damage and a little over two years from the discovery of the neuroretinitis. The evil prognosis accompanying either neuroretinitis or the onset of definite renal symptoms in hyperpiesia is well recognized.

The clinical association of hypertensive neuroretinitis with renal failure⁴⁸ on the one hand and with cerebral vascular catastrophes⁴⁹ on the other has been emphasized by many observers, and has a solid foundation in fact. Although it is true that neuroretinitis may exist for considerable periods with apparently normal renal function⁵⁰ (as in the case cited), and without evidence of cerebral arteriosclerosis, yet, provided such cases be kept under observation, provided they be not carried off by cardiac failure or intercurrent malady, evidence of renal or cerebral damage will become manifest within a period of two years. The onset of neuro-retinopathy is the writing on the wall which proclaims the onset of the malignant and final phase of the disease. The pathological changes in disk and retina are but an index of co-ordinated arteriolar disease in other vascular fields.⁵¹

The arteriolar system of the body may be compared with the extended front line of the last war. Always under steady pressure, it is at any time liable to intensified attack. The line will yield first at the weakest point, the retinal area; but this is not a vital spot, and the line as a whole stands. As the strain is maintained the line gives at an area essential for its existence—cardiac, renal, or cerebral—with resulting disaster. As to the mysterious agency which causes this speeding up in the degeneration of the arterioles throughout the body, and converts a comparatively benign condition into a rapidly fatal one, we are still absolutely ignorant. Unless a case of malignant hypertension has been under observation before the onset of renal insufficiency it may be quite impossible to differentiate it, clinically or biochemically, from chronic nephritis. Even at necropsy, even after histological examination, pathologists may differ. But then indeed the problem is one of academic rather than of practical importance, for at this stage the prognosis is equally hopeless.

REFERENCES

- ¹ Allbutt, T. Clifford: *Arteriosclerosis: A Summary View*, 1925, p. 44.
- ² Johnston, George: *Med.-Chir. Trans.*, 1868, li, 57.
- ³ Gull, W. W., and Sutton, H. G.: *Ibid.*, 1872, lv, 273.
- ⁴ Jones, L.: *Virchow's Arch. f. Path. Anat.*, 1904, clxxviii, 367.
- ⁵ Evans, G.: *Quart. Journ. Med.*, 1920-1, xiv, 215.
- ⁶ Fishberg, A. M.: *Hypertension and Nephritis*, second edition, 1931, p. 179.
- ⁷ Kernohan, J. W., Anderson, E. W., and Keith, N. M.: *Arch. Int. Med.*, 1929, xlv, 395.
- ⁸ Gull, W. W.: *British Medical Journal*, 1872, ii, 673, 707.
- ⁹ Gray, J.: Medical Research Council, Special Report Series, 1933, No. 178, p. 121.
- ¹⁰ Hueck: *Munch. med. Woch.*, 1920, lxvii, 835.
- ¹¹ Gross, L.: *Journ. Med. Research*, 1917, xxxvi, 327.
- ¹² Bradford, J. Rose: *Journ. Physiol.*, 1899, xxiii, 415.
- ¹³ Richards, A. N.: *Kidney Function*, Harvey Lectures, 1920, vol. xvi.
- ¹⁴ Mahomed, F. A.: *British Medical Journal*, 1874, i, 585.
- ¹⁵ Huchard, H.: *Traité clinique du cœur et des vaisseaux*, third edition, 1899, i, 45-126.
- ¹⁶ Riseman, J. E. F., and Weiss, Soma: *Amer. Journ. Med. Sci.*, 1930, clxxx, 47.
- ¹⁷ Paullin, J. E., Bowcock, H. M., and Wood, R. H.: *Amer. Heart Journ.*, 1926-7, ii, 613.
- ¹⁸ Fishberg, A. M.: *Loc. cit.*, p. 546.
- ¹⁹ Janeway, T. C.: *Arch. Int. Med.*, xii, 755.
- ²⁰ Addis, T., and Oliver, J.: *The Renal Lesion in Bright's Disease*, 1931, p. 96.
- ²¹ Christian, H. A., and O'Hare, J. P.: *Oxford Medicine*, iii, p. 772 (38).
- ²² Bright, Richard: Goulstonian Lectures, *Medical Gazette*, 1833, xii, 381.
- ²³ Dunn, J. Shaw: *British Medical Journal*, 1922, ii, 1166.
- ²⁴ Shaw, H. Batty: *Hyperpiesia and Hyperpiesis*, Oxford Medical Publications, 1922.
- ²⁵ Ellis, A. W. M., and Marrack, J. R.: *Lancet*, 1923, i, 891.
- ²⁶ Calvert, E. G. B.: *British Medical Journal*, 1925, i, 64.
- ²⁷ Hunt, T. C.: *Lancet*, 1929, ii, 751.
- ²⁸ Korányi: *Zeit. f. klin. Med.*, 1897, xxxiii, 1.
- ²⁹ Volhard, F.: Mohr and Staehelin's *Handbuch der inneren Medizin*, Berlin, 1918, iii, 1197.
- ³⁰ Calvert, E. G. B.: *Loc. cit.*
- ³¹ O'Hare, J. P., Walker, W. G., and Vickers, M. C.: *Journ. Amer. Med. Assoc.*, 1924, lxxxiii, 27.

