

Section of Physical Medicine

President—GEOFFREY HOLMES, M.B.

[January 15, 1937]

The Peripheral Circulation in Chronic Rheumatism

By G. D. KERSLEY, M.D., M.R.C.P.

ABSTRACT.—A series of cases of rheumatoid arthritis, osteo-arthritis, gout and fibrositis have been investigated by means of the sedimentation rate, Arneth count, saline absorption test, glucose tolerance test, and direct observation of the capillaries, in order to correlate any abnormality of the peripheral circulation with the type and activity of the disease.

The sedimentation rate test, in which a wide bore tube was used, was of great value as an estimation of activity in the rheumatoid arthritic cases, but a small group showed a normal reading. In the gouty subjects it was usually low but was liable to vary greatly within a short time. In the osteo-arthritic and fibrositic groups it was normal.

The Arneth count did not parallel the sedimentation rate; it was usually normal in the gouty subjects but showed abnormalities in the rheumatoid arthritics and sometimes in the osteo-arthritics (a shift usually to the left, but sometimes to the right).

The saline absorption test was valueless except in cases of gross circulatory disturbance.

The glucose tolerance test, although producing some abnormal curves, in both the osteo-arthritic and the rheumatoid arthritic groups gave normal curves, taking an average of a large number of cases.

Observation of the capillaries—notes being taken of their number, shape, &c., with a drawing eyepiece and photographs—showed a wide variation in normal individuals. This was so remarkable that the only clear-cut findings were a slight increase in tortuosity in the osteo-arthritic group—probably due to the increase in the average age of this group—and an increase in the visibility of the full-length of the capillary loop and of the basal meshwork in the rheumatoid arthritics, probably due to trophic thinning of the epidermis.

RÉSUMÉ.—La rapidité de la sédimentation globulaire, la formule leucocytaire d'Arneth, l'absorption de chlorure de sodium et la tolérance du glucose furent étudiés dans une série de cas d'arthrite rhumatoïde, d'ostéo-arthrite, de goutte et de fibrosite, et les capillaires furent examinés directement pour déterminer les relations entre les anomalies de la circulation périphérique qui peuvent se trouver avec le type et l'activité de la maladie.

La sédimentation globulaire, étudiée au moyen d'un tube à grand calibre, s'est montrée très utile comme index de l'activité des cas d'arthrite rhumatoïde, mais dans quelques cas les chiffres furent normaux. Chez la majorité des goutteux l'indication était basse d'habitude, mais pouvait varier beaucoup en peu de temps. Chez les ostéo-arthritiques et les fibrositiques la sédimentation se montra normale.

La formule d'Arneth ne suivit pas la sédimentation. Chez les goutteux elle fut le plus souvent normale, mais dans l'arthrite rhumatoïde, et quelquefois dans l'ostéo-arthrite elle se montra anormale (déviations vers la gauche le plus souvent, mais quelquefois vers la droite).

L'épreuve de l'absorption du chlorure de sodium se montra sans valeur, sauf en cas de perturbation circulatoire manifeste.

Quant à la tolérance pour le glucose, quoique quelques courbes anormales furent observées, la courbe moyenne dans un grand nombre de cas d'arthrite rhumatoïde et d'ostéo-arthrite se montra normale.

L'observation des capillaires (leur nombre, leur forme, etc., enregistrés au moyen d'un oculaire à dessin et de photographies) montra de larges variations chez des sujets normaux. Ces différences furent si considérables que le seul résultat défini chez les malades fut une légère augmentation de la tortuosité des capillaires chez les ostéo-arthritiques, probablement due à l'âge moyen plus élevé dans ce groupe que dans les autres, et une augmentation de la

visibilité de la longueur entière de la boucle capillaire et du réseau basal dans l'arthrite rhumatoïde, due probablement à un amincissement trophique de l'épiderme.

ZUSAMMENFASSUNG.—Bei einer Reihe von Fällen von rheumatoider Arthritis, Osteoarthritis, Gicht und Fibrositis wurden Blutkörperchensenkungsgeschwindigkeit, Arneth'sches Blutbild, Glukosetoleranz, Kochsalzresorption sowie das Verhalten der Kapillaren beobachtet, u. zw. im Hinblick auf etwa vorhandene Beziehungen zwischen Anomalien des peripheren Kreislaufs und Art sowie Aktivität der verschiedenen Erkrankungen.

Die Bestimmung der Blutkörperchensenkungsgeschwindigkeit—verwendet wurde eine Röhre mit weitem Kaliber—erwies sich bei den Fällen von rheumatoider Arthritis als sehr wertvoll um einen Anhaltspunkt über die Aktivität der Erkrankung zu gewinnen; bei einer kleinen Zahl von Fällen wurden indessen normale Werte gefunden. Bei Gicht waren die Werte meist niedrig, zeigten aber eine Tendenz zu erheblichen kurzfristigen Schwankungen. Bei Osteoarthritis und Fibrositis waren die Werte normal.

Es bestand kein Parallelismus zwischen Arneth'schem Blutbild und Senkungsgeschwindigkeit; während es bei Gicht meistens normal war, zeigte es bei rheumatoider Arthritis und zuweilen auch bei Osteoarthritis pathologische Veränderungen (meistens im Sinne einer Links-, bisweilen aber auch einer Rechtsverschiebung).

