X

Thesis.

"Gout – what is its true aetiology?"

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GOUT — what is its TRUE AETIOLOGY?

"A knowledge of the real nature of gout and of its kindred malady rheumatism is, in my opinion, at the very foundation of all sound pathology." — Todd.

DEFINITIONS of the DISEASE.

"Gout", says Duckworth,(1) "is a constitutional or diathetic malady, manifesting itself in very varied aspects. In its acute forms it usually, but not invariably, presents the characters of localised inflammation, accompanied by peculiarly intense pain; the inflammation in its course, and the attendant pain, being of a specific nature. In its chronic forms there may be no manifest inflammatory features, and even no pain. The male sex, chiefly in the third decade, is most frequently the subject of the disorder in the acute form, and the articular system not seldom bears the brunt of its incidence. In the earlier manifestations the inflammatory trouble seizes especially upon the first joint of the great toe, spreading subsequently to other articulations, and a suppurative stage but very rarely occurs. The digestive system is largely involved, and in the fully developed forms of the malady, hardly any of the viscera or textures are unaffected. The nervous system is

(1) A treatise on Gout, p. 2, London, 1890.

likewise specially implicated—whether primarily or not is, as yet, a vexed question.

The disorder is either inherited, or newly acquired. In most of its manifestations it is plainly associated with perturbed relations of uric acid in the economy, and the inflammatory attacks are accompanied by deposits of urate of sodium, for the most part in articular cartilages and fibrous structures. A measure of pyrexia commonly forms part of the acuter gouty processes, but profound, though slow, nutritional changes may proceed quietly in the chronic forms of the malady without any febrile movement".

"Gout", writes Charcot[1], "is a chronic and constitutional affection, most often hereditary, and always connected with a peculiar dyscrasic state; for the presence of an excess of uric acid in the blood constitutes one of the principal characters of the disease. It is incontestable that most of the morbid manifestations which give to gout its peculiar physiognomy arise from this special condition: this is the case, for example, with regard to the diseased joints . . . . . But independently of these joint affections, and of this special state of the blood, gout may give rise to numerous and varied visceral affections, sometimes structural, sometimes merely functional. There is even reason to think that, in some cases, rare however, the diathesis merely produces internal troubles of this kind during

(1). Clin. Lect. Senile and Chronic Diseases, pp. 50 — 51. New Syd. Soc., London, 1881.

the whole evolution of the disease, without ever producing those external manifestations on which we are accustomed to reckon.

This is what old writers used to call irregular, as opposed to regular, gout, which corresponds to the classical type of the disease. Yet, even in it we come across visceral disturbances; sometimes they appear suddenly in the midst of an attack (retrocedent gout), or in the interval (misplaced gout); sometimes, on the contrary, it is by a slow, progressive, almost latent, development, that those profound organic lesions are formed, which are so often met with in gouty people. (Chronic Bright's, fatty heart.)".

"Gout", says Woods Hutchinson[1], "may be defined as a toxaemia of varying causation, usually 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 neutralise the poison — in other words, being the measure of the resisting power of the body 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."

CHRONIC NATURE OF GOUT.

The terms acute and chronic, as applied to Gout, are useful clinically as describing the two chief

(1) Lancet, Jan. 31: 1903.

phases of the malady, but gout is an essentially chronic affection, and may assume a chronic form from the outset, although, as a rule, it as such, only follows several attacks of acute gout. On the other hand, a patient, after an apparently complete recovery from an acute attack, may flatter himself that the disease has exhausted itself in a single paroxysm, and that, with care, he will have done with it, but unfortunately any one who has once had a typical gouty seizure must, as a rule, regard himself as goutily disposed for his lifetime.

The interval between the attacks may be very considerable — thus Roberts[1] mentions the case of a Yorkshire squire in whom the first attack occurred at the age of twenty-seven; the next attack befell him in his eighty-ninth year.

The prevalent impression from time immemorial has been that gout is particularly an appanage of the rich and leisured classes. — Thus Shakespeare makes Rosalind (As you like it, Act III.,Sc. 2.) say "Time ambles with a priest that lacks Latin, and a rich man that hath not the gout"; and Sydenham in his most graphic account of Gout says: "Great kings, emperors, generals, admirals, and philosophers, have all died of the gout. Hereby nature shews her impartiality since those whom she favours in one way she afflicts in another".

Nowadays, however, gout is more democratic, and

(1) Allbutt's System of Med.,Vol. iii., p. 156.

attacks the half-starved seamstress as well as the squire — it is no respecter of persons: high, low, rich, and poor, are all liable to its attacks, although it usually defers its onset until the third decade, and affects the male sex more frequently than the female.

As regards "poor gout" or "poor man's gout", which occurs in persons who may be very temperate, but who have a weak constitution and faulty circulation and digestion, some of those cases are undoubtedly true gout, and some are cases of chronic rheumatoid arthritis. All authorities are not, however, agreed on the point whether gout and chronic rheumatoid arhtritis are quite separate affections or not: some — e.g., Haig—contend that rheumatism and gout are similar diseases — both due to uric acid—, and that chronic rheumatoid arthritis is a third modification also due to it. Women often suffer from "poor gout", and at the same time, in my experience, suffer from chronic constipation or leucorrhoea, or both.

Dr. Billings[1] more than sixty years ago wrote: "Temperate persons have gout, because they have, whether hereditarily or not, a feeble nervous system and weak digestion. Abstemiousness will not cure such gout, which is called "poor gout", that which has come on in constitutions without excess."

Experience teaches that this is quite true, and, at the present day, many cases can fully enter into

(1). Principles of Medicine, p. 183.

Horace Walpole's feelings when he grumbled at being the victim of gout, and said "It is an absolute upstart in me; and,what is more provoking, I had trusted to my great abstinence for keeping me from it".

HISTORY of GOUT.

Gout can,at least, claim a long pedigree — our common ancestor Adam having succumbed to it; at least Duckworth[1] quotes from a pedigree extant at the Herald's College that Adam died of the"Gowte"! From the writings of Hippocrates, it is evident that gout has been known in Europe from the most ancient times — it appears to have become rampant during the reigns of the early Caesars. The writings of Ovid,Seneca[2](who was a victim to the disease), Galen,and many others,show that gout in the first and second centuries was a well recognised malady, and in the third century "an edict of Diocletian exempts gouty persons from the public burdens when they are suffering from articular deformities so considerable as to interfere with the ordinary functions of life — a circumstance which seems to demonstrate both the extreme frequency of gout at that period and the immutability of the chief symptomatic characters".[3]

(1) Treatise on Gout, p. 129. (2) Seneca relates that at the time of the decay of the Roman Empire, women practised such excesses, that they were as subject to gout as the men.
(3) Charcot, Clin. Lect. Senile and Chronic Diseases, New Syd. Soc., p. 110.

