health, except that she had simple goître for many years, and had been subject to occasional attacks of catarrhal cough.

On January 5th, 1902, she had an attack of vomiting, with pains in the right back, which slowly subsided. But from January 22nd to 26th she had a series of rigors in the daytime, followed by feverishness at night. Subsequently for ten days there recurred feverishness at night, followed by remission in the morning, the temperature ranging between 99° and 102.5°, and the pulse between 60 and 68 per minute.

On the fifteenth day from the first rigors, after careful examination of the patient and consultation with my friend Dr. John Davies of Aberayron, nothing could be found to account for the pyrexia. Noon temperature 99°, pulse 56, night temperature 101°, pulse 76. Sulphate of quinine (3 gr. every four hours), and phenacetin (5 gr. at night) were administered.

On the thirtieth day, after continuance of similar symptoms, we agreed that the pyrexia was probably due to the thyroid enlargement. At noon the temperature was 100°, pulse 72, night temperature 101.5°, pulse 64. Thyroid extract was tried with phenacetin, but the same symptoms persisted till the seventy-first day, when the circumference of the neck over the thyroid swelling measured 15 in., the swelling extending vertically about 4 in., and the lower part of it on the left side becoming red and painful.

On the eighty-eighth day—that is, three months after the first rigor—the swelling on the left side had become redder and softer, but the temperature lower and the pulse slower. After consultation with Drs. Davies of Aberayron and Evans of Green Grove, the abscess was lanced and a considerable quantity of pus escaped. A large drainage tube was introduced into the wound, and it was dressed antiseptically. This operation gave considerable relief to the patient, and she improved much in appearance, but the temperature became subnormal afterwards for some days. The wound continued to discharge, and did not finally heal until three months after opening, but the affected side of the thyroid tumour disappeared entirely, and the patient recovered her usual health.

November 26th, 1904 (sixteen months after the last report). The general health of this lady has continued very satisfactory. There is no perceptible swelling on the left side of the neck, and the swelling on the right side is much diminished, being less than a hen's egg in size. The circumference of the neck over the tumour now measures only 12½ in., being 2½ in. less than it was a week before the abscess was opened.

CASE II.

Mr. G. J. D., aged 42, occupation schoolmaster, had an enlarged thyroid (goître) for many years which used to swell and become irritable with colds, etc.; otherwise he had been in good health.

On July 11th, 1903, he was first attended by me, having been ailing for two or three days, suffering from feverishness, with pains in the head, erythema on the left elbow, and other symptoms, which were concluded to be owing to influenza. He was treated with aperients, salicylate of soda, and tepid sponging to allay his feverishness, and an occasional dose of phenacetin or phenazone to relieve pain. However, these symptoms continued with temporary abatement till the twelfth day of illness, when at 6 p.m. the temperature was 104°, pulse 84, and the respirations 23 per minute, and crepitation was heard on auscultating over the base of the right lung; no cough or stitch in the side. The case was also seen on this day by my friend, Dr. Evans, of Green Grove, who likewise diagnosed influenza, and recommended 5 gr. of quinine sulphate to be taken three times a day in addition to the other medicines.

On the fifteenth day, 6.30 p.m., the temperature was 104.3°, the pulse 68, and the respirations 9 to 15 per minute. No crepitation then heard over the right back. For last two days observed considerable swelling and redness of the left side of the goître, together with tenderness on pressure. The circumference of the neck over the goître measured 17 in.

On the eighteenth day, 5.30 p.m., temperature 100.8°, pulse 60; the swelling in the neck more tense, and extending downwards as far as the manubrium; turgid veins seen coursing across the swelling. There is distinct fluctuation to be felt in the centre of the swelling. The patient is easier, and now sleeps without phenacetin.

On the nineteenth day, after due antiseptic precautions had been taken, the abscess was freely opened, and a saucerful of pus escaped. A large drainage tube was introduced into the wound, which was afterwards dressed with carbolized gauze and boric wool.

On the next day at noon the temperature was 98.2°, pulse 52 per minute. The patient felt much better, but an uncertain crepitation was again heard over the base of the right lung. There was copious purulent discharge from the abscess.

On the ninth day, subsequent to opening the abscess at 6 p.m., the temperature was 99.8°, and the pulse 68 per minute. There was still free discharge from the abscess, but it was difficult to keep the opening patent, so a plug of double cyanide gauze was substituted for a drainage tube.