Mit Ausnahme der Fälle von vorgeschrittener Kreislaufstörung erwies sich die Bestimmung der Kochsalzresorption als wertlos.

Die Untersuchung der Blutzuckerkurve ergab sowohl bei Osteoarthritis als auch bei rheumatoider Arthritis einen normalen Befund, sofern man die Mittelwerte einer grossen Anzahl von Fällen zugrunde legt; gelegentlich wurden allerdings abnorme Kurven gefunden.

Die Untersuchung der Kapillaren—hinsichtlich ihrer Zahl, Form, usw., mittels Zeichnungsookular und Photographien—ergab auch bei normalen Individuen grosse Verschiedenheiten. Diese waren so ausgesprochen dass der einzige unzweideutige abnorme Befund bei den Fällen von Osteoarthritis in einer leichten Zunahme der Schlingelung—wahrscheinlich eine Folge des höheren Durchschnittsalters dieser Gruppe—und bei den Fällen von rheumatoider Arthritis in einer Zunahme der Sichtbarkeit der Kapillarschlingen in ihrer ganzen Länge und des basalen Netzwerkes bestand; letzteres dürfte wahrscheinlich auf einer trophischen Verdünnung der Epidermis beruhen.

MUCH clinical evidence has been produced suggesting changes in the peripheral circulation as a prominent factor in various types of chronic rheumatism. In certain cases of rheumatoid arthritis a tendency to vascular spasm is an early feature, and in osteo-arthritis there are often vascular changes. Moreover, any treatment calculated to improve the circulation—whether it be massage, heat in its various forms, alternating heat and cold, moderate exercise or sympathectomy, is helpful in the treatment of chronic rheumatism provided that it does not at the same time traumatize the affected joints.

Various workers, largely American, have added pathological tests to substantiate the clinical evidence, and I have tried to repeat some of these observations and correlate them with clinical findings, in conjunction with the sedimentation rate and Arneth count, in clear-cut cases of chronic rheumatism. I might say, from the first, that my results have not been dramatic, that I have failed to find such clear-cut demarcations between the rheumatic subjects and normal controls as have been found by certain other observers, and that my observations have proved destructive rather than constructive. The tests used were the saline-absorption rate, the glucose tolerance, and finally direct observation of the capillary circulation of the nail bed.

Two other clinico-pathological tests have also been used by other workers in the desire to throw light on the same problem, namely, blood-counts on drops of blood issuing from a finger stab directly after puncture, and after these drops have been wiped away, and observations on temperature change in the nail bed. In the former test in normals it was found that the count was slightly higher in the first sample of blood but that in arthritics the reverse was usually the case. This is interpreted by the authors, Pierce and Pemberton (1927), as being due to increased capillary spasm, slow issuing of the blood, and hence undue dilution by tissue fluids.

As regards temperature observations it was found by Wright and Pemberton (1930) that in arthritics the temperature of the nail bed was slightly lower than in normal individuals and that on cooling the whole body, the fall in temperature of the periphery was slower, and the return to normal slower than in normal subjects. This of course also suggests poorness of the peripheral circulation.

In considering the pathological tests of the most value in assessing the activity and type of a rheumatic infection, one may take a lead from the observations made by Houghton (1936) on their value in pulmonary tuberculosis, a condition having many points in common at least with rheumatoid arthritis. He studies the value of the differential count, the sedimentation rate, and the nuclear count, in assessing the state of the disease. In the former he considers an increase in the number of monocytes an indication of tubercle-formation (a liability), in that of the polymorphonuclears an indication of decomposition and pus-formation (a liability), in that of the lymphocytes a reaction (an asset) and similarly in that of the eosinophils a reaction (an asset). He thus considers the blood picture as an indication of what is happening in the diseased tissues.

The sedimentation rate he takes to be a gauge of the constitutional disturbance and increase in metabolism, and the nuclear count whether estimated as the Schilling count, Arneht count and weighted mean, or the Bonsdorff count (the latter being the same as the weighted mean multiplied by 100), as an indication of the degree of auto-inoculation and toxæmia. In the present series of cases insufficient observation has been carried out on the differential count, but the sedimentation rate and Arneht counts have been performed in all cases and have been used in conjunction with the clinical data in order to assess the activity and type of the disease. The former was carried out by collecting 15 c.c. of venous blood into a syringe and tube, each rinsed out with 10% potassium oxalate, and then placing 10 c.c. of this in a conical tube graduated in tenths of a c.c. This was read at half-hour intervals and any fall below 90% at the end of an hour was considered abnormal, and below 80% markedly so. All estimations were also carried out in parallel with the Westergren and capillary methods, but we have found that the wide-bore tube appears to give a more delicate and accurate measure of the clinical activity than the narrow tube methods, and that the capillary method is almost useless. The Arneht count was carried out by the usual technique and the weighted mean, or average number of nuclear lobes per polymorphonuclear cell, has been used as the index.