From the third century down to the present time, gout has maintained its sway, although it is generally admitted that, since the commencement of the last century, classical podagra is less frequently met with than it was perviously, and appears to have taken refuge mainly in England, Germany, and America. But even in England, acute gout is less common than in the time of Sydenham[1] — this is largely due to the "softening of our manners" (in the language of Charcot), and to the better hygiene, dietetic and otherwise, of the times we live in. The two-and three-bottle man has disappeared, more temperate principles prevail, and no longer is a man considered no gentleman if, after an evening function, he be able to walk upstairs to bed unassisted!

Nowadays, less and lighter wine is consumed, and there is a great increase in the consumption of water, both as such and in the forms of mineral and effervescing waters: the inception of which latter we owe to the genius of the late Dr. Joseph Priestly, who, eminent divine as he was, will perhaps be remembered more through his chemical researches than through his sermons.

In Scotland and Ireland, gout is exceedingly uncommon, except in the luxurious livers, in Germany it apparently is on the increase, in America it certainly is on the increase.[3] From my personal observations of the very mixed dietary and express speed methods of living in America, it would be, to me, passing strange if

(1) Duckworth, Treatise on Gout, p. 253.
(2) Futcher, Practitioner, July, 1903.

such were not the case.

GENERAL SYMPTOMS.

The cardinal signs and symptoms of Acute Gout are so well recognised that it is hardly worth while to recount them. The picture of the swollen, red, tense, and exquisitely painful, great toe joint with turgid dorsal veins, and the accompanying explosive temper of the patient, is one which indelibly fixes itself in the student's mind; even if, as is often the case in Scotland, he has never actually seen a case. Thrice happy is he if he never personally experience the pains of acute gout. I never realised the full significance of Cruikshank's famous cartoon until I fell a hapless victim to the malady.

The premonitory symptoms may be marked, or, on the other hand, not appreciable. It is commonly said that premonitory symptoms are few and little marked in the earlier attacks, and more pronounced in the later attacks. The reason of this is, I believe, that, as a rule, once a patient has had an acute attack of gout he is very careful to find out the danger signals, and to recognise them as they occur. An old patient of mine used actually to welcome any precursory symptoms, of which he had compiled a nice little list. As he expressed it, an attack of gout made a "new man" of him for some time,— unfortunately for him, a time shorter and shorter after each attack. Unfortunately also for him, he refused to

be persuaded that "building up his strength" with old port and whisky was not conducive to averting attacks, and this state of affairs went on until cirrhosis of the liver and cardiac failure brought on the final scene.

"Those" writes Duckworth,(1) " who study carefully the multiform phases of any one malady lay themselves open to the charge of seeing signs and symptoms of it in almost every case of disease . . . . . Taunts such as I have already alluded to are freely cast at those who see "gout" everywhere, and are perhaps not unfairly cast. The competence and honesty of the observer can alone shield him from such charges".

According to Crabbe, who was, I believe, at one time, a physician —

> "Some to the Gout ascribe All human pain,
> They view it raging in the frantic brain,
> Find it in fevers all their efforts mar,
> And see it lurking in the cold catarrh"!

There is no denying the fact that the uric acid diathesis has been very often made a scrap-basket for improperly diagnosed cases. Yet just as the gouty diathesis may be perfectly developed in individuals who never see its local manifestations of uratic deposit, there may occur symptoms in an individual who may never have had an attack of gout, which to an observer who has had a certain amount of experience of gout in its many phases, may appear very suggestive of an impending acute attack, and often prove to be so — symptoms which a casual observer might not regard as being of premonitory importance — at

(1) Treatise on Gout, p. 4.

least, as regards impending gout.

Inasmuch as the power of prophetic opinion (if it be fulfilled!) from apparently insufficient data is a valuable asset to a practitioner, I think the premonitory signs and symptoms of gout are well worthy of consideration.

THE PREMONITORY SIGNS AND SYMPTOMS of gout, when they occur, are very diverse. The most common are digestive troubles. "Its only forerunner is indigest--ion and crudity of the stomach, of which the patient labours some weeks before", says Sydenham. Loss of appetite, sense of fulness at the epigastrium (very often, in my experience, associated with Indicanuria), acidity and irregularity of the bowels — usually confined, but sometimes relaxed as if Nature were trying to expel some toxic matter. As a rule, before an attack, the urine is scanty, and concentrated, but sometimes there is free emission of pale watery urine before an acute articular attack. Very often the prominent symptoms are nervous and circulatory. There may be headache, irritability of temper, or great mental depression, various neuralgic pains, hemicrania, palpitations, persistent weariness, or drowsiness, or yawning; "fidgets" or constant restlessness — nocturnal or otherwise; deep-sighing, pricking pains in joints or limbs, and deep-seated pains in various parts.

General pruritus may be complained of, and is

supposed to be characteristic of gout, as also are pain in the calcaneum and plantar fascia. As regards the pain in the calcaneum and plantar fascia, I have so often noticed them in cases of mitral disease in which there was no appreciable gout nor goutiness, and no history, on careful investigation, of gout or "rheumatics", that I feel inclined to dispute Duckworth's dictum that those pains are characteristic of gout, especially as in all those cases of mitral disease all specific gouty treatment failed to relieve the pain.

Other symptoms which have been recognised are cramps in the legs, lumbar pain, pain in sound teeth, sharp fleeting pain in the tonsils, sallow face and icteric tinge of conjunctiva, conjunctivitis and sclerotitis.

Personally my prodromata have been occipital headache, violent vertigo ("gouty semicircularitis" according to an eminent specialist!), temporary hemianopsia, nasty taste in the mouth, with a triangular patch of yellow fur on the dorsum of the tongue, also irritability of temper, and, more particularly, great depression of spirits associated very often with the presence of Indican in the urine.

All these signs and symptoms have been recognised antecedent to an acute attack of gout — needless to say, although ~~suggestive~~ *Suggestive*, they are by no means pathognomic. On the other hand, the impending victim may feel perfectly well — perhaps better than he has done for years —, when suddenly this "euphoria" *is* superseded by

by an acute attack and excruciating torture.

Many writers on Gout appear to have copied from Sydenham, who copied from Nature, and their description of the onset represents, no doubt, what is very often the typical sequence of events as regards the regions invaded, the time of day, and the season of onset, etc. But as Duckworth[1] truly says, "the classical attacks described by Sydenham are by no means the rule. Even in the first onset, and in cases that may be termed sthenic, all authorities agree that, in the great majority of cases,[2] the primary acute attack is in the great toe joint — the right great-toe joint according to many authorities, but, in my experience, more often the left.

SEAT of PRIMARY ATTACK.

I believe, however, that, nowadays, more frequently than ~~that~~ one is led to believe from ordinary text-book accounts, the primary acute attack affects parts other than the great-toe joint.

