Types in Relation to Disease.†

The distribution of the serological types in relation to the lesion which they caused is given in Table I. Out of a

TABLE I.—Showing the Types of Pneumococci Associated with Different Lesions (Cambridge, 1924-29.)

Lesion.	Type I.	Type II.	Type III.	Group IV.	Total No.
Lobar pneumonia	7	2	0	2	11
Broncho-pneumonia	2	0	2	1	5
Empyema thoracis	24	4	2	1	31
Terminal pneumonia	0	0	2	2	4
Post-operative pneumonia	0	0	1	2	3
Nasal catarrh	0	1	0	3	4
Conjunctivitis	0	1	1	3	5
Bronchitis	0	2	2	8	12
Meningitis, together with otitis media and cerebral abscess	9	1	2	1	13
Other lesions, including abscesses, arthritis, peritonitis, etc.	3	0	1	3	7
Total No. of strains	—	—	—	—	95

total of 47 strains recovered from lobar pneumonia, broncho-pneumonia, and empyema, 33, or 70.5 per cent., belong to Type I; 6 strains, or 12.5 per cent., to Type II; 4, or 8.5 per cent., to Type III; and 8.5 per cent. to Group IV. Such minor lesions as nasal catarrh, conjunctivitis, and

* Summary of an investigation: report to the Science Committee of the British Medical Association, 1929.

† The type agglutinating serums used from 1927 onwards were kindly supplied by the Rockefeller Institute, New York. Previous to this I was using Types I and II serums prepared by Dr. R. R. Armstrong, which were, as I showed from time to time, active agglutinators for the homologous American type cocci at the titres employed in the research.

* Work carried out during the tenure of a Beit Memorial Fellowship. Completed under a grant from the Medical Research Council, and to be published shortly in the *Journal of Physiology*.

bronchitis are associated with strains which usually possess a lower order of virulence, and mostly (66 per cent.) belong to Group IV. Type I strains have never been found in this minor kind of lesion. Terminal pneumonia and post-operative pneumonia, arising in persons who are already ill or suffering from shock, are associated with strains which belong only to Type III and Group IV; in 3 out of the 7 cases in Table I they were comparatively avirulent. Type I is therefore the most consistently virulent group, and remains the most important in the production of lobar pneumonia and empyema.

A comparison of the relative virulence of the different types of pneumococci based on the minimal lethal dose for mice is given in Table II. It is again obvious that Type I organisms are consistently of high virulence (the average M.L.D.= 10^{-5} c.cm. of broth culture). Type I is also the numerically predominant group. Type II and Group IV show a relatively low order of virulence, which is in agreement with Gaskell's conclusions.³

TABLE II.—Showing the Virulence and the Relative Predominance of the Different Types of Pneumococci.

Type.	Proportion of Highly Virulent Strains; M.L.D. = 10^{-5} c.cm. or less.	Proportion of Feebly Virulent Strains; M.L.D. > 10^{-5} c.cm.	Average M.L.D. in c.cm. of Broth Culture.	Total No. of Strains.
I	Per cent. 100	Per cent. 0	10^{-5}	39
II	50	50	10^{-2}	11
III	87	13	10^{-4}	15
IV	32	68	10^{-2}	28
Lister's "A"	1 strain	1 strain	—	2
Total No. of strains ...	—	—	—	95

During the current year I have been able to obtain 11 strains which appear to belong to Type II. In the first three months of 1929 there occurred in Cambridge a number of cases which were diagnosed as acute bronchitis. The patients, both young and old, presented rather unusual symptoms in that they were often very ill, sometimes for a period of several weeks, although the temperature was never very high. At no time did the physical signs yield evidence of any consolidation of the lung, though broncho-pneumonia was suspected. Nevertheless the prostration, the severity and length of the illness, and the persistent cough with copious sputum suggested some involvement of the alveoli of the lung, and this view was favoured by the fact that one patient contracted an empyema as a complication. It is of particular interest that in the sputa of five of these patients pneumococci were found in great abundance, and that practically pure cultures of pneumococci were obtained which possessed an intermediate grade of virulence. Three of these strains agglutinated with Type II serum and two with Type III serum. I suggest that these strains, which showed a lower order of virulence than the lobar pneumonia strains, were able to set up a particularly toxic form of infection of the bronchioles, which probably extended to patches of lung too small to be differentiated from the rest by percussion and auscultation—a low-grade broncho-pneumonia. The patients all recovered, though slowly. The peculiarly toxic properties of Type II pneumococci have been noted by American workers, and also by Gaskell³ in his research on experimental pneumonias in rabbits; he found that Type II strains behaved differently from Type I, and that though the amount of lung substance involved in the infection was small the animals were seriously ill for a time and then recovered. These Type II strains were able to set up only minor lesions, yet were highly toxic in their effects. Hence a clear distinction must be drawn between virulence, or the power to grow in the host's tissues, and the power to elaborate toxin.