Hill (1931) found a shift to the left or low-weighted mean in nearly all cases of rheumatoid arthritis (average 1.9), to a less degree in subacute rheumatism, climacteric arthritis and gout, and no abnormality in fibrositis. His normal controls ranged from 2.4 to 3.0 and he found a tendency to return to normal with clinical improvement. Collins (1936) taking a weighted mean below 2.40 as a slight shift to the left, found a reduction of weighted mean in cases of rheumatoid arthritis and those cases of osteo-arthritis with cyst formation and also notes that this abnormality does not improve readily with decrease of clinical activity.

Schulhof (1937) in a paper read to the I.S.M.H. at their meeting in Austria this year, dealt with the effect of the "bath reaction" on the Arneht count. Examining this in 100 cases he found a definite shift to the left, or decrease in the weighted mean about the end of the first week of treatment, that the shift was not altered by salicylates and analgesics used to control the clinical reaction, and that there was later a tendency to return towards normal correlating, to some extent, with the clinical progress of the individual. This is not the place, nor have we followed up enough cases, to warrant a discussion on the relationship of the sedimentation rate and Arneht count, but it may be said that like most others we find the sedimentation rate of the utmost use in distinguishing early cases of rheumatoid arthritis, but there is a certain small group we are following up carefully where the sedimentation rate is persistently normal but which otherwise very closely resemble that disease.

A parallel instance is noted by Houghton as occurring in tuberculosis. Moreover, the rate is usually lowered in gout but in this condition it is much more prone to marked variations over short periods of observation. The Arneth count, taking as index the weighted mean, is more difficult to interpret. It did not run parallel to the sedimentation rate, was seldom far from normal in the gouty subjects, but some markedly low results—and also a few high results—were found among both the rheumatoid arthritics and the osteo-arthritics. So far the results obtained during bath treatment have been rather confusing, some showing a definite shift to the right.

The saline absorption test is carried out by injecting intradermally in two piqûres 0.20 c.c. of normal saline and noting the time taken for its absorption, the end-point being read by palpation. In a normal person this is usually estimated as being more than 50 to 60 minutes, but there are many fallacies. The type of skin injected, the exact depth of the injection, and the amount of trauma due to the needle, are all variable, and make any slight deviation from the normal of little

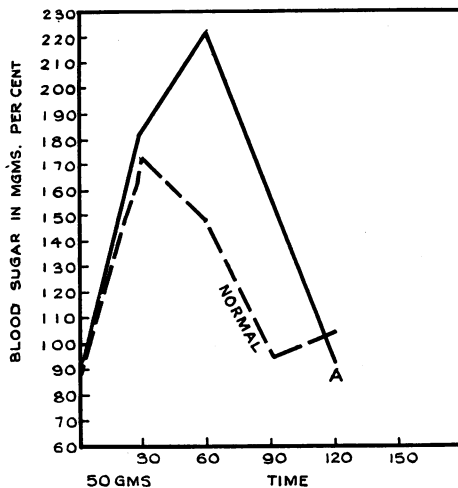


CHART I.

value. The test was used by Aldrich and McClure (1924) and again by Cohen and Applebaum (1926) and the latter workers found a definite decrease in the time of absorption in localized anoxæmia, cardiac and renal disease, and when advanced vascular changes were present.

In 14 cases of rheumatoid arthritis four showed a drop in absorption time below 50 minutes but this abnormality did not parallel the clinical degree of activity or the fall in the sedimentation rate. Eight cases of osteo-arthritis all showed normal results as did eight cases of gout. Of normal controls taken from a fracture clinic, the part fractured being remote from the area punctured, eight out of nine gave normal results and the ninth, who had slight cardiac symptoms, gave the lowest result recorded. Four cases of empyema were also examined and two of these gave results as low as any of the rheumatoid cases, namely, thirty minutes. It therefore appeared that the group of rheumatoid arthritics, the only group of rheumatic disease that gave an abnormal result, was comparable with that of sick and toxic patients suffering from other infections.

According to Pemberton (1920) the glucose tolerance test shows a delayed sugar removal and hence a high curve (Chart I), rapidly returning to normal in 60% of arthritics, and potentially so if the circulation of the extremities is reduced by both

legs and one arm being suspended above the level of the heart, in another 25%. He, however, used 100 gm. of glucose for this test-feed and took his upper limit of normality as 150 mgm.%. Any abnormal curves obtained may be due to delayed sugar removal from the blood or increased speed of absorption from the gut, and in order to disprove the latter hypothesis Pemberton (1925) administered at the same time urea and potassium iodide. He found no greater increase in the non-protein nitrogen of the blood or the nitrogen or iodine content of the urine than in normal controls and hence assumed that increased speed of absorption was not the cause of any increase in the blood-sugar. He therefore interprets this finding as evidence of delayed sugar-removal by the tissues, owing to vasoconstriction of the smaller blood-vessels to those tissues, and hence less contact of the blood with them. He states that after removal of sepsis there is often a rapid fall of the sugar level to normal with improvement in the patient, and that this delayed sugar removal occurs in sepsis and toxæmic states unassociated with arthritis.