In two cases out of fifty of which I have notes on this point, the primary attack was tonsilar, in one case conjunctival, in one case cephalalgic, and in one case (the patient being myself) the left thumb was primarily affected.

In all those cases there was intense pain with the "chaplet of little attacks, strung together, but separated by intervals of remission" (in the language of Charcot describing a "typical" acute articular attack),

(1) Treatise on Gout - p. 247. (2) Scudamore (quoted by Charcot — Senile Diseases, p. 73) showed that 512 cases of gout the great toe was affected 373 times at the first attack, either alone, or along with other joints; and, out of those 373, there were 341 in which the symptoms were limited to one joint.)

and in all those cases there was metastasis to the opposite side.

CASES The first case of "Acute tonsillar gout" was E.L. — commercial traveller —, a robust man, aet. 30, who consulted me one forenoon for "violent pain on the left side of his throat". To my knowledge he was temperate, although I had never attended him professionally. He told me that he was subject to slight sore throats, and, feeling his throat rather sore, on the recommendation of a friend, he had taken two glasses of port wine. Four or five hours afterwards the pain became so intense that he consulted me. On examination, the fauces were slightly congested, both tonsils enlarged, chiefly on the left side, but the patient informed me that his tonsils had been rather enlarged 'owing to frequent colds'. No history of articular rheumatism — gout (or syphilis). The local signs seemed out of proportion to the local symptoms.

I prescribed Calomel gr. ij, to be followed in due course by Mist. Sennae Co. ℥ ij — and locally a solution of Cocain and Glycerine. The same evening the left tonsil was very inflamed and enlarged; the right in statu quo. T. 101° F. I proposed scarification of the left tonsil which was refused. The patient 'howled' so much with pain, that I administered morphia hypodermically. On the following morning the tonsil was still much inflamed, but the pain was much abated — On enquiring into the family history. I was told that the father, who was

from home, suffered from "rheumatics". I therefore, prescribed Sod. Salicyl. — and Guaiacum Lozenges (to be sucked frequently). Towards night the agonising pain recurred, and the father having then returned I examined him, and found well marked tophi on his ears. I promptly prescribed (for the son) Colchicum and Pot. Cit., which according to the patient was 'grand stuff'. The pain for two days afterwards recurred to a slight extent towards night, but five days after the onset of the attack, the patient expressed himself as being "all right". The left tonsil had shrunk back to its apparently chronically slightly enlarged condition — the colchicum mixture was, however, continued at greater remissions of time.

Three days afterwards very acute pain was experienced in the other tonsil, but the second attack only lasted three days.

One year afterwards the patient had a'classic' attack of gout in his left great toe, which attack lasted a week. The patient described the pain as being identical with that he had experienced in his tonsils. Up to five years afterwards the patient had had no repetition of the attack, either in his tonsils or great toe — since that time I have lost sight of him, he having left the district.

The second case of acute tonsillar gout was F.M., aet. 38 — foreman at a cloth mill and an amateur vocalist—,who one morning, practising his high notes, felt a sudden pain in the back of his throat, and immediately

consulted me, thinking "something had broken". What the "something" was he did not know, but he suspected it was one of his vocal cords! As he volubly described the course of events and the violence of the pain, I assured him that, at least, his vocal cords must be intact; but, being a very nervous man, he insisted upon a laryngoscopic examination, which revealed nothing abnormal. The pharynx and tonsils appeared quite healthy, but the tongue was furred, and the patient complained of feeling "blown up with wind".

Family history — Father and Mother both dead — father died of acute pneumonia at 50; he used to drink "a lot of beer, and suffered cruelly from rheumatics in his feet". Mother died in confinement at 38. Patient never had any serious illness , and said he was abstemious.

I prescribed Blue Pill, to be followed by Mist. Sennae Co.; and promised a visit on the same evening.

On examining the throat in the evening, I found the right tonsil inflamed, and acutely tender. T. in mouth 102°F. As the conditions were so similar to those in the case of E.L., I prescribed Tinct. Colchici, and Pot. Cit. and Cocain Lozenges. The case progressed much as that of E.L., but there were nocturnal remissions for six days, and two days afterwards the other (left) tonsil became affected, and this secondary attack lasted for four days.

In this case, on recovery, the tonsils shrunk back to the normal size. The patient refused to

believe in my diagnosis of "gout in the tonsils", until he, like E.L., had a typical attack of podagra — six months afterwards, also in his left great-toe joint. Three years afterwards he had another attack of gout in his right great-toe, lasting one week — since then, as far as my knowledge goes, he has had no more attacks.

The case of acute primary gout in the conjunctiva was W.M., aet. 50, who had conjunctivitis in the right eye with violent pain in the eyeball and all round the orbit. An ophthalmic specialist examined both fundi, but found nothing which would account for the violent pain — he suggested that the conjunctivitis was of rheumatic origin, but there being a family history of gout on the father's side. After a Blue Pill and Mist. Sennae Co., I prescribed Colchicum and Pot. Cit., which apparently in two days cured both the pain and the conjunctivitis, but the very next day there was a metastasis to the other eye. The pain was so excruciating that I had to administer Morphia: at the end of five days from the secondary onset all pain and inflammation had completely disappeared, and the patient said he felt better than he had been for a long time.

He was, however, so terrified at the thought of a recurrence of the ocular pain, that he for two months put his feet in mustard and hot water every night, to try and induce an attack of gout in his toe, but it was of no avail until a horse trod on his left foot, and the next day violent pain attacked his left great-toe

joint, and a "regular" attack ensued. He has since had several attacks in his toes, but only one more attack in his conjunctivae (two days duration in each conjunctiva). He, however, has had attacks in his tarsus, scalp, hands, and knees — in short, he is now hardly ever long free from gouty twinges in some part of his body.

One morning I was asked to visit Mrs. E.A. (aet. 48), and on visiting her found her in great agony with pain in her head. She had gone to bed feeling in her ordinary state of health and had slept fairly well, but on waking at 7.30 felt very dizzy, and half an hour afterwards pain "like sticking knives into her head" came on, — so acute that she stayed in bed. I saw the patient at 9 o'clock. T. 101° — throbbing pain all over the head — pulse full and bounding — tongue furred. No history of indiscretion in diet, nor any other immediately possible cause, except that the patient had been very anxious about her husband, who had lately suffered much from gout. I prescribed Antipyrin gr.x, to be repeated in one hour, and, along with the first dose, gr. ij of Calomel, to be followed in due course by a Seidlitz powder. Diet — milk and lithia water. During the day the pain became easier, but became worse towards night; and it being apparently neuralgic in character, I prescribed Quin. Sulph. with Acid Hydrobromic and Tr. Gelsemii. The patient had a "terrible night", and, at my morning visit, I found the scalp hot and tender on pressure. T. 102°F. Finding no organic cause to account for the violent symptoms, I suspected Gout, and promptly prescribed Colchicum and

Pot. Cit., which, according to the patient, gave more relief than anything that had been tried. The "chaplet of attacks" lasted for two more days, a sharp attack of diarrhoea came on, and the patient quickly recovered, only two months afterwards to have a typical podagra (left toe). Ever since Mrs. E.A. has been subject to periodic attacks — but always in her great-toes. She has had occasional headaches, but never in any degree as acute as her primary attack. The family history in this case revealed "rheumatism" in her father, but the patient seemed a most unlikely subject for gout — being a life-long teetotaler, very abstemious in diet, of an active and sunny disposition; very fond of outdoor exercise, and lastly being very fair-haired. On this point I may mention that, I have only in one other fair-haired patient observed gout to occur — the other patient curiously enough being Mrs. E.A.'s nephew by marraige. I have observed a similar immunity from rheumatism in fair-haired people.