In about a month after opening the abscess the patient was able to go away for change of air to the wells, etc., the sinus still discharging. The circumference of the neck over the thyroid then measured 16½ in. Afterwards the patient returned home much improved in general health, and was able to resume his occupation in less than three months, but the sinus did not finally close until six months had elapsed. The circumference of the neck had reduced over 2 in.

November 19th, 1904. This gentleman has been in good health during the past year. The goître on the left side has now completely disappeared, and on the right side it has much diminished, so that now he requires a collar of only 14½ instead of 15½, used before the illness.

It will be seen that in both these cases the persons were of middle age, and that both recovered slowly from the suppuration, followed by the disappearance of the goître on the affected side, and diminution of it on the opposite side. The first case appeared to have been spontaneous in its origin—commencing with rigors, then running a chronic obscure course, characterized by mild evening pyrexia and morning remission, so that the cause of the symptoms could not be determined for the first month, then running on for two more months before the abscess was mature for evacuation, and taking another three months to discharge before finally closing.

The other case, which appeared to have been secondary to an attack of influenza, ran an acute course with high fever, and the abscess matured for evacuation on the nineteenth day; but the sinus did not finally close until six months afterwards.

In both these cases, the suppuration occurred on one side only, and both recovered their general health satisfactorily. It would be interesting to know what would have been the effects if the suppuration had occurred on both sides.

In the *Practitioner* for April, 1901, p. 415, Dr. Walter Edmunds says, "In the treatment of an ordinary goître, if an operation is decided on, one lobe is generally removed. The operation is frequently followed by atrophy of the opposite lobe." But he shows that excision of the whole thyroid gland has been followed by grave symptoms like myxoedema, and even by death in one case. Mr. Bernard Pitts (in Treves's *System of Surgery*, vol. ii, p. 376) recommends in cases of solid goître the removal or division of the isthmus only, but not to remove the whole gland.

REASONS FOR ABANDONING THE URIC ACID THEORY OF GOUT.

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IF we may judge from the discussion on the chemical pathology of gout held at the meeting of the British Medical Association in 1904, it would appear that the uric acid theory still occupies the foremost place in the mind of most investigators of this disease. Whatever place this theory occupies in the mind of those who are seeking to determine by the aid of laboratory methods the exact rôle of uric acid or its allies, it must be admitted that the theory has been abandoned by many clinicians of wide experience in the disease. Dr. Goodhart, in an address on Acidity, published in the *Lancet* in 1900, writes as follows: "For myself, I cannot but think that had it not been for our eagerness to get hold of something to 'treat,' the uric acid theory that is dominant at the present day would never have become the fetish that it has." My object in this paper is to submit facts gained from research which strongly support this teaching of clinical experience as to the minor rôle of uric acid in the production of gout.

My investigations were commenced in 1898, and with a bias strongly in favour of uric acid. As the research developed, however, the defects of this theory became more and more apparent. I am now convinced that the general adoption of the uric acid theory has been attended by two unfortunate results. In the first place, the prominence given to this theory has unduly narrowed the field of inquiry relative to the disease; and in the second place, it has obscured the significance of the facts actually observed. The grounds for these two statements will be shortly stated. These can, perhaps, best be submitted in the form of an epitome of the steps which have led me to abandon the view that uric acid is an important etiological factor in the disease. For a fuller account of the various points the reader is referred to the original papers. The investigations deal in turn with (*a*) chemical, (*b*) histological, and (*c*) clinical questions.

OBSERVATION I.—*Uric Acid in the Blood of Birds.*

The first point investigated was the presence of uric acid in the blood of birds. Sir A. B. Garrod, using older methods of investigation, failed to find uric acid in the blood of birds. Dr. Luff, in his valuable Goulstonian lectures, gives the results of his investigations on this point. He states that "after most careful examination of very large quantities of the blood of the turkey, goose, duck and fowl, I have never been able to detect any uric acid in the blood of these birds," and he interpreted this as "conclusively supporting the view that

uric acid is normally produced in the kidneys." Dr. Luff further utilized this result as the main basis of his view as to the renal origin of gout. As the question of the existence of uric acid in the blood of birds appeared to me a vital one, I made a series of investigations on this point. Five observations were made, four on the blood of birds and one on the blood of a snake.[1] In each instance the presence of uric acid was determined, a weighable quantity being obtained on three occasions (see Table I).

TABLE I.

	C.cm.	Grams H_2U.
Duck	1,750	0 0352 gram.
,, ...	50	Qual. reaction only.
Goose	1,650	0.0428 gram.
Turkey	1,500	0.0328 ,,
Snake	1,500	Qual. reaction only.