- ³² Turnbull, H. M.: Quoted by Ellis and Marrack, *loc. cit.*
- ³³ Lewis, T.: *Diseases of the Heart*, 1933, p. 234.
- ³⁴ Moore, R. Foster: *Medical Ophthalmology*, 1922, p. 154.
- ³⁵ Evans, P. J.: *Brit. Journ. Ophthalmol.*, 1933, xvii, No. 5.
- ³⁶ Allbutt, T. Clifford: *Loc. cit.*, p. 54.
- ³⁷ Christian, H. A.: *Journ. Amer. Med. Assoc.*, 1926, lxxxvii, 931.
- ³⁸ Bell and Clawson: *Arch. Path.*, 1928, v, 939.
- ³⁹ Granger: *Journ. Amer. Med. Assoc.*, 1929, xciii, 820.
- ⁴⁰ Lewis, T.: *Loc. cit.*, p. 64.
- ⁴¹ Allbutt, T. Clifford: *Loc. cit.*, p. 64.
- ⁴² Fishberg, A. M.: *Loc. cit.*, p. 544.
- ⁴³ Volhard, F. and Fahr, T.: *Die Brightsche Nierenkrankheit*, Berlin, 1914.
- ⁴⁴ Fahr, T.: *Virchow's Arch. f. Path. Anat.*, 1919, ccxxvi, 119.
- ⁴⁵ Idem: Heucke and Lubarsch's *Handb. d. Path. Anat. u. Hist.*, Berlin, 1925, vii, 405.
- ⁴⁶ Volhard, F.: *Verhandl. d. deut. Gesellsch. f. inn. Med.*, 1923, xxxv, 134.
- ⁴⁷ Keith, N. M., Wagener, H. P., and Kernohan, J. W.: *Arch. Int. Med.*, 1928, xli, 141.
- ⁴⁸ Fishberg, A. M., and Oppenheimer, B. S.: *Ibid.*, 1930, xlvi, 901.
- ⁴⁹ Moore, R. Foster: *Loc. cit.*, p. 59.
- ⁵⁰ Wagener, H. P., and Keith, N. M.: *Arch. Int. Med.*, 1924, xxxiv, 374.
- ⁵¹ Salus: *Med. Klinik*, 1931, xxvii, 1885.

REPORT ON TWO CASES OF PSITTACOSIS

BY

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With a Note on the Serological Investigation of the Two Cases by S. P. BEDSON, M.D., M.Sc.

The two cases described occurred in Huddersfield during April, 1933, in the house of a local millowner. Resident in the house were the owner and his wife, their son, and two maids, one of whom (S. H.) and the mistress (E. H.) contracted the disease.

CASE I

S. H., a female aged 41, had a chronic duodenal ulcer. On April 10th, 1933, she complained of chilliness and headache. She was first seen on April 12th, when her temperature was 103° F., and she was complaining of generalized aching, especially in the back, and of severe occipital headache. A troublesome dry cough was present, but except for a furred tongue there were no physical signs. On April 13th the air entry to the right base was diminished, but it was not until the 17th that definite signs of consolidation in the right base appeared. During this first week the temperature remained high, the pulse rate was not correspondingly raised, and the respiration rate was never more than 37. The aching passed away, an irritating cough with very little sputum persisted, the tongue remained thickly furred, and the bowels were loose. The patient had vivid hallucinations during this week. On April 19th the temperature reached 105° F., the pulse rate was 108, and the respiration rate 35.

On April 20th a Widal test was performed for typhoid, paratyphoid A and B, *B. aertrycke*, *B. enteritidis* Gaertner, and *Br. melitensis*; also the blood was cultured aerobically. The Widal reaction was negative for all except *Br. melitensis*, which organisms were agglutinated to a titre of 1 in 50, with slight agglutination to a titre of 1 in 125 after standing overnight. The blood culture proved sterile. At this stage, in view of the presence of several budgerigars in the house, an infection by psittacosis virus was thought to be possible. Accordingly sputum was collected on April 21st for bacteriological examination and for injection into mice as described later. No tubercle bacilli were detected in the sputum. Direct Gram films showed some streptococci and pneumococci, and cultures confirmed the presence of these organisms. On the same date the faeces were examined for organisms of the typhoid-paratyphoid groups, with negative results.

During the second week of illness the patient's general condition was poor. There was cyanosis at times, and the pulse was intermittent. Insomnia was troublesome, there was profuse perspiration, and the stools were frequent, fluid, and most offensive. On April 26th the temperature dropped

from 102° F. to 98.6° F. in four hours, the pulse rate from 120 to 76, and the respiration rate from 36 to 24, and the patient was collapsed. On April 27th a leucocyte count showed a leucopenia of 4,000 per c.mm., the differential count being 75 per cent. neutrophil polymorphs, 18 per cent. small lymphocytes, 2 per cent. eosinophils, and 5 per cent. transitional cells. The red cells showed some degree of polychromatic staining. The Widal test and a bacteriological examination of the faeces were repeated on this day. The

stools on several occasions. There were a few doubtful and transient "rose spots." The patient was very voluble, often delirious, and suffered from hallucinations. During this week it was noticed that she was somewhat deaf and mentally dull. Her speech was noticeably slower than normal, and there was cyanosis at times.

The typhoid state persisted into the third week, when the temperature fell by lysis: the pulse rate, which throughout the second week was about 72, became slower still, and on the twentieth day of illness was 48. The respiration rate, which had shown extraordinary variations, became slower, and reached 24 on the twenty-eighth day. During the third week she developed cystitis; this was a lighting-up of a long-standing infection. Convalescence was protracted but satisfactory.

A parallel series of pathological investigations was carried out as in Case I. The findings were similar. On April 24th the Widal reaction was positive for *Br. melitensis* in a dilution 1 in 25, and on April 27th it was positive, 1 in 25, for both *Br. melitensis* and *B. abortus*, and, as in Case I, this was not regarded as a specific agglutination. The leucocyte count showed a leucopenia, the figures being 5,800 per c.mm., with 81 per cent. polymorphs, 16 per cent. lymphocytes, and 3 per cent. transitional cells. The red cells, as in Case I, showed some slight degree of polychromasia. The urine was examined by Ehrlich's diazo test, with negative results. There was heavy pus and *B. coli* infection in the urine.

faeces again showed no abnormal organisms. The Widal reaction was also negative except for *Br. melitensis*, which was again agglutinated to a titre of 1 in 50, and it was thought that this was either an auto-agglutination—not a specific reaction—or that it was due to some prior infection. Notwithstanding, the milk supply was kindly investigated by the medical officer of health, Dr. John M. Gibson, and samples of blood and milk were sent for examination from the only suspected cow in the herd. These were examined bacteriologically and serologically for *Br. melitensis* and *B. abortus*, with negative results.

During the third week the general condition began to improve, though a mitral systolic bruit was heard for the first time, and the pulse rate tended to be somewhat higher. On May 8th the patient had some epigastric discomfort and vomited; the vomit contained altered blood and some red blood cells. Convalescence has been prolonged.

CASE II

E. H., aged 48, had had encephalitis lethargica in 1923, and as a result had a persistent useless cough and a tic involving the levator ani muscles. She had also had attacks of cholecystitis. She first became ill on April 13th, 1933; her temperature was then 99.4° F. She complained of general aching, but not much headache. The irritating cough was much intensified, the sputum being extremely scanty, and on one or two occasions "rusty." There was insomnia, anorexia, constipation, and abdominal distension, and the tongue was thickly furred. No physical signs were detected in the lungs during the first week. The temperature rose daily, reaching 104.4° F. on the fifth day, with a pulse rate of 80 and a respiration rate of 32.

On April 24th, the eleventh day of illness, crepitations were heard at the left apex, and a patch of consolidation developed; another patch was later detected at the left base. During the second week the general condition became worse, and she presented, clinically, the appearance of typical typhoid. The temperature remained high, the pulse rate was disproportionately slow, and the respiration rate increased. The tongue was coated and the constipation gave way to diarrhoea, with very offensive fluid stools, closely resembling the "pea-soup" stools of typhoid. Blood was present in the

TREATMENT OF THE SPUTUM FOR INOCULATION INTO MICE

The sputum from both cases, collected on April 21st, was treated separately in the following manner. It was ground up with sterile sand, and filtered through a Seitz filter; the filtrate was tested for sterility, and 1 c.cm. was inoculated into the peritoneum of three mice. When these died, the spleens, livers, and lungs were similarly

treated, and a further series of mice was inoculated; in this way the presence of a filterable virus, capable of killing mice, was demonstrated. Passage was obtained through more than six generations of mice in the case of S. H., and through four generations in the case of E. H. In addition to inoculation of the spleens and livers, etc., from each series of mice, histological examination of these organs was carried out. Care was taken to show that the mice were not dying from bacterial infection.

The features common to all the mice which died from what was assumed to be the effect of the virus were as

follows. The liver showed marked fatty changes, with areas of focal necrosis, and around the areas of necrosis infiltration by lymphocytes and polymorphonuclear cells; there was also diffuse necrosis of the cells. The spleen was congested and showed a marked endothelial-celled proliferation, while there was often some flaky lymph to be seen in the peritoneum, and the intestines appeared congested. Cultures from the peritoneum, however, proved sterile.

The order in which the various series of mice died was interesting. Three mice were inoculated with the filtered sputum of "S. H." on April 23rd and all died on May 1st—that is, on the tenth day after inoculation. Retransmissions were made from the spleen, livers, etc., of these animals to three sets of two mice. The two mice from one set and one mouse from another died on May 5th; these were not retransmitted. The remaining three mice died on May 15th; retransmissions were made from these on May 16th, all of which died on May 18th. Three further rapid transmissions were obtained, after which the virus seemed to lose virulence, and mice, since inoculated, have remained alive to September, 1933. Whether this loss of virulence was in any way due to the storage of the livers and spleens of the last series in the ice-chest for several days before reinoculation we do not know.

In the case of the sputum from "E. H." the virus obtained never reached the same degree of virulence, the first set of mice inoculated not dying for thirty days, and no set of retransmissions dying in less five days. Moreover, this strain suffered the same fate as that from "S. H." after it had been stored for some days in the ice-chest.

When the first set of mice died on May 1st inquiries into the antecedents of the budgerigars elicited the following facts. The birds, about ten in number, were bought from a local dealer in February and were home bred. In March, 1933, one of the hens was "egg-bound" and died. To replace this bird another hen was obtained from Blackpool, and the mate of this hen became ill and died at the end of March. Both "S. H." and "E. H." handled this bird before and after death. The period of incubation in these cases appears to be ten and thirteen days respectively (approx.). From these investigations there seems little reason to doubt that the two cases described were cases of psittacosis, and confirmation of the diagnosis was obtained from the complement-fixation tests carried out by Dr. S. P. Bedson, to whom and to Dr. E. L. Sturdee of the Ministry of Health we are much indebted for help and suggestions.

SEROLOGICAL INVESTIGATION

It is now well established that viricidal antibody is developed in response to infection with a filterable virus. The presence of this antibody can be demonstrated not only by the neutralization reaction, but also by such purely test-tube reactions as agglutination, precipitation, and complement-fixation in current use in bacteriology. In psittacosis the neutralizing power of human convalescent serums is of an extremely low order,¹ and one would hardly have expected the complement-fixation reaction to be of any use, since in the case of most viricidal serums neutralization is more readily demonstrated than complement-fixation. However, one or two tentative experiments² suggested that convalescent psittacosis serums might fix complement specifically, despite the absence of detectable neutralizing power, and subsequent work has fully confirmed this.¹ The reaction is not given by every case, but a positive result in a carefully controlled test is of undoubted significance and the reaction a valuable aid to diagnosis.

Technique of the Test.—The technique of the complement-fixation reaction for psittacosis is carried out

according to the method devised for viruses by Bedson and Bland.³ Specific antigen consists of a 5 per cent. suspension of virulent mouse spleen in phosphate buffer or saline. A control antigen, made from normal mouse spleen or the spleen of a mouse suffering from some other virus infection such as ectromelia, is invariably used. This control antigen is of particular importance, because serums from individuals with a positive Wassermann reaction will give a false positive result with the psittacosis antigen; they fix complement equally well with the control antigen, however, and so reveal themselves. A known positive serum and one or more normal serums are included in the test.

Result of Test.—Serums were collected from these two cases on the fourteenth day of disease. The complement-fixation reactions tabulated below show that both serums contained psittacosis antibody, and leave little doubt that these were both cases of psittacosis.

Serum		2 M.H.D. Complement +			
Designation	Dilution	5 per cent. Virulent Mouse Spleen in Phosphate	5 per cent. Normal Mouse Spleen in Phosphate	Saline	
S. H.	1/1	++++ +++	—	—	
	1/2	++++ +++	—	—	
	1/4	++++ ++++	—	—	
E.H.	1/1	++++ +++	—	—	
	1/2	++++ +++	—	—	
	1/4	++++ ++++	—	—	
P. 112 (Hyperimmune guinea-pig)	1/4	++++ ++++	—	—	
N. 21 { Normal human	1/1	—	—	—	
N. 22 { Wassermann negative	1/1	—	—	—	
Saline		—	—	—	

Degrees of fixation indicated by signs + + + +, + + +, and so on to —. Two readings taken, one after 30 minutes at 37° C. (upper row), and a second after standing overnight at room temperature (lower row).

REFERENCES

- 1 Bedson, S. P.: *Brit. Journ. Exp. Path.*, 1933, xiv, 162.
- 2 Bedson, S. P., and Western, G. T.: Reports on Public Health Medical Subjects, 1930, No. 61.
- 3 Bedson, S. P., and Bland, J. O. W.: *Brit. Journ. Exp. Path.*, 1929, x, 393.

CHORIONIC CARCINOMA

BY

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Individual cases of this rare condition seem worth recording, as it is only by collating such reports that the full clinical picture and the results of treatment can be obtained. Chorionic carcinoma varies much in malignancy, but the highly malignant type predominates. The case here described followed a hydatidiform mole, and has remained free from recurrence five years after operation.

The patient, a woman of 32, who had had a normal confinement in 1920 and no previous illness, was admitted to Northampton General Hospital on April 5th, 1928, with a history of slight uterine haemorrhage for seven weeks, followed by two floodings; her last menstrual period had occurred fourteen weeks previously. When admitted she was in poor condition. The uterus reached 1 inch above the umbilicus, and was smooth and symmetrical. The cervix admitted one finger, and a boggy structure was felt; some vesicles escaped,