All those cases would doubtless by the leading authorities be included under the heading of irregular gout; but, from the signs, symptoms, and course of events manifested in them — almost identical with those of a regular acute articular attack—it would be more accurate to describe them as being cases of acute primary abarticular gout. May it not be contended that the tonsils, conjunctiva, and scalp be related embryologically with the particular structures in joints usually affected in Gout?

A noticeable feature in the tonsillar and conjunctival cases was that, although they were primary attacks,

the gout was metastatic to the corresponding parts on the opposite side, a feature which, in my experience, is not common in primary articular attacks.

Perhaps those "exceptional" cases are more common that might be inferred from the stereotyped literature on the subject. If not, it is curious that I, who, even with twenty years' experience of general practice, must, of necessity, have met with much fewer cases of gout than do specialists in large centres, especially London, have been able to observe such comparatively large proportion of acute primary gouty attacks which differed so in locale from the ordinary routine.

TIME of ONSET.

As regards the time of onset, my experience leads me to agree with Duckworth when he says "the nocturnal paroxysm is less often met with than would be imagined if the ordinary accounts of the text-books were to be implicitly relied on"[1].

In my Yorkshire experience, I have found the attacks to be almost as often diurnal as nocturnal — especially after the disorder is fully established, and think that the time of onset largely depends on the time at which the gout-producing meals are taken.

In Yorkshire among the well to-do middle classes breakfast is taken at 8 or 8.30 o'clock — dinner at one o'clock —"high tea" (often an extraordinary meal!) at 5.30 — and light supper — if any — at 9. The main meal is the one o'clock dinner, after which the older members

(1) Treatise on Gout, p. 247.

of the family, having done the brunt of their work in the forenoon, are at leisure in the afternoon — in many cases having at one o'clock eaten and drunk more than was physiologically necessary. If the one o'clock meal in those goutily disposed, be not sufficient to provoke an occasional acute attack, which in many cases occurred about five o'clock in the afternoon, the"high tea" which is often practically another meat dinner with the addition of tea often provoked a sudden attack which might occur shortly after rising from the meal or four or five hours afterwards. In those cases the train was laid, and only needed the match to produce an explosion. The nocturnal attacks were usually due to some special late function, at which the gout-provoking nature of champagne was mentally put to one side in the festive exhilaration of the moment. In London, of course, dinner is taken late in the evening — hence doubtless the frequency of nocturnal attacks.

"Nothing" remarks Sir James Paget, "can show better than gout sometimes does, how exactly health is, in some persons, just maintained: how nearly balanced in them are health and disease, comfort and misery." Those good-hearted, hospitable, and frequently injudiciously eating and drinking Yorkshiremen would suffer much more from gout than they do were they not firm believers in the ~~in the~~ efficacy of outdoor exercise, and of Blue Pill and Black Draught, to which they have frequent resort — as well as being usually a very jovial and non-despondent

1. Clin. Lect. and Essays, p. 354.

disposition.

THE NATURE of GOUT.

What is Gout? This is a most momentous question, which has excited the interest and attention of all medical men from the earliest ages. Galen said that gout was a disease which none but the gods could understand. Since his days, as centuries rolled on, innumerable theories and remedies have been suggested, but no man has yet earned the monument as high as St. Paul's, as wide as the Thames, and as lasting as Time, which Johnson declared was the fitting reward to the man who could discover a panacea to the gout.

Sydenham, two hundred years ago, wrote a classical treatise on the subject, and wrote with feeling, as he was a martyr to gout for thirty-four years. His account of the paroxysms was drawn from nature, and has been largely copied by subsequent writers. Sydenham wrote, "The more closely I have thought upon gout, the more I have referred it to indigestion, or to the impaired concoction of matters both in the parts and juices of the body. At one and the same time the energy of the spirits, which are the instruments of digestion, is diminished. The viscera are over-worked, and then the spirits, which have long been giving way, are prostated. If it were not so; if it were a simple weakness of the spirits; children and women, and the victims of long illness, could be equally gouty: on the contrary, however, it is the hearty and robust. These it attacks during the decline

of their best and natural spirits. When this takes place, a congestion of the humours supervenes. From the two together the due concoctions are vitiated and prevented".(1)

Sydenham, who lived long before the days of experimental chemistry and bacteriology, and recognition of ptomaines, etc., was perhaps not far off the mark — and after two centuries how much more do we know definitely of the real essence of gout than he did?

Authorities from time to time in quick succession promulgate theories, intricate and with much polysyllabic phraseology, only to be flatly refuted by a fresh crop of experimentalists or theorists, who even if they agree on most points, absolutely differ on at least one — entertaining apparently the same sentiments towards each other on the matter of opinions, as did the old Quaker famed in sotry, who said to a boon-companion "All the world is queer except thee and me, and thou art a little queer"!

After this conflict of opinion, when at last an apparent residuum of solid fact is established, another prophet looms on the horizon, who avers that all pre-existing ideas are wrong, that the residuum arrived at after years of controversy is not solid, and that the whole subject ought to be re-investigated de novo — in other words that, all previous seekers after the truth have been vainly following an "ignus fatuus" which has led them far from the straight path!

(1) R.G. Latham's translation of Greenhill's edition of Sydenham's works. Syd. Soc., London, 1850.

This condition of affairs has prompted Clifford Allbutt to write — in his usual happy vein, "When that able physician who knows so well how to combine abstract science with practice — Dr. Luff—,when Dr. Luff tells us that the "gouty individual is one whose general metabolism is instable, and that this instability may be present in one or more of the great physiological systems — the digestive, the nervous, the circulatory, etc."; and when Dr. Bannatyne, out of a rich experience at Bath, tells us that "in gout we have a disease which may give rise to almost any symptom, or affect almost any organ or function," we are pleased to think how thankful Sydenham would have been for a vision of the explicit results of two hundred more years of progress"![1]

STAGES of INVESTIGATION.