In this country the glucose-tolerance test is usually made with only 50 gm. of glucose and even then the upper margin of normality is usually placed in the region of 165 rather than 150 mgm.%. Shackle and Copeman (1933) using 50 gm. of glucose repeated this work on arterial and venous blood in 50 cases, and stated that they obtained curves in nearly all cases of rheumatoid arthritis similar to the one illustrated in their article where the blood-sugar rises to 316 mgm.%. One wonders whether these high curves might be due to a low carbohydrate diet employed in the course of treatment, and whether sepsis had been less completely eliminated.

In the present series of cases the test was carried out at 9 a.m. after an overnight fast and the blood was collected by blood gun puncture in tubes containing deposited oxalate and a minute pinch of fluoride. The estimations were carried out by Wallis's modification of Folin and Wu's method and after the first blood test 50 gm. anhydrous glucose was given in 250 c.c. water.

In about 100 classified chronic rheumatic cases the glucose tolerance test has been performed. In Chart II are shown plotted the average curves of 47 rheumatoid arthritics, 16 osteo-arthritics, 11 fibrositics, and 8 goutis. It may be seen that, although in this series there were abnormal curves, among the rheumatoid arthritics five and the osteo-arthritics three, rising to or above 200 mgm.% yet the average curves are not abnormally high. There seemed to be no relation between the height of the curve and the sedimentation rate, but one showed a dramatic fall after the removal of a septic focus. The group of cases showing the highest average curve was that of the osteo-arthritics, and the only possible abnormality in the average curves was the tendency for them to rise to their highest point at the hour rather than earlier. In order to correlate these results with those of the American workers a short series of cases had glucose tolerance tests performed on them within a few days interval using both 50 and 100 gm. of sugar and the result of the average curves of these cases showed the curve in the latter to be about 10 mgm.% higher than in the former and that there was a definite tendency to a lag in the fall (Chart III).

The method of examination of the capillaries of the nail bed was first suggested by Lombard (1912) and was improved by Wright and Duryee (1933). It consists of placing a drop of oil on the back of the finger and examining the thinned cuticle overlying the nail with the $\frac{1}{2}$ objective and $\times 8$ or $\times 10$ eyepiece, and using a light focused on the surface by means of a convex lens. As in many things, practice is essential and it is not until many cases have been examined that the maximum detail is obtained. On a little practice, however, the terminal loops of the capillaries may be clearly seen but their number, regularity, diameter, the difference between the afferent and efferent stems, their length, their degree of tortuosity, speed of progression of the corpuscles, and general visibility, all vary greatly.

In some cases the spasm of the vessels produces temporary stasis and apparently

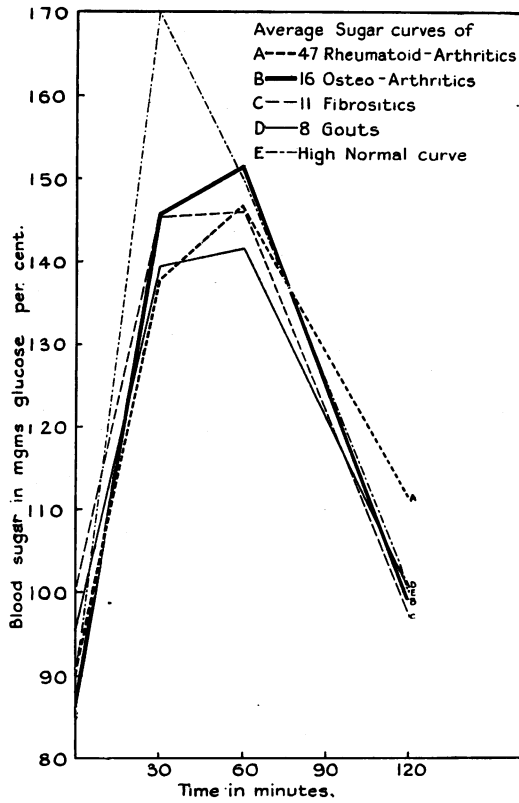


CHART II.

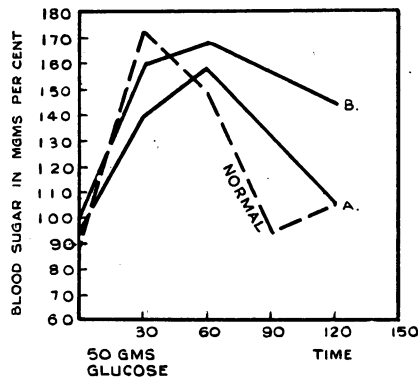


CHART III.

interrupted circulation and Pemberton suggests that this is present in 25% of arthritics but in only 2% of normal controls. His other main differences consist of general pallor of the field, fewer capillaries, less contrast between the arterial and venous part of the loop and slower blood-flow.