These results show conclusively that uric acid is normally present in the blood of birds; they also negative the view that uric acid is normally formed in the kidney; they further indicate that the theory of the renal origin of gout, so far as this rests on the absence of uric acid in the blood of birds under normal conditions, cannot be entertained. It is right to add that Dr. Luff has in later writings abandoned this view.

OBSERVATION II.—*Uric Acid in Pathological Fluids.*

The second point selected for investigation was the examination of the blood or tissue fluids from a number of diseased states, with the special object of determining the presence or absence of uric acid. Six observations were made[2] (see Table II).

TABLE II.

	Sex.	Age.	Fl. Oz.	Grams H_2U.
Chronic Bright's disease	F.	60	10	0 0068
Malignant disease	M.	55	30	0 0155
Aneurysm (aortic)	M.	40	19	0.0087
Ulcerative endocarditis	M.	30	26	0 0075
Lobar pneumonia	M.	22	10	qual.
,, ,, ...	M.	40	33	0.0170

A glance at Table II shows that in a number of diseased states which have no known relationship to gout, uric acid was present in weighable quantity in the limited amount of blood or pleural fluid examined. This result merely confirmed the work of previous investigators. When we further consider the thoroughly-established fact that in leukaemia uric acid may be present in the blood to an extent greater than obtains even in aggravated cases of gout, and yet that disease is unaccompanied by either the clinical or pathological features of the gouty state, we are forced to conclude that Garrod's original theory, which was based largely on the presence of uric acid in the blood, needs very material modification. It is idle to contend that in leukaemia the uric acid is excreted as fast as it is produced. There is no proof that this is the case; and even if it were so, Dr. Ringrose Gore has well pointed out that uric acid can be no exception to the general law that a substance acts as a poison in direct proportion to the amount of it present in the circulating fluids. Consideration of these points shows that in focussing attention on uric acid in its relation to gout the field of inquiry has been unduly restricted. Further proof of this was obtained in the course of the next investigation dealing with the excretion of uric acid in the urine in acute gout.

OBSERVATION III.—*Uric Acid Excretion in Gout.*

The necessity of investigating this point was obvious from the fact that the uric acid theory was to a great extent based on the view held by Sir A. B. Garrod that the excretion of uric acid is diminished during the paroxysm, this being associated with a retention of uric acid in the system. A detailed analysis of the urine was made in two cases of typical gout, a daily examination of the urine being made for many weeks. In addition to the urea and uric acid, the amount of P_2O_5 was also estimated.[3] The results of this investigation showed no disturbance in the uric acid elimination either before, during, or after the paroxysm (see Tables III and IV).

TABLE III.—*Case I. Uric Acid Excretion in Acute Gout.*

	Urea.	H_2U	H_2U—Urea Ratios.	Average of Days.
	Grams.	Grams.		
Acute attack*	28	1 15	1—24	5
Acute attack—three weeks later	24	1.39	1—17	8
In the interval...	21	1.31	1—16	3

* Last five days of a severe attack (see temperature chart later).

TABLE IV.—*Case II.*

	Urea.	H_2U.	H_2U—Urea Ratios.	Average of Days.
	Grams.	Grams		
Interval—mixed diet ...	24	0.39	1—63	6
Interval—mixed diet and thymus administration ..	21	0.35	1—69	4
Acute attack—mixed diet...	25	0.65	1—39	3
After acute attack—milk diet	33	0 55	1—59	4

Other observers have recorded a like result. We may therefore conclude that there is no striking change in uric acid elimination in acute gout, and accordingly we are justified in stating that one of the main premises on which the uric acid theory was based is erroneous. (The results of these investigations further appear to show that the tissues of gouty subjects reacted to nuclein administration in the same manner as healthy tissues.)

Reference may appropriately here be made to the other main pillar of the uric acid theory—namely, the diminished alkalinity of the blood during the acute attack. The researches of Magnus Levy have clearly proved, even to the satisfaction of those who still pin their faith to the uric acid theory, that there is no diminution in the alkalinity of the blood during the acute attack. If, then, as has been shown, the main premises of the uric acid theory are untenable, it is evident that further investigation on the traditional lines could not be fruitful in its results. Attention was therefore directed to the histological appearances of the disease.