I shall now give an epitome of the various stages of investigation from the time of Cullen down to the present day, afterwards giving my own views on the subject, — drawn from nature, and from clinical observation of gout in patients — observations as exact as are compatible with the exigences of a busy practice. / Difference.

"The theories formulated about gout during the whole of the seventeenth century, and part of the eighteenth, are essentially connected with Humoralism: with a few variations, it is the doctrine of Sydenham. There exists a morbific matter in the economy; it is the result of imperfect coction, conducted either in the primae or secundae viae; and the efforts of nature to eliminate

(1) Practitioner, July, 1903.

this peccant matter (phlegm, bile, tartar) constitute the symptoms of gout"(1)

EARLY NOMENCLATURE. The earliest names by which the malady was known were "podagra" and "fotadle", "fotadl" or "foot-addle", the latter names being Saxon. The term "gout" (French "goutte", German "Gicht") is derived from the Latin "gutta" a drop, and was first used about the end of the thirteenth century — the pathological belief being that an acrid morbid material was dropped from the blood into the joints — the term expresses in one word the doctrine of the humoralists. Cullen in 1784 was the first to dispute the humoral pathology of gout. He admitted the presence of a morbific matter in some gouty patients who had suffered long from the disease, but he regarded it as the effect, and not the cause, of the disease. Tophi, one of the "strong cards" of the humoralists were, according to Cullen quite accidental occurrences in a disease which he held was primarily a disorder of the nervous system, — a kind of plethora with a loss of tone in the extremities. He admitted that his ideas were inspired by Stahl of Halle.(2)

Cullen's doctrine excited muct interest and carried weight, especially in England, but did not prove convincing to the humoralists, who still contended that some morbific matter in the bodily ecomony was the "fons et origo mali". Lithic acid had been long suspected of being the particular "materia peccans", and in 1775 Scheele had discovered lithic acid in urinary calculi and in urine.

(1) Charcot. Senile Diseases, p. 125.
(2) First lines of the Practice of Physic, Vol.ii., pt. 1, Chap. xiv. Edited by John Thomson, M.D. Edinburgh, 1827.

In 1793 Murray Forbes[1], on account of the relationship between gout and gravel, opined that uric acid existed in the blood of the gouty, and in 1797 Tennant and Wollaston[2] proved that tophi are composed of urate of soda.

Scudamore, in a treatise on gout published in 1819, in the main agreed with the veiws held by Cullen, and he regarded gout as a kind of plethora with no relation to the excess of uric acid in the blood. Inasmuch as in 500 cases he found tophi in only 45 of them, he considered them to be exceptional phenomena in gout. Cruveilhier[3] regarded the deposition of urate of soda as the cause of gout. Pearson[4], Andral[5], Rayer[6], and Holland[7], amongst others, regarded gout as having a presumably intimate connection with the presence of lithic (uric) acid, and finally in 1848 Garrod[8] definitely demonstrated the fact and established the uric acid theory of gout on a firm basis.

Garrod's theory on the relationship of uric acid to gout is shortly :

1. That in acute and chronic gout there is an excess of uric acid in the blood.
2. That from the first attack urate of soda is deposited in the inflamed part, the deposit being interstitial.

(1) A treatise upon Gravel and upon Gout, etc.
(2) On Gout and Urinary concretions, Philosoph. Trans., ii, 386, 1797.
(3) Atlas d'anatomie pathologique, 4e livraison, planche iii.
(4) Phil Trans., 1798.
(5) Précis d'anatomie pathologique, 1829, vol: i., p. 553, and vol. ii., p. 387.
(6) Traité des maladies des Reins, 1839, vol. i., p. 243.
(7) Medical notes and reflections, p. 252, 1839.
(8) Med.-Chir. Transactions, 1848.

infiltrated and permanent, and being the cause, and not the effect, of the gouty inflammation.

3. That during the attack there is a sensible diminution in the excretion of uric acid by the kidneys, which are probably deranged functionally in the early stages, and certainly structurally in the chronic stages of gout.
4. That the predisposing causes of gout are those which increase the formation of uric acid or favour its retention in the blood.
5. That the exciting causes of gout are those which induce a less alkaline condition of the blood, or increase the formation of uric acid, or such as temporarily check renal elimination.
6. That true gout is the only disease in which urate of soda is deposited in the tissues.

He allows, however, that those views are not by themselves sufficient to explain all the phenomena of gout.

Most of Garrod's views are now generally accepted, but some of them are still the subject of debate, and in characteristic style from time to time various authorities of more or less importance have claimed to have disproved or at least qualified first one and then another of them, and lately more than one ~~aurhtoity~~ authority has tried to show that most of Garrod's views can be disproved, and doubts whether the excretion of uric acid is the all-important factor either in acute or chronic gout.

W. Gairdner,[1] did not agree with Garrod's views, and regarded the accumulation of uric acid in the blood as being only a frequent symptom and consequence of gout.

Charcot[2] remarks that Garrod's facts do not, as yet make a physiological theory of gout possible. He accepts Garrod's facts in the main, but believes that the local inflammation is not due to the deposition of urate of soda, but is the result of the general change, and that gout is a chronic and constitutional affection, and always connected with a peculiar dyscrasic state.

Barclay[3] regarded the uric acid theory as "far too mechanical". He doubted that true gouty inflammation is always associated with, or caused by, the deposit of urate of soda. He believed that in gout the first change was in the blood globules, the result of errors of diet, and that the retention of uric acid is merely a symptom — a consequence of gout, and not its cause. The good living and stimulants do not simply cause an excess of uric acid to be formed, but they end by causing some more permament change, and probably one affecting the blood globules, which reacts on the kidneys, putting a stop to the excretion of uric acid and causing its retention in the serum, where, passing in the round of the circulation, it is very apt to become deposited as urate of soda.

Parkes believed that there was an increased formation of uric acid in the system, and that the elim-

(1) Gout; its History, its Causes, and its Cure; London, 1849, p.99, 3rd edit. p. 88. 1854.

(2) Clin. lect., Chronic and Senile Diseases, p. 127, New Syd. Soc., London, 1881.

(3) On Gout and Rheumatism in Relation to Disease of the Heart, 1866, p. 3 et seq.

ination was impeded, not through renal inadequancy, but owing to some unnatural combination in the blood or organs which held the uric acid back.[1]

Edward Liveing[2] doubts whether an excess of uric of uric acid in the blood is either causative or pathognomic of gout — a disease which he believes to be often of nervous origin.

Sir William Roberts[3] agrees with Garrod's views. He thinks that diminished alkalescence of the blood is possibly the cause of renal inadequacy as regards the elimination of uric acid. According to Roberts, uric acid normally circulates in the blood, and is excreted in the urine, in the form of a quadriurate, which is quite soluble. In gout, either from renal inadequacy or from overproduction of urates, the quadriurate accumulates in the blood. This detained quadriurate, meeting with Sodium Carbonate, is converted into the biurate which is less soluble, and less easily excreted by the kidneys. The biurate, therefore, accumulates in the blood, and, at a certain point of accumulation, is precipitated in a crystalline form. This, says Roberts, occurs chiefly in synovial sheaths and other situations where there is a relatively high percentage of sodium chloride, and where the circulation is poor, and the temperature low.