Such experimental findings indicate a close parallelism between human and experimental infections with Type II pneumococci. The amount of consolidation of the lung in the experimental animals was so trifling as to be unrecognizable by methods of auscultation and percussion.

Conversion of Strains of Low Virulence into Strains of High Virulence.

The question whether strains recovered from such minor infections as nasal catarrh, conjunctivitis, or bronchitis can be converted by laboratory processes into strains of sufficient virulence to produce lobar pneumonia in healthy subjects has been further investigated. A number of strains of this kind have been inoculated into animals by a variety of methods, and with numerous passages, but no appreciable increase of virulence has resulted. The methods used by Griffith⁴ for converting his avirulent, "rough" strains back into their virulent, "smooth" phase have been found ineffective. Whereas it is comparatively easy to recover the virulence of strains whose original virulence has been suppressed or temporarily lost, to enhance the virulence of strains which have been from the first of low virulence has so far proved an impossible task.

Pneumococcal Otitis Media Produced Experimentally in Mice.

As noted in my last report,¹ certain feebly virulent strains of pneumococci when inoculated into the peritoneal cavity of mice have occasionally been found to produce a subacute type of infection. This condition has received further study.

Only one mouse out of a dozen inoculated may be affected. The animal usually remains well for as long as a week, but sooner or later it shows signs of inco-ordination pointing to an affection of the semicircular canals. A unilateral effect is produced and the mouse holds its head twisted to one or other side, tends to rotate in the same direction on its long axis when stimulated, and shows a coarse tremor of its head when attempting to move. Occasionally it moves in circles. Usually it dies within seven to twenty-one days after inoculation, and always of pneumococcal septicaemia. Pneumococcal pus is found in one or the other middle and internal ear, sometimes in both, but usually there is more pus on one side than on the other. If the animal is killed before the disease is far advanced one or the other middle ear is found to contain pus which gives pure cultures of pneumococcus and contains no other organism. The heart blood at this stage is usually sterile on culture. The pneumococcus so recovered gives the same serological reactions as the one inoculated into the peritoneum and shows no alteration in virulence.

A similar condition occurring spontaneously in laboratory rats afforded further clues to the anatomical distribution of the lesions in the mice, which was discovered partly by serial sections and partly by cultures and films. In the rats, of which eight have been examined, the symptoms were identical, and pus was found constantly in one or both middle and internal ears. Blood cultures were sterile. In rats the infection appears to run a very chronic course. The organisms obtained from the pus in the ear were not the same in each rat, and they included Gram-negative bacilli, as well as Gram-positive diplococci, which in one case closely resembled pneumococci but were insoluble in bile. A rabbit also showed the same symptoms spontaneously, but unfortunately the animal was thrown away in error before a post-mortem examination could be made.

Laboratory rodents are known to be susceptible to middle-ear infections, but I have been unable to find references to such infections following intraperitoneal injections of pneumococci. It is evident that the middle ear is a site of election for the pneumococcus both in man and in the mouse. I have one case recorded in which otitis media apparently followed a vaginitis in a child of 8. A practically pure culture of pneumococcus was obtained from the vagina and from the ear, and in each instance the strain belonged to Type I and possessed a minimal lethal dose of 10^{-5} c.cm. of broth culture.

The pathology of the mode of infection has yet to be worked out, and I hope to make this research the subject of a separate paper.

Summary.

1. Primary lobar pneumonia and empyema due to pneumococci are invariably caused by strains of high virulence. In the period under examination (1924-1929) 70.5 per cent. belong to Type I.

2. Type II and Type III strains have exhibited relatively great toxicity together with a rather lower order of virulence, particularly noticeable in the first three months of 1929. These organisms may infect a comparatively small amount of lung substance and yet produce a fairly severe and prolonged illness. They therefore differ in their behaviour from the Type I strains.

3. The task of converting strains of low virulence, recovered from cases of nasal catarrh, conjunctivitis, and bronchitis, into those which are sufficiently virulent to set up lobar pneumonia in healthy subjects has again proved impossible by any of the known experimental procedures for raising virulence. No support is therefore given to the theory that these strains of low virulence may become sufficiently pathogenic to produce pulmonary lesions, though such a possibility cannot be finally excluded.

4. A condition of subacute otitis media with involvement of the semicircular canals has been set up in mice by the introduction of pneumococci of moderate or feeble virulence into the peritoneal cavity. The condition bears the closest resemblance to the spontaneous otitis media occurring in laboratory rodents. Though the pathology of the infection has not been worked out in detail, it is clear that the pneumococcus has a special predilection for the middle ear both in man and mouse.

I wish to thank Dr. J. F. Gaskell for his frequent advice, and Professor W. E. Dixon both for the hospitality of his laboratory and for help in drawing up this report. I wish also to record my gratitude to the British Medical Association for the generous assistance afforded me by a grant for the research.

REFERENCES.

- ¹ Whittle, C. H.: *British Medical Journal*, 1928, ii, 153. ² Idem: *Journ. Hyg.*, 1928, xxvii, 412. ³ Gaskell, J. F.: *Journ. Path. and Bact.*, 1928, xxxi, 613. ⁴ Griffith, F.: *Journ. Hyg.*, 1928, xxvii, 113.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

CONTINUOUS DRAINAGE OF A HYDRONEPHROTIC ONLY KIDNEY.