OBSERVATION IV.—*The Histological Appearances of Gout in Lower Animals.*

At the outset it is important to bear in mind that the classical description of the histological appearances in gout dates from a time prior to our knowledge of general and local infective processes. It is therefore natural that the histological records of the disease, as given in the classical works, are, from the standpoint of modern pathology, remarkably incomplete. Some years ago I had the rare opportunity of studying the histological appearances of the tissues in a case of acute gout in a fowl, and have recently recorded the results of this examination.[4] The facts may be here summarized. The gouty deposit in the tissues, the changes in the synovia, the widespread thrombosis, and the characteristic areas of necrosis in the kidney in this case clearly indicated the nature of the disease. It was a typical case of gout. At the time of publication doubts were expressed by some critics as to the genuine gouty nature of the renal and other lesions. These doubts did not appear to me to be well founded. In this connexion it is of interest to note that recently in the course of a repetition of Ebstein's classical experiments on gout, kidney lesions were established identical with those described and illustrated in this paper. From the clinical and pathological record of this case we are "driven to the conclusion that we have to deal with a case of pure gout in which the disease had run a natural course, in which an examination of the tissues shows that the *post-mortem* appearances generally are characteristic of an infection by bacteria or their products." The facts learned from this investigation indicated the importance of reinvestigating the histological appearances of chronic gout in man.

OBSERVATION V.—*The Histological Appearances of Chronic Gout in Man.*

The results of this inquiry were embodied in a paper published a few months ago.[5] These results were in the main an independent confirmation of those previously obtained by Dr. Berkart. The main facts may be summarized:

(*a*) In gouty deposits in the subcutaneous tissues, the appearances of the tissues warrant the statement that we have no

more right to assign etiological significance to uric acid than to other substances of an unknown nature found in the structureless material left after removal of the crystals.

(*b*) An examination of gouty tendons showed that the necrotic areas had a definite relation to the vessels of the part. The appearances in the tendons indicate that the necrotic areas are to be accounted for by an infection by the blood stream.

(*c*) The erosion of cartilage was due not to the presence of uric acid but to the action of small rounds cells of the granulation tissue type.

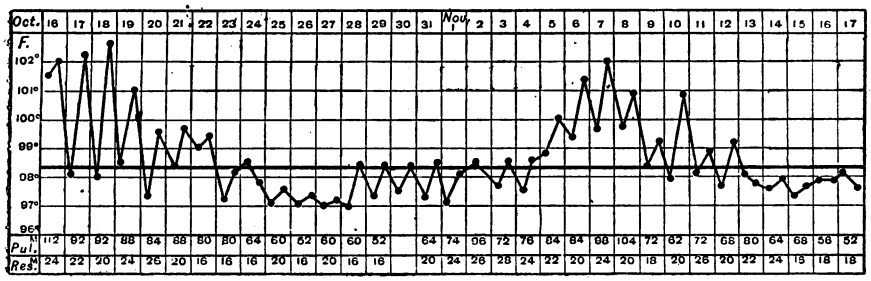
(*d*) At the gouty deposits in the bone, attention was directed to (1) the richness of the blood supply, (2) the general character of the giant cells, and (3) the great accumulation of small round cells of the nature commonly associated with the action of bacterial toxins.

(*e*) Stress was laid on the alterations in the interior of the bone, more especially on the disappearance of the marrow proper and rarefaction of the bone trabeculae.

The general conclusion in this paper was that "the *tout ensemble* of the pathological pictures is strikingly similar to that seen in chronic infective diseases. From this point of view the uric acid is regarded as the feature which gives the inflammation its specific character." A study of the facts recorded in this and the preceding paper showed to my mind conclusively that the adoption of the uric acid theory had obscured the significance of the facts actually observed.

OBSERVATION VI.—*From the Clinical Standpoint.*

When it became apparent that the results obtained from these histological investigations did not support the uric-acid theory, but rather suggested an infective condition, the point at once presented itself for consideration whether the latter hypothesis would conflict with the teaching of clinical experience. It does not. I submit that, on the contrary, this hypothesis more adequately explains the phenomena of acute gout than does any other theory.



In the clinical picture of acute gout, the manner of onset, the course of the temperature curve, the changes in the blood indicating disturbances of the marrow function,[2] and the marked liability to relapses, all strikingly recall the picture of an acute infective disorder. This is illustrated in the chart of one of the cases recorded in Observation III.

GENERAL CONCLUSIONS.

From the foregoing we conclude that the evidence of the laboratory is in harmony with the teaching of clinical experience, and shows that uric acid is not an important etiological factor in the production of gout. The author believes that (1) there is an infective element in the disease; and (2) the uric acid is the feature which gives the inflammation its specific character. According to this view the chief source of infection is the alimentary tract, and an injudicious dietary—meat or drink—acts mainly in virtue of its influence on the bacteria present in the digestive tract. This view by no means minimizes the importance of the hereditary factor in the disease.

In concluding this summary, I must refer to a very suggestive paper on gout recently published in the *Lancet* by Woods Hutchinson. The keynote of this paper is, I think, to be found in its definition of gout as a "Toxaemia of gastro-intestinal origin accompanied by the formation of an excess of urates, this excess of urates being due to the breaking down of the leucocytes and fixed cells in the attempt to neutralize the poison—in other words, being the measure of the resisting power of the tissues. The formation and introduction of the toxins, be it well understood, are by no means confined to the gouty; it is only the nature of the resistance of the body to them that gives the character of gout."

Dr. Woods Hutchinson rightly lays stress on leucocytosis, the main bone-marrow function. The importance of this function and the correctness of Dr. Woods Hutchinson's conception of gout have been strongly emphasized to me by the results of some clinical and therapeutic observations on bone marrow which I have carried out coincidently with the investigations referred to in this paper.

It only remains for me to refer to the likely lines for fruitful investigation. Reliable evidence for or against the general theory put forward in my paper should, I think, be looked for along the following lines:

(*a*) It is advisable to investigate the influence of (1) a meat diet and (2) a carbohydrate diet, on the digestive secretions and on the ductless glands. Special attention should be directed to the thyroid gland and the bone marrow.

(*b*) It appears advisable to repeat Ebstein's experiments with the aid of skilled bacteriological methods.

REFERENCES.

[1] BRITISH MEDICAL JOURNAL, January 28th, 1899. [2] Ibid., January 6th, 1900. [3] Ibid; also *Journal of Pathology and Bacteriology*, December, 1900. [4] BRITISH MEDICAL JOURNAL, January 9th, 1904. [5] Ibid., July 16th, 1904.

A NOTE ON SENILE SYMMETRICAL ATROPHY OF THE SKULL.

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A CURIOUS condition of symmetrical circumscribed thinning of the parietal bones, generally regarded as a form of senile atrophy of the skull, has been described, with or without illustrations, by Virchow,[1] Maier,[2] Sauvage,[3] Meyer,[4] Féré,[5] Eve,[6] Humphry,[7] and others. Most examples have occurred in old persons, especially women, but Meyer mentions commencing atrophy of the parietal bones in a melancholic man only 44 years of age, and I have met with a typical instance in a woman only 55 years old, the subject of biliary cirrhosis and jaundice of four years' duration, whose case I described in the BRITISH MEDICAL JOURNAL for April 25th, 1896. In all cases the change in the skull is the same in kind, the only difference consisting in the degree of thinning of the parietal bones and in the size of the thinned areas. The thinning is due to a circumscribed depression with shelving edge on the outer surface of the parietal bone, due, as Mr. Targett[8] pointed out in the specimen I gave to the Royal College of Surgeons, to removal of the outer table over the affected area and wearing away of the diploë, so that the inner table forms the floor of the depression. The inner surface of the skull is generally unaltered.

In the museum of the Royal College of Surgeons are Egyptian and other skulls showing these symmetrical areas of atrophy. One of these skulls, presented to the museum by Mr. Flinders Petrie, is from Gurob (Fayoum) in Egypt, probably of about 1,300 years or so before the Christian era, and has been described and figured by Mr. F. S. Eve in the *Transactions of the Pathological Society of London* for 1890. Sir G. M Humphry,[9] who, in his book on the *Human Skeleton*, in 1858 attributed the condition to a peculiarity of congenital conformation, afterwards, in 1890, before the Royal Medical and Chirurgical Society of London, described it as probably a result of senile changes. Ziegler,[10] in the ninth German edition of his well-known textbook of pathological anatomy, gives an excellent illustration of symmetrical parietal depressions, and thus refers to the subject: "Lacunar absorption affecting large portions or the whole of the skeleton takes place first in old age, and is, therefore, called senile atrophy. The process is sometimes especially advanced in the flat bones of the body, the skull, the shoulder-blades, and the pelvis, notably in parts which are not covered by muscles. In the skull the absorption of the parietal bones may proceed so far that the whole of the outer table and the diploë become destroyed, and finally portions of the inner table, and at spots here and there even both tables, completely disappear."

But the question arises, Is this symmetrical atrophy of parietal bones merely a senile change, and if so, why does it sometimes occur in younger persons? Bernard Hollander[11] collected a number of cases associated with melancholia, and regarded the condition as due to trophic influences accom-