Bissett and Woodmansey (1932) carried out a like investigation on rheumatic cases—including fibrositis, rheumatoid arthritis, and osteo-arthritis—and normal

controls, and noted in the former fewer and less-filled loops, less tortuosity, greater length and better visibility, owing to the thinner epidermis. Wright and Duryee draw attention to the fact that by reflected light the thin endothelial wall and widely spread meshwork of muscle of the capillaries are not visible, but only the blood within, and likewise lay stress on the effect of age on conformation, the capillary loops gradually become elongated and more tortuous. They investigated many cases of cardiovascular disease and found that in high blood-pressure the vessels might be straight or tortuous, but the flow was rapid and uninterrupted. In low pressure the vessels were usually straight and moderately dilated and the flow was slow with frequent cessations. In arteriosclerosis there was nothing pathognomonic but interruptions were fairly frequent. In conjunction with Kovacs (1933) they examined the capillaries of a series of arthritics and found no significant abnormality except in the neighbourhood of Heberden's nodes and actually swollen fingers, and here the number of capillaries was decreased and cessations in flow were more frequent. They took a much broader view than other authors and are less inclined to treat minor variations as abnormalities. Griffiths (1932) records that of 600 cases including 31 neurasthenics seven, all in the last category, showed disorderly capillary arrangement and variability in size to a very marked degree.

The problem on commencing this investigation was how to avoid bias and obtain a record on a large number of cases without undue expense and wasting of time. Photography of the nail bed is very difficult and although with help from Messrs. Ilford, Ltd., I have obtained a number of photographs—using a carbon arc lamp and cooling system—it was impracticable to use this method for every case. I therefore obtained a drawing eyepiece and in addition to making notes in columns as to the presence of tortuosity, interrupted circulation, &c., I took a drawing of a sample field in each case so that these might be classified on their merits, irrespective of what type of case they represented.

The first striking thing was the error obviously presented by the effect of occupation on the thickness of the skin and also by the effect on the first layer of capillary loops in the nature of shortening and increase in tortuosity on pressing back the cuticle. Secondly the extreme variation in the fields of normal individuals was most striking and perhaps one of the most typical "arthritic" fields with interrupted circulation that I have observed was in my own nail bed. So far I have no symptoms of rheumatism.

The cases investigated were grouped into the categories of rheumatoid arthritis, gout, osteo-arthritis and controls and every type of capillary arrangement could be found in each group. Tracings of capillary fields were examined and classified without relation to the clinical diagnosis and no significant preponderance of any clinical group was found in any morphological group.

In 43 cases the length of the capillary loops, their number and the presence or absence of regularity in disposition, interruption of circulation, tortuosity, and visibility, were all noted and these features were each considered in turn in relation to the clinical picture. The length of the loops visible and the number was slightly greater in the group of rheumatoid arthritics. As regards regularity of arrangement and visibility there was no significant difference between either group. Tortuosity was slightly more marked in the osteo-arthritics and interrupted circulation perhaps a little more in the rheumatoid arthritics, but the variation between the four groups was so slight as to be barely worthy of notice. Certain experiments were also carried out, the capillaries being examined at room temperature before and after immersion of the hands in hot and cold water, but no significant difference was noted between the reaction of the various groups.

In the osteo-arthritics, the group with the highest average age, there was a slight tendency to increased tortuosity; and in the rheumatoid arthritics the full length of the capillaries and the basal meshwork was rather more easily seen, owing

PHOTOGRAPHS OF TYPICAL CAPILLARY FIELDS

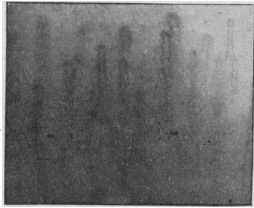


FIG. 1.—A normal field.

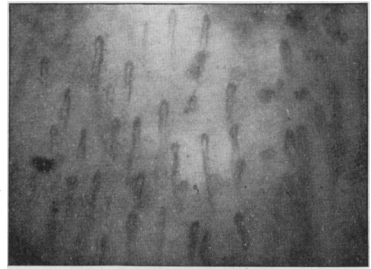


FIG. 2.—Normal field showing good definition of arterial and venous loops.

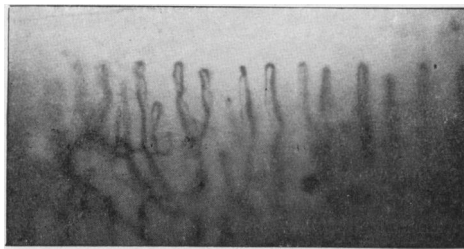


FIG. 3.—Basal venous network (from normal individual).

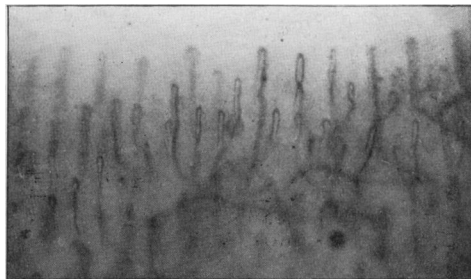


FIG. 4.—Basal venous network in rheumatoid arthritis.

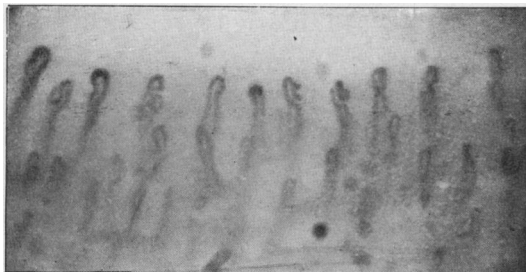


FIG. 5.—Field showing tortuous loops rather congested (from an osteo-arthritic).