(1) On Urine, p. 298. E.A. Parkes, M.D.; London, 1860.
(2) On Megrim, Sick headache, and some allied disorders, p. 404; London, 1873.
(3) St. Thomas's Hosp. Reports, New series, Vol. iii., p. 227; 1872; Med. Times and Gazette, vol. i., p. 233; 1874.

Roberts's theory seemed very plausible until Tunnicliffe and Rosenheim[1] subjected the salts of uric acid to fresh chemical examination. Their conclusions were —

1. That there is no evidence of the existence of quadriurates, either in the artificial or amorphous urinary deposits, or in the fluids of the body.
2. That the substances obtained artifically under the conditions supposed to produce quadriurates consist of uric acid and biurates, or of pure uric acid, or pure biurates alone.
3. That natural amorphous urinary deposits consist of a mixture of uric acid with urates of sodium, ammonium, potassium, calcium, and magnesium (containing in most cases, in addition, phosphoric acid).
4. That the property of some amorphous urates of showing the formation of uric acid crystals under the influence of water, is due to the dissolving out of the more soluble biurate moiety, and a change in physical state of the remaining uric acid.
5. That any theory concerning the pathology or treatment of gout or the uric acid diathesis built up on the assumption of the existence of quadriurates requires reconsideration.

1. Lancet, June 16: 1900.

Ord[1] believes that gout arises from a specific tendency to degeneration and abnormal transformation of certain tissues, especially the firboid tissues, wherein an excessive formation of urate of soda occurs which escapes into the blood, and is also deposited in cartilage and such structures as are feebly vascular. "The local gouty degeneration and inflammation tend to infect the rest of the system through the blood, and to set up similar actions elsewhere through reflex nervous influence." Gouty paroxysms, in Ord's opinion, are due to local causes, such as injuries and exposure to cold.

Ralfe[2] believes that "the first step in the process lies in the failure of the tissues to reduce the uric acid (to urea) as occurs in health. In the large glands, or where the current of the circulation is free, the uric acid is carried into the blood and gradually reduced to urea: in tissues outside the current of the circulation the insoluble uric acid is not so readily carried off, and so, on the slightest disturbance, is deposited, as is the case in cartilages of the joints, the ear, etc.".

The tissues and blood become loaded with effete products, which at last disturb some special nerve-centre, which disturbance constitutes the determining cause of the gouty attack. Ralfe doubts Garrod's theory that renal inadequacy is the prime cause of the

(1) St. Thomas's Hosp. Reports, New Series, vol. iii, p. 227; 1872; and Med. Times and Gazette, vol i, p. 223; 1874.
(2) Clinical Chemistry, p. 295; 1883.

~~of the~~ retention of uric acid in the system, believing that the deposition of uric acid is due rather to the insolubility of uric acid than to the excessive production of it.

Murchison[1] regarded gout as merely a result or variety of lithaemia due to functional hepatic inactivity whereby "the normal process by which albuminous matter becomes disintegrated in the liver into urea is persistently deranged." He believed that, given the above conditions, articular gout is a local accident. In gout, he believed (like Garrod) that there was an accumulation of uric acid in the blood, which the kidneys, although at first healthy, failed to eliminate.

Milner Fothergill's views[2] were much the same as Murchison's. He believed that the accumulation of uric acid in the blood (lithiases, as he termed it) was partly due to imperfect oxidation, partly due to impaired renal activity perhaps aggravated by defective action of the skin.

Latham also believes in the hepatic origin of gout, and is of opinion that the imperfect metabolism of glycocine (a derivative of Glycocholic acid) is the prime and essential defect. Unchanged, it passes from the alimentary canal, or elsewhere into the liver: there, under the action of the gland, it is conjugated with urea, resulting from the metabolism of the other amido-bodies, leucine, etc., and is converted into hydrantoin, or a kindred body, then passes on to the kidneys, to be combined there with another molecule of urea, forming ammonium

(1) Lect. on Diseases of the Liver, 2nd edit., p. 588; 1877.
(2) Practitioner's Handbook of Treatment, 2nd edit., p. 267 et seq.; 1880.

urate, a portion of which overflows into the circulation, and is converted into sodium urate. Given this metabolic defect, Latham believes that some disturbance of the central nerve centres determines the attacks, their incidence on the joints, and probably the hereditary nature of gout.(1)

Jonathan Hutchinson(2) believes that gout and rheumatism spring from a basic arthritic diathesis. "I believe that gout and rheumatism go together; you never have gout without rheumatism, though you may have rheumatism without gout, and gouty subjects suffer from arthritis from rheumatic causes. Gout must be divided into special forms, some being attended with free deposition of urate of soda in the joints, and others not so. The formation of urate of soda is a very special thing indeed, and comes about only by heredity, often quite irrespective of the habits of the person on which the mantle has descended; but slight errors in diet may manifest the disease, even though the patient has been most careful in every other respect. For instance, many total abstainers have gout. The gout process is partly due to defective assimilation, and partly to deficient excretion, and it is probably only when the kidneys are decidedly affected that any great tendency to the formation of tophi is witnessed. It is possible, indeed

(1) On the Formation of uric acid in animals; its Relation to Gout and Gravel. Cambridge, 1884 — vide also Croonian Lectures, 1886, Royal College of Physicians, London, 1887.

(2) On the Relations which exist between Gout and Rheumatism. Trans. Internat. Med. Congress, London; 1881. Vol ii. p. 92 — vide also Clin. Journal, Sept. 30th., 1896 — p. 354.

probable, that in some of the inherited forms neither digestion nor excretion is much impaired, and that the inheritance is of peculiarity in tissue."

Ebstein[1] considers that there is a primary articular gout and a primary renal gout.

Primary articular gout develops itself first under the influence of a retention of uric acid: this retention is localised because it affects only one or more parts of the human body. In primary renal gout there is a generalised retention of uric acid, which consequently affects all parts of the body; it is always caused by a primary and material change in the kidneys.

After studying the affected tissues in gout, Ebstein maintains that, firstly, there is a nutritive tissue disturbance leading to complete death of the damaged tissue, and that in this necrotic area the urates are deposited. He has never seen uratic crystallization in healthy tissues. He believes that urate of soda is a poisonous irritant wherever deposited — the injurious results depending on the amount and concentration of the deposit and the vulnerability of the tissue affected.