THE following case of a patient who for seven years has passed urine through a catheter introduced into the renal pelvis by way of a lumbar incision is, I think, instructive enough to deserve recording.

On August 12th, 1922, I was called to see a married woman, aged 45, who gave a history of complete anuria for two days. She had had no pain or vomiting, and was not feeling ill; her temperature and pulse were normal. Examination revealed no distension of the bladder, but there was a large, tender, tense swelling in the left lumbar region. In the right loin there was an old scar, and the right kidney could not be felt; I was informed that the kidney had been removed at the Westminster Hospital ten years previously for tuberculous disease. The patient stated that during the whole of the intervening period she had been free from urinary symptoms. No evidence of tuberculous disease was found elsewhere.

The patient was admitted to the Hornsey Central Hospital, where catheterization proved that the bladder was empty, and the diagnosis of hydronephrosis of a single kidney was made.

I operated as soon as possible, exposing the left kidney through a lumbar incision, and found the pelvis distended with nearly a pint of clear urine, which I drained by a tube passed through the cortex. The renal tissue appeared normal, and there was no evidence of stone or tuberculous infection. The patient made a good recovery.

During the three days following the operation urine drained freely through the tube, and a small quantity passed naturally. On the fourth day the tube became dislodged and could be replaced only with great difficulty. As the patient remained free from pain and passed normal quantities of urine through the bladder, the wound was allowed to heal. A radiogram revealed no stone or other abnormality, and the patient returned home apparently well after three weeks.

All went well until the end of the following September, when the condition returned, though the swelling was much smaller than on the previous occasion. I operated again within twenty-four hours, and once more the patient made a good recovery. This time, however, fearing a further return of the obstruction, I decided to attempt prolonged or permanent drainage, and at the end of a fortnight, when the wound had nearly healed, I replaced the tube by a No. 12 rubber catheter. Later Messrs. Bailey and Son fitted a rubber belt and urinal into which the catheter drained.

The patient has now worn this apparatus for seven years. She is able to remove and cleanse it unaided, and suffers no incon-

venience from leakage. Only occasionally an ounce or two of urine is passed naturally. The urine is usually alkaline, and sometimes contains a considerable deposit of pus, but it quickly improves with the use of acid sodium phosphate. During the whole of this period the patient has led an active life, doing all her own housework. Her condition compares very favourably with the best I have ever seen after suprapubic drainage of the bladder.

The case presents the following interesting features: the excellent results of the nephrectomy for unilateral tuberculous seventeen years ago; the coincidence of hydronephrosis from unknown but probably congenital causes in a solitary kidney; the continued functioning of the kidney after pressure and repeated injury; and the comfort of the patient under these conditions.

London, N.

FRANK MANNINGTON, F.R.C.S. Eng.

FOREIGN BODIES SWALLOWED INTENTIONALLY.

THE following case is unusual and seems worthy of placing on record.

The patient, a man aged 27, was admitted to this hospital on April 2nd, 1929, with the history that while in prison in September, 1928, he swallowed a piece of copper wire about 4 inches long, a

Skiagram taken on April 3rd (reversed in reproduction).

large needle about the same length, and a dinner fork. He was operated upon and the fork was removed during September, 1928. While still in prison, on March 5th, 1929, he swallowed another fork, which had not been removed.

On examination directly after admission the patient appeared to be well developed and nourished. An upper abdominal mid-line scar from the previous laparotomy was seen. Nothing abnormal was discovered on abdominal palpation except some general thickening in the epigastric region. Under x-ray examination the fork was shown apparently in the stomach. An article like a needle was seen in the upper right quadrant of the abdomen. The piece of copper wire was seen in the region of the descending colon.

On April 7th the abdomen was opened, the old scar being excised. A general examination of the stomach and the abdominal cavity was then made. An adhesion was found running from stomach to liver; when this was divided it was found to have a piece of metal in its midst. This, on close examination, proved to be the remainder of the needle swallowed in September, 1928. The fork, a large dinner one, 7½ inches long, was found to be lying with the handle at the pyloric end of the stomach. A small incision was made in the stomach over the handle and the fork extracted. The opening in the stomach was then closed. Next, a search was made for the third foreign body seen in the radiogram. The colon was especially subjected to close examination, but no trace of this foreign body could be found. The abdomen was then closed.

The patient made a satisfactory recovery and was discharged from hospital on May 1st.

On examining the fork after the operation, the handle half was seen to be unaffected by its long stay in the stomach, but the other half, which had been pointing towards the cardiac end, was corroded and black in colour.

I am indebted to Mr. H. Morton Anderson and Dr. William Graham for permission to publish this case.

DONALD A. P. MACALISTER, M.B., F.R.C.S. Ed.,
Assistant Medical Officer, Gulsan Road Hospital, Coventry.