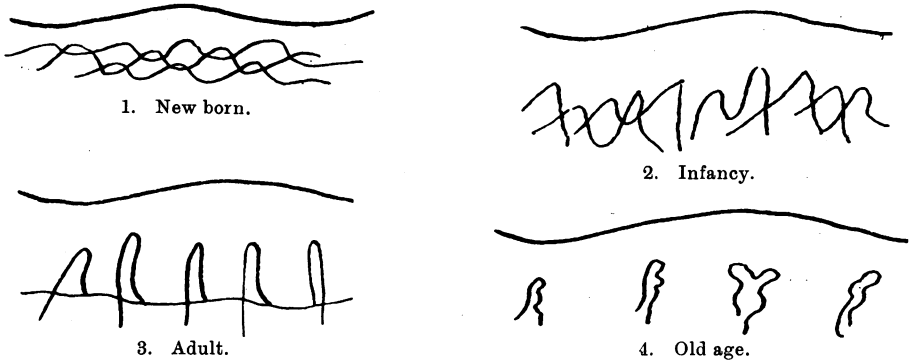


FIG. 6.—Diagrammatic representation of the development of capillary loops.

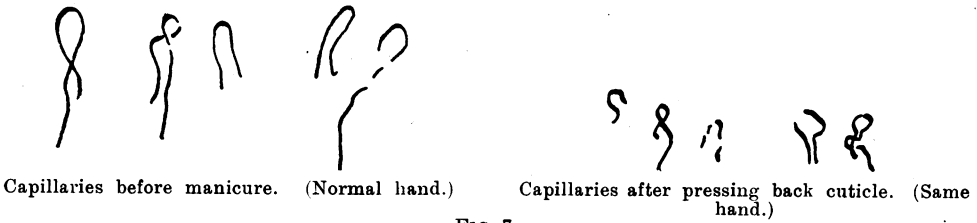


FIG. 7.

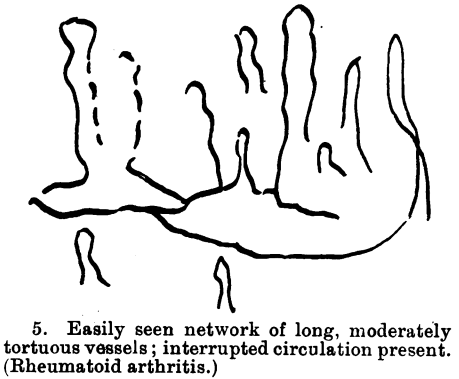
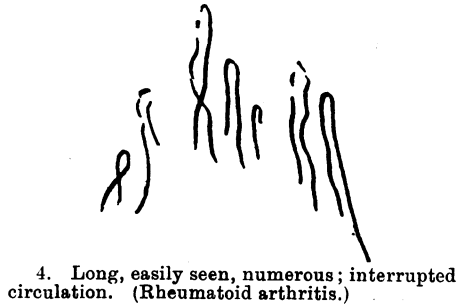
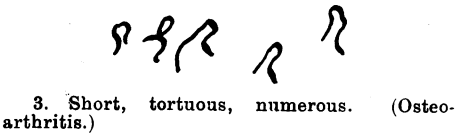
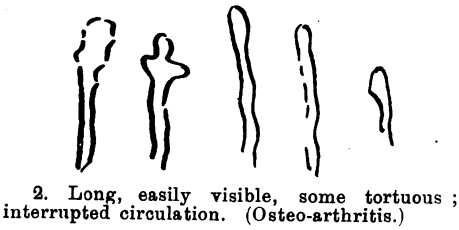
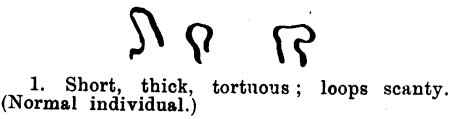


FIG. 8.—Tracings made with drawing eyepiece of capillary loops.

to the trophic thinning of the epidermis, but no other significant abnormalities could be distinguished.

[I wish to express my thanks to Dr. Hubert Gibson for his invaluable help, and also to Messrs. Ilford, Ltd., for assistance with the photography of the capillaries.]

BIBLIOGRAPHY

- ALDRICH, C. A., and MCCLURE, W. B. (1924), *J. A. M. A.*, **82**, 1425.
 BISSETT, A. A., and WOODMANSEY, A. (1932), *Lancet* (ii), 620.
 COHEN, M. B., APPLEBAUM, H. S. J., and HAINSWORTH, E. L. (1926), *J. A. M. A.*, **86**, 1677.
 COLLINS, D. H. (1936), *Acta rheumatol.*, **28**, 3.
 GRIFFITHS, J. O. (1932), *Am. Journ. M. Sc.*, **183**, 180.
 HILL, L. (1931), *Acta rheumatol.*, **10**, 6.
 HOUGHTON, L. E. (1936), *Brit. M. J.*, **2**, 1246.
 KOVACS, J., WRIGHT, I. S., and DURYEE, A. M. (1933), *J. A. M. A.*, **100**, 1018.
 LOMBARD, W. P. (1912), *Am. J. Physiol.*, **29**, 335.
 PEMBERTON, R., "Arthritis and rheumatoid conditions", London, 1935.
 PEMBERTON, R., CAJORI, F. A., and CRONTER, C. Y. (1925), *J. A. M. A.*, **85**, 1793.
 PEMBERTON, R., and FOSTER, G. L. (1920), *Arch. Int. Med.*, **25**, 245.
 PIERCE, E. G., and PEMBERTON, R. (1927), *Arch. Int. Med.*, **39**, 421.
 SCHULHOF, O. (1937), *Arch. M. Hydrol.*, **1**, 234.
 SHACKLE, J. W., and COPEMAN, W. S. (1933), *Brit. M. J.* (i), 268.
 WRIGHT, I. S., and DURYEE, A. M. (1933), *Arch. Int. Med.*, **53**, 554.
 WRIGHT, I. S., and PEMBERTON, R. (1930), *Arch. Int. Med.*, **45**, 147.

Discussion.—Dr. C. W. BUCKLEY said that he had been impressed by the results of some recent researches by Professor Talalajef of Moscow, who found that excess of carbohydrate in the diet materially affected the sensitivity of dogs, as measured by the Arthus phenomenon. In view of the difference in glucose-tolerance curves shown by Dr. Kersley according to whether 50 or 100 grm. of glucose had been taken, and the generally accepted view that carbohydrate excess was bad in certain forms of rheumatic disease, this might be due to increased sensitivity to the rheumatic infection caused by the diet. It would be interesting to see whether the sedimentation rate and the Arneth count were modified by variation of carbohydrates in the diet.

Dr. G. L. KERR PRINGLE said he thought that one of the chief reasons why Dr. Kersley's findings with the glucose-tolerance test had differed from those of Pemberton and others was because he had not differentiated between those of rheumatoid arthritis with a focus of infection and those in which the focus had been removed—as, for instance, after tonsillectomy. Also to a lesser degree differentiation should be made between severe, mild, and convalescent cases. In the series of 100 cases¹ which he had investigated the difference in the graphs was most marked and followed closely those of Pemberton.

Referring to the Arneth count in osteo-arthritis, it was possible that the unequal findings were due to the probability of there being two distinct types, the senile degenerative and the more active cystic types.

Dr. J. BARNES BURT: The whole question of the peripheral circulation is of great importance in the study of rheumatism, from the point of view of ætiology, progress of the disease and, above all, of its physical treatment, for the action on the blood-vessels is the basis of nearly all physical treatment.

During this century the idea of infection and focal infection has tended to blind the physician to the importance of other factors, in spite of the fact that Dr. Pemberton has shown that something like 60% of cases of arthritis in the world war were precipitated by exposure to wet and cold, and that rather more cases of arthritis improved without removal of focal infection than when the focus of infection was removed, and also in spite of the work on the peripheral circulation carried out by Sir Thomas Lewis.

Lewis stated that there are four factors which control the peripheral circulation: *Factor 1*. The central nervous system, by means of the sympathetic system; this is a most difficult subject because our knowledge is still so uncertain. With regard to the other factors we are on much more certain grounds. *Factor 2* is the presence of metabolites, which have a stronger action than anything else in promoting dilatation of the capillaries. *Factor 3* is the local effect of cold and heat upon the limbs. *Factor 4* is the general effect of heat and cold, thus, by heating the trunk the small capillaries of the limbs are caused to dilate. Under

¹ "Glucose-tolerance in chronic arthritis", Pringle and Miller, *Lancet*, 1923 (i), 171.

certain conditions these factors antagonize one another, and one of the results of this may be the production of some form of rheumatism.

For example: A man goes to sleep in a train, sitting up; his head is supported in an uncomfortable angle by his head muscles; a draught from the window plays on his neck, and his feet are cold. After some fifteen minutes of sleep he wakes up and finds his neck stiff. This passes off with a little rubbing, but the next day he has a severe fibrositis of the neck muscles. What has happened? In supporting the head, the neck muscles have produced quantities of metabolites, and this according to factor 2 ought to have produced a dilatation of the capillary system; but a cold draught is playing on this area and factor 3 comes into play, namely vasoconstriction, as a result of local cold. If the railway carriage is cold, factor 4 also comes into play, namely, vasoconstriction of all the peripheral blood-vessels. In severe cases there is a fifth factor; if tissues are cooled below 50° F., hæmoglobin fails to part with its oxygen. Thus in the above case the tissues of the neck muscles suffer from an accumulation of metabolites, which ought to have been carried away by the dilated capillaries and veins, but local and general cold has prevented their removal by setting up vasoconstriction. The initial stiffness was due to the excess of metabolites, the later stiffness was due to inflammatory changes necessary to repair the tissues damaged by excess of metabolites.

There is, of course, no experimental proof for these statements; it is a question of deduction and clinical experience. In ought, however, to be possible to prove experimentally what is the relation of fibrositis and arthritis to exposure to damp and cold, and Dr. Kersley's paper indicates a beginning in that direction.

Dr. JOHN BODMAN said that he too had to thank Messrs. Ilford Ltd. for their help and advice. He suggested that the simplest means of obtaining routine capillary photographs of good definition was by means of the Leitz capillary microscope, which would plug into any mains circuit, and which was very portable, and using Ilford "double X-press" plates on which, with this particular instrument, good negatives could be obtained at an exposure of 1/25th second; he had found that prints were best made on Ilford "extra contrasty glossy" bromide paper.

He had been struck by the similarity between the osteo-arthritic and the arteriosclerotic type of capillaries, and by the same type of similarity between the rheumatoid capillary with that seen in acrocyanotic tendency.

He had been still more impressed with the investigations being carried out, particularly in Germany on routine photography of the capillaries in school children, which was tending to show that capillary development proceeded along definite lines in childhood, and arrest at one or other stage could be demonstrated as being associated with arrest in development in other directions of the child's physical or mental state.

[A series of drawings were shown illustrating these several stages of development, and further illustrated by actual capillary photographs, in which arrested development could be made out at various stages in arthritic conditions. A preliminary scheme was suggested for typing capillaries morphologically from their appearance, stress being laid on the different appearance in the photographed structure.]

In conclusion, he suggested that the solution of the problem of the relation of capillary structure, in particular as applicable to rheumatism and arthritis, lay firstly in accurately assaying the anatomical variations and arrests in developments, according to some such scheme as he had put forward, and then by applying this type of classification to photographs from definite clinical groups.

Dr. PHILIP ELLMAN said that, with Dr. H. J. Taylor, he had described a method for estimating the subcutaneous tissue oxygen and carbon-dioxide tension in man.¹ In cases of chronic rheumatic joint disease the results had shown that the diffusion of oxygen and carbon dioxide was normal. This indicated that there was no capillary stasis in these cases, and that the flow of blood was a normal one.

With regard to the blood sedimentation rate, his observations in cases of rheumatoid arthritis indicated that the rate of sedimentation of the red corpuscles was a valuable guide in estimating the degree of activity of the disease.

In a closely allied infective disease—pulmonary tuberculosis—he had found that the sedimentation rate was less valuable from the point of view of prognosis than it was in rheumatoid arthritis. Hence, Houghton, working at Colindale Hospital, had used a blood

¹ *Journ. Hygiene*, 1935, 35, 3.

index as a method of estimating prognosis in pulmonary tuberculosis and considered it to be of greater value. Houghton's formula represented three blood items, namely, the sedimentation rate, the von Bonsdorff count, and the polymorphonuclear-lymphocyte-monocyte ratio.

In a few cases in which this index had been applied to rheumatoid arthritis he had not found it to be so valuable as it undoubtedly was in pulmonary tuberculosis, indeed it was questionable whether the work involved in estimating this index justified its use over and above the sedimentation rate alone.

Dr. H. J. GIBSON that, as the results of the sugar-tolerance tests were completely at variance with those of other workers, the question of the technique of the tests arose. He had carried out those reported by Dr. Kersley, and he would be pleased to answer any question regarding the methods used.

Dr. L. C. HILL said that he had been particularly impressed by the care taken to avoid any bias in favour of the hypothesis of circulatory deficiency.

One of the most interesting portions of the paper had dealt with the question of diminished sugar tolerance. In so far as the speaker was concerned, Dr. Kersley's investigations did not entirely dispel the fog which surrounded this problem.

The investigations of Pemberton and his co-workers appeared to prove in a logical and satisfactory manner the presence of a diminished sugar tolerance in at least 75% of cases of rheumatoid arthritis. Having found that 60% of rheumatoid arthritics showed a diminished power of absorbing 100 gm. of glucose, the peripheral circulation of the remaining 40% was hampered by the process of elevating two legs and one arm for a period of one hour. Under these circumstances, 40% (the speaker said he could not vouch for the actual figures) of the remainder now showed diminished absorption, which number added to the original 60% made a grand total of over 75%. A similar procedure of limb elevation carried out in a number of controls did not reveal carbohydrate intolerance in a single case. The final stage in the experiment occurred when, by giving vasodilators regularly over a period, the rate of glucose absorption had been appreciably improved.

His (Dr. Hill's) experience at the Devonshire Royal Hospital had been similar to Dr. Kersley's in that while a considerable number of cases of rheumatoid arthritis showed diminished absorption, the figures were nothing like so high as those obtained by Pemberton. Some part of the explanation might lie in the giving of 50 gm. of glucose instead of the 100 gm. given by the American workers, as suggested by Dr. Kersley, but this could hardly be the whole explanation.

Dr. W. S. C. COPEMAN said he agreed with Dr. Kersley that the blood-sugar curve in rheumatoid arthritis did not invariably assume the form illustrated in the paper to which Dr. Kersley had referred.¹ It did so, however, in a great majority of active cases. He (Dr. Copeman) suggested that the cases investigated at Bath had possibly not been in such an active phase as those in his own series.

He suggested on the basis of a small number of investigations which he had since made, that the reduced sugar tolerance found in these cases was not due, as was generally supposed, to a diminution in the area of the capillary beds due to spasm.

¹ "The glucose tolerance in rheumatoid arthritis," *Brit. M. J.*, 1933 (i).