Riehl[2], opposing the views of Ebstein, says that in gout urate crystals are deposited in unaltered living tissues, and that the assumption that necrosis of the tissue must precede the deposit of the salts must be given up. He thinks that the failure of others to find urates in the healthy tissues is due in part to their

(1) Die Natur und Behandlung der Gicht. Wiesbaden, 1882.
(2) Med. Klin. Woch., No. 34, 1897.

having examined tissues from the cadaver, and, in part, to their faulty methods of hardening.

Haig[1] contends that the "uric acid diathesis" is a myth, and that gout is but a symptom of poisoning by flesh and tea and similar substances which introduce uric acid into the body in very considerable quantities. (2) That the uric acid so introduced may not only remain in the body, but may prevent the excretion of uric acid formed in the body.

(3) That, as a result, the body becomes more or less saturated with uric acid, which may irritate its fibrous tissues (gout or rheumatism), or may obstruct its capillaries, causing high blood pressure and defective capillary circulation and their results, such as the great group of circulation diseases, the uric acid headache, epilepsy and mental disease, anaemia, Bright's disease, Raynaud's disease, etc., all of them being mere results of the enormous influence which uric acid asserts on the circulation of the body by obstructing its capillaries. Haig believes that gout and rheumatism are identical, both being due to uric acid, and that rheumatoid arthritis is a third modification, also due to it.

Luff[2] considers that the first step in the pathogenesis of gout is a failure on the part of the kidneys from functional or organic mischief, perfectly to excrete the uric acid formed in them, and that consequently absorption of the non-excreted portion took place from

1. Med. Rec., Jan. 26; 1901. Practitioner, July, 1903.
2. Brit. Med. Journ., Jan. 13th., 1898.

them into the general circulation, where it first existed in the form of sodium quadriurate and formed the source from which the gouty deposit was derived. Luff believes that uric acid is formed in the kidneys by the combination of urea with glycocin or with one of the derivatives of the latter body. He disbelieves the views held as to a diminution of the alkalinity of the blood promoting uratic deposition, whilst increased alkalinity of the blood is supposed to cause solution of the deposit, and claimed that in the light of recent experimental evidence such views were untenable. Dietary indiscretions in his opinion cause gout by their effect on the liver by increasing the amount of glycocin passed to the kidneys, and so causing an increased production of uric acid in those organs.

Later[1] Luff says, "Gout I regard as a disease which is due to faulty metabolism, probably intestinal and hepatic, as a result of which certain poisons (probably the purin and other bodies, but of which we at present know very little) are produced and lead to an auto-intoxication, which is an early factor in the development of the gouty condition. This auto-intoxication coincides with, or is followed by, in the majority of cases a deposition of sodium biurate in certain of the joints or tissues, which constitutes the climax of the gouty attack. Certainly I think that with our increasing knowledge and experience uric acid and its salts will in all probability

(1) Clin. Journ., Oct. 7th: 1903.

have to be relegated to a position of subsidiary importance in the pathogenesis of gout. The joint manifestations are probably dependent upon much more general and much larger conditions than a mere excess of uric acid in the blood. The deposition of sodium biurate is possibly merely the sign of the disease, not the essence of it."

Sir Willoughby Wade,(1) speaking of acute podagra, believes that the lesion may arise from injury or from the presence of some toxic agent in the blood. A neurosis is the primary and essential element — if a sensory nerve be attacked, we get pain and tenderness; if a motor nerve, we get redness and swelling; if the nutritive nerve of a joint, we get changes in the joint; one result of which may be a deposit of urate.

Duckworth(2) writes, "It may be confidently asserted that according to our present knowledge no conception of this malady is possible which should exclude from its purview the part played in it by uric acid." Again he writes, "Gout is something beyond the resultant effects of aberrant relations of uric acid; it consists in something more than a perversion of animal chemistry; it is not to be explained as a mere outcome of gastric or hepatic distemper; it is not the appanage only of the middle-aged or elderly high-liver and intemperate drinker, because, as is well known, it affects also, sometimes in early life, the high-thinker and the laborious bread-winner." Duckworth considers that a paroxysm of gout, the sites of

(1) Med. Times and Hospital Gaz., July 24: 1897.
(2) Treatise on Gout, p. 15.

its occurrence, and its metastases, are determined by nervous influences, probably dominated from the bulbar centre, and that the local attacks alight either in the joints or in textures which have been weakened by impaired nutrition owing to past injury or overuse. This central neurosis is an essential and transmissible feature in the pathogeny of gout, and pertains to the arthritic diathesis generally. He considers that the urichaemia of gout is peculiar and unlike that induced by other morbid conditions, but that th e occurrence of urichaemia in the gouty is by itself inadequate to induce attacks of gout. He doubts Garrod's theory that a functional renal inadequacy as regards the excretion of uric acid is one of the causes exciting a gouty fit. He believes that uratic deposits in any part of the body may disappear in time, but are apt to be permament in the least vascular tissues, and that the local processes are not always dependent upon those deposits, it being largely a quantitative question with due regard to the personal factor, and he believes that in gout, to use the words of M. Rendu, there is a "primordial vice of nutrition", leading to imperfect elaboration of the food taken. In short, Duckworth is a firm believer in the gouty diathesis as expressed in (1) a neurosis of the nerve centres which may be inherited(primary) or acquired (secondary), and (2) a peculiar incapacity for normal elaboration within the whole body, not merely in the liver or in one or two organs, of food, whereby uric acid is formed at times in

excess, or is incapable of being duly transformed into more soluble and less noxious products.

Croftan[1] is an advocate of Duckworth's neuro-humoral theory. He believes that the formation of uric acid in man is mainly analytical, and that its accumulation is more often due to non-destruction than to over-production, and that the deposits are determined by local causes.

Critzman[2] concludes that:

1. The so-called gouty kidney is the primary cause of gout, and just as there can be no gout without uric acid, with uric acid there can be no gout without chronic nephritis.

2. The tubuli contorti may be affected for years before nephritis is clinically evident, and that in such a case the existence of gout is sufficient evidence of nephritis though it may be in a very early stage.

3. Uric acid is not a normal constituent of the blood, though constantly to be found just before or during a gouty attack, when the amount excreted by the kidneys is just as constantly diminished. As, in Critzman's opinion, healthy kidneys are capable of excreting several times the normal quantity of uric acid, this diminished excretion is pathognomic of diseased renal tissue.

4. Uric acid is formed in the kidneys, chiefly or solely from the deconposition of the nucleins present in

(1) New York Med. Journ., Nov. 1: 1902.
(2) Brit. Med. Journ. Epit., March 11: 1899.

the body; thus, it is evident that, given a nephritis and consequent retention of uric acid, a diet rich in absorbable nucleins,or the onset of any disease accompanied by leucocytosis,will produce a precipitation of uric acid in the tissues, already weakened in their nutrition by the presence of blood containing toxic substances. Critzman believes that alcohol does not lessen the excretion of uric acid until it has deranged the kidneys,and he quotes the experiments of Luthje and Weintraud as showing that the same conditions apply to the absorption of salts of lead.

Woods Hutchinson(1) believes that gout is a chronic toxaemic process resulting in the production of uric acid and urates from the katabolism of body nucleins under the influence of poisons, such as alcohol and lead, and that most of the toxins are of intestinal origin and treatment should aim at intestinal antisepsis.

In this opinion Thorne(2) agrees with Woods Hutchinson,and believes that a prolonged deficiency of pigment in the faeces is a pathognomonic indication of excessive intestinal putrefaction.

Von Noorden,in a very able address at the British Medical Association meeting at Oxford in 1904, said that in his opinion uric acid is a poison determining inflammation in the surrounding tissues, but only when

(1) Lancet,Jan. 31: 1903.
(2) Lancet,April 11: 1903.

the solution reaches a certain concentration. The solid needles do not irritate the tissues, alteration of the alkalinity of the blood and tissues cannot explain the deposition and the solution of the crystals: this solution of solid needles is a phagocytic process, and that probably the crystals are deposited before the acute attack, and that the acute gouty inflammation depends on sudden solution of the needles.

He referred to the hypothesis of Minkowski that, in gout, substances of a kind that bind the uric acid firmly, and make it easily soluble and easily excreted, are formed in too small quantities in the blood and in the gouty foci. Von Noorden suggested the following amplification of Minkowski's hypothesis:—

The normal organism has at its disposal a certain number of organic substances with "haptophore" side-chains for catching and solving uric acid.

In this form the uric acid is removed from the place of its origin and passed through the blood. Out of those combinations the kidneys eliminate the uric acid, while the uric acid salts as such are eliminated with difficulty. Two deviations from the normal may arise — firstly, the amount of the uric acid binding substance is normal but the influx of uric acid into the blood is too great — hence we find loosely bound uric acid in the blood, as in case of excessive disintegration or ingestion of nucleins or in nephritis. Secondly — the amount of the uric acid binding substance is too small; hence the

characteristic anomaly of gout. A certain part of the uric acid formed in the body does not meet with molecules bearing "haptophore" side-chains for uric acid — it with difficulty is excreted, therefore accumulates in the blood, and in certain tissues a deposition takes place.

The amount of those organic substances, says Von Noorden varies much in gout; increase of them is indicated by increase of uric acid in the urine, as a sign that it is a toxin — producing process, and also by an increase of nitrogen and phosphoric acid. When the influx of uric acid binding substance increases suddenly and largely, then acute local inflammation due to dissolved uric acid and a genuine febrile reaction accompany it — hence the typical gouty paroxysm.

Walker Hall[1] contends that "gout cannot be regarded as a state of simple malnutrition; it is rather a condition of insufficient cellular resistance against the absorption of intestinal poisons or auto-toxines, characterised by the production of imperfectly formed metabolites, which act on some tissues as irritants and in others excite degenerative changes that permit uratic infiltration, as the processes of absorption, assimilation, and elimination, are closely associated, quantitative changes in any one function will produce qualitative changes in

(1) Practitioner, July, 1903.

the other two. So, while the increased activities of the purely metabolic organs may lead to widespread cellular changes, the results produced, themselves sufficiently abnormal, may be complicated by the secondary factors of deficient ingestion or excretion."

P. Le Gendre[1] is of opinion that "it is probable that there exists in the gouty subject a defective elaboration of nitrogenous material, an inaptitude of the tissues to destroy albumen thoroughly. Among the consequences of the incomplete destruction of refuse must be included the incumbrance of the organism, both by certain acids (oxalic, acetic, lactic, etc.), which can diminish the solubility of uric acid without that substance being necessarily in excess in the blood, and by certain organic bodies the toxicity of which may contribute to the production of the manifold accidents of gout.

Chalmers Watson as a result of a series of investigations, concludes that: (1) The alkalinity of the blood is not diminished during the attack; (2) The excretion of uric acid is not diminished during the attack, but the reverse; there is therefore no ground for the supposition that there is temporary diminution in the capability of the kidneys to excrete uric acid; (3) The amount of uric acid in the blood is not greater during the attack than in the intervening period; and, if those points be accepted, we must start de novo in search of the cause of the acute paroxysm. It would be well, he thinks, if less attention were centred on the excretion

(1) Brit. Med. Journ. Epit., Aug. 11: 1900.

of uric acid alone as the all-important factor in the disease, whether in its acute or chronic form.

AUTHOR'S VIEWS and DEDUCTIONS.

When one reviews all these different opinions regarding the true nature of gout — the role which uric acid plays, the origin of uric acid, the influence of dietary, and various other points, one is forced to come to the conclusion that gout is a disease which as yet is not generally understood.

When Garrod first promulgated his, now well known, views on the relationship of uric acid to gout, he allowed that they were not by themselves sufficient to explain all the phenomena of gout; and, after a prolonged series of attempts to fit in the missing links by the uric acid theory, there has been of late years a perfectly justifiable tendency in some authorities in the direction of regarding uric acid as being merely a secondary product, and not the prime cause of the disease.

Others, however, not only adhere to the uric acid theory, but attempt to imbue uric acid with toxic properties even when held in solution in the fluids of the body; it having, they say, not only an aetiological relation to gout, but to many other maladies which are apparently clinically unrelated, e.g., Raynaud's disease ,

Epilepsy, Mental diseases, etc. (Ebstein, Haig).

Most of the views of the numerous authorities which I have quoted are beyond the pale of criticism of a general medical practitioner such as I am. It has not been my privilege to have access to a laboratory, it has not been in my power, owing to the exigences of busy general practice to conduct a series of quantitative analyses of urine in gout, still less has it been my inclination to test the truth of Haig's well-known views by swallowing measured doses of uric acid three times a-day — Nature has made quite enough experiment in me without my trying to experimentally induce further attacks. As a matter of experience, I have never found moderate use of meat or tea to have ever had prejudicial effects, except in cases of renal complication, impaired digestion, or where an idiocyncrasy existed.

Haig apparently suffers from a particularly physiologically-damaged economy to which meat and tea are prejudicial, and many authorities far better qualified to criticise than I am, are not convinced by his arguments.

Woods Hutchinson(1) expresses doubts as to the correctness of Haig's "uric acid filter" views. "The overwhelming consensus of opinion among physiologists is that the process by which his theory would have us believe that uric acid is deposited in the tissues when the blood is acid — which it never is — and dissolved out into the blood stream again when this becomes alkaline, is practically impossible in the living body, or

(1) Lancet, Jan. 31: 1903.

at all events there is no shadow of evidence that it actually occurs . . . . . "

Although Duckworth[1] says "the essential elements in any case of gout relate, threfore, to peculiarity of diathesis, to diminished alkalescence of blood owing to impregnation with uratic salts, and to the deposition of the latter, especially in the textures of joints" — on the other hand Robert Hutchison[2] