Suggested New Nomenclature.

Chronic Arthritis (A, Monarticular; B, Polyarticular).

(1) *Synovial Type* (O.T., Rheumatoid arthritis).—The disease commences and remains more marked in the synovial membrane. The cartilage and bone may be invaded secondarily. Every gradation may be seen between the chronic types and the more acute forms which lead to ankylosis.

(2) *Chondro-osseous Type* (O.T., Osteo-arthritis).—The disease commences and remains more marked in the articular end, the synovial membrane being involved later.

(3) *Mixed Type*.—The disease commences simultaneously in synovial membrane and articular end and the changes advance *pari passu*.

In all three types osteophytes may form at the articular margins, but in the synovial type they occur comparatively late in the disease, and in the more acute forms which lead to ankylosis are usually absent. The suggested nomenclature is obviously a primary classification. It is probable that further research will justify us in subdividing each type.

E. THE NEED OF RESEARCH INTO ETIOLOGICAL ASPECTS.

Clinical evidence often appears to point to an infective or toxic origin in many cases of chronic arthritis. In a certain proportion obvious infective foci are present, the treatment of which may produce amelioration or cure of the joint condition. In other cases a careful search fails to reveal any primary focus, but it should not be forgotten that this fact by no means negatives the possible infective nature of the disease. For instance, chronic polyarticular arthritis may be ushered in by an attack of tonsillitis. The latter may entirely subside; yet the arthritis remains, and the supposition is that micro-organisms have entered the circulation via the tonsil and have settled in the synovial membrane, where they proliferate and form their toxins.

A young man came under my care suffering from chronic gonorrhoea with gleet. Gonococci were present in the prostatic smear. While under treatment he developed a spindle-shaped swelling of the interphalangeal joints of the hand exactly similar to rheumatoid arthritis. At this stage, however, examination of prostatic smears for organisms was persistently negative. The infective nature of his arthritis was therefore obvious on clinical grounds, although it could not be demonstrated bacteriologically.

Similarly in tuberculous disease of a joint the primary focus is usually a matter of assumption rather than actual demonstration. It is clear that any possible primary focus should be treated not only for these special reasons but because thereby the general health of the patient is improved.

At the same time we must bear in mind that the treatment of the primary focus need not necessarily bring about the desired result if the organisms were already entrenched in the synovial membrane and joint structures, as on clinical and bacteriological grounds sometimes appears to be the case. In these cases the treatment applied to the joints themselves is of even greater importance than concentrating on primary foci. How often the efforts of the medical man are devoted to the latter while the joints are allowed daily to become more stiff and deformed—an excellent example of a policy of "straining at a gnat and swallowing a camel."

The bacteriological aspects of the problem are clamouring for complete and scientific investigation. The important pioneer work of Blaxland and Poynton and Paine requires following up. From time to time bacteriological investigations of the synovial fluid have been made and have been usually negative. However, as an argument against the infective nature of these forms of chronic arthritis this fact is quite valueless; for we know that in the form of chronic arthritis occurring in such infective conditions as gonorrhoea the fluid is usually sterile. What is required is examination of the synovial membrane and other joint tissues. The extent of the operative field in chronic arthritis has increased of late years, and if every surgeon would make a point of having all tissues removed from the joint systematically examined by a bacteriologist the evidence obtained might be of great value. This is one line upon which my own investigations are now proceeding.

In conclusion, let me repeat that the stage is now set for

the bacteriologist and chemical pathologist in conjunction with the surgeon to march forwards, inspired by the immortal advice of John Hunter to Jenner, who was "thinking" of investigating vaccination: "Do not think but try: be patient, be accurate."

It is my pleasant duty to thank all those who have assisted me in my researches. To Sir Arthur Keith I am indebted for permission to work at the Royal College of Surgeons of England and for much help. Professor Shattock has been ever ready with advice on pathological points. To my colleagues at the hospitals with which I am connected, and especially in the Medical and Surgical Units of University College Hospital, I owe a debt of thanks.

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A CASE OF FEVER DUE TO *B. PARATYPHOSUS C*.

BY

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PARATYPHOID C fever appears to be rare in England, and only two previous cases have been described—one by Dudgeon and Urquhart (1920) and another by Andrewes and Neave (1921). Possibly the disease is commoner than is imagined, but in many cases (as pointed out by Dudgeon and Urquhart) agglutinins are not formed in the blood, and often the diagnosis can be made only by isolation of the organism from the blood stream, or more rarely from the faeces.

A girl, aged 13½ years, was under the care of Dr. Benson Young of Plymouth, to whom I am indebted for the clinical particulars. She had had the symptoms of a mild "influenzal" attack for three to four days—temperature 100° F., pulse 120, cough, sweating, and joint pains. The temperature steadily rose, until seven days after the onset of the disease it was 106° F., pulse 124. The patient was semi-delirious, the tongue furred and dry; there were scattered areas of consolidation over the lungs, and slight diarrhoea was present. The spleen was not enlarged and no spots were noted.

At this stage I saw the patient in consultation with Dr. Young. A blood count gave the following figures: Leucocytes 4,440 per c.mm., polymorphs 54 per cent., lymphocytes 44 per cent., large hyalines 2 per cent. Agglutination to *B. typhosus* and *B. paratyphosus* A, B, and C was negative in a dilution of 1 in 25. The urine contained no pus and was sterile on cultivation. No pathogenic organisms were isolated from the faeces. From the blood a Gram-negative bacillus was isolated which gave the reactions of *B. paratyphosus* B with the exception that dulcitate was not fermented. On subculture, however, acid and gas were produced from dulcitate, though this took about seven days. Acid and gas were also produced in dextrose, maltose, mannite, and xylose; no change was produced in inositol (unlike *B. paratyphosus* B); an alkaline reaction was produced in litmus milk.

The organism was tested with some *paratyphosus* C serum kindly sent me by Professor L. S. Dudgeon. It was agglutinated to the end point of this serum, whereas with *paratyphosus* B serum, with an end point of 1 in 8,000, agglutination only took place up to a dilution of 1 in 400. On saturation of this stock *paratyphosus* C serum with the bacillus isolated from the patient the following result was obtained.

The titre of stock *paratyphosus* C serum before saturation with the patient's bacillus on its homologous antigen was 1 in 8,000. The titre of the above serum after saturation with the bacillus isolated from this patient on the same antigen was 1 in 100 = trace; 1 in 200 = 0. Although the patient's serum did not agglutinate the stock *paratyphosus* C antigen, her own bacillus was agglutinated slightly (1 in 100, trace) by her own serum.

Course of Illness.

The temperature slowly subsided and was normal in ten days from the onset of the disease. No complications ensued. The pulse throughout was high; it was over 120 during the first week of illness, and a fortnight elapsed before it was below 100.

Frequent examinations were made of the faeces, using both the brilliant green enrichment method, direct plating, and the method of drying (Wordley, 1921); in no instance was *B. paratyphosus* C isolated. Fourteen days after the first agglutination was performed the patient was again bled and her serum tested on *paratyphosus* C antigen, with a negative result.

The source of infection was not discovered and no other cases of unexplained fever arose. The faeces of the other members of the family were examined, but no pathogenic

organisms were isolated. As a precaution the other inmates of the house were inoculated with a *paratyphosus* C vaccine, and, as stated above, no fresh cases of infection arose.

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THE RELATIVE CONCENTRATION RATIOS OF SOME CONSTITUENTS OF THE URINE.

(Abstract.)*

BY

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THE "filtration-reabsorption" theory of renal secretion states that the glomeruli filter off from the plasma its dialyzable constituents, some of which are reabsorbed, together with water, by the tubules, thus leading to a concentration of the remainder: the former are described as "threshold," and the latter as "no-threshold" bodies respectively.¹ If two "no-threshold" substances are present together in the plasma, are filtered off by the glomeruli, and are concentrated in the tubules by the absorption of water, the degrees to which they are concentrated should be the same in each case. The "concentration ratio" is the ratio of the amount present in the urine to that in the plasma (expressed in percentages).² The experiments to be described were performed to determine the relative concentration ratios of some of the so-called "no-threshold" constituents of the urine; urea, inorganic phosphate, and creatinine were chosen for this purpose. They are present in a "free" (that is, dialyzable) condition in the plasma, and appear to be equally distributed between plasma and corpuscles *in vivo*, so that estimations made on the plasma give the amounts available for filtration through the glomeruli at that moment. As, however, it has been stated that urea and inorganic phosphate are present solely in the plasma *in vivo*, entering the corpuscles after the blood is shed, unless precautions are taken to avoid injury to them,³ some preliminary experiments were performed on the distribution of these three substances between plasma and corpuscles in the blood of the cat, since this animal was used for the later experiments. It was found that urea and creatinine were evenly distributed under normal conditions: after injection intravenously, the same even distribution might be found, or there might be more in the plasma, while there was always more inorganic phosphate in the plasma than in the corpuscles after it had been injected into the blood stream.

The experiments on the concentration ratios were performed on decerebrate cats: a solution of the substances about to be examined was injected intravenously, a blood sample taken shortly afterwards, and a further sample after a variable length of time, during which the urine was collected; in some experiments further samples of blood and urine were obtained. The blood samples were oxalated and centrifuged, and the plasma used for the analyses. For calculating the concentration ratio the plasma percentage was taken as the mean of the analyses of the two samples obtained at the beginning and end of the period during which the urine was collected.

It was found that the creatinine was always concentrated to a greater extent than the urea—from two to five times more in the different experiments. This occurs whether the plasma or urinary concentrations vary or remain constant during the course of an experiment. The fact that the results obtained when the plasma concentrations are constant are comparable with those obtained when these concentrations vary, suggests that taking the mean plasma concentration for calculating the concentration ratio introduces no appreciable error.

Comparing the concentration ratios of inorganic phosphate and urea, it was found that the phosphate might be concentrated to about the same extent as the urea, or up

to about three times more; but it was always found to be concentrated to a less degree than the creatinine in the same experiment. The degree of concentration seemed to depend directly on the amount of phosphate injected, being greater when the kidney had to remove a larger amount from the blood stream. If the concentration ratio of urea is taken as unity, those of creatinine and inorganic phosphate relative to this as standard can be plotted on a chart, and it is seen that there is a general parallelism between the ratios of the latter two, which possibly depends on the rate of blood flow through the kidney.

The fact that urea, inorganic phosphate, and creatinine may be concentrated to different degrees by the kidneys during excretion is difficult of explanation on the filtration reabsorption hypothesis. If the modification be accepted that the urea is partly reabsorbed in the tubules,⁴ these experiments show that the hypothesis must be still further modified to admit of partial reabsorption of the inorganic phosphate also. It seems more probable that the tubule cells secrete these substances independently, according to the requirements of the moment. On the other hand, the facts are consistent with the view that selective reabsorption takes place in the tubules, the fluid absorbed varying in composition at different times. A fairly definite relationship was found between the excretion rates of the three substances in experiments in which several samples of urine were obtained: the factor correlating the excretion rates is presumably the blood flow through the kidney.

The experiments give data for calculating the rate of disappearance of the injected substances from the blood stream, taking the initial blood volume to be 5 per cent. of the body weight. Within two minutes of the completion of the injection, 75 to 90 per cent. of the injected urea and creatinine is no longer to be found in the blood; the loss is most rapid at first, and then the rate slackens until a balance is struck between the concentrations in the blood and in the tissues; the concentration in the blood may now remain fairly constant in spite of excretion in the urine, since the tissues act as a reservoir of the substances in question. The injected inorganic phosphate leaves the blood more slowly, and only about 65 to 80 per cent. disappears into the tissues.

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THE DIFFERENTIAL DIAGNOSIS OF SMALL-POX AND CHICKEN-POX.

OBSOLETE DIAGNOSTIC CRITERIA.

BY

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ANYONE who wishes to gain a really sound grounding in this subject will be well advised to assign beforehand their true value to certain traditional criteria with which he may have been equipped as a student. There are certain phenomena which frequently occur indeed, but are not pathognomonic in the hour of trial for the purpose of distinguishing between small-pox and chicken-pox. Into this category fall umbilication, shottiness, palatal and buccal lesions, lesions on the sole of the foot, cropping, uniloculation. Not one of these is a real friend in need; and the first four may prove to be very unreliable in the matter of the assistance which they offer.

In my article in the Jenner Memorial Number of the *BRITISH MEDICAL JOURNAL*, dated July 5th, 1902, on "The differential diagnosis between variola and varicella," the following observations were made: "It is well at once to say that the words 'shotty' and 'umbilicated' are mere broken reeds to lean upon in the matter of diagnosis. The expressions are pernicious in two ways: Their absence in a case suspected to be small-pox is taken as evidence against that disorder, and their presence in a case otherwise suggestive of varicella is held to negative that disease. The words are fetishes, or objects of superstitious worship, which help their devotees as little as do most idols, and

* The full paper is published in the *British Journal of Experimental Pathology*, 1923, vol. 4, pp. 87 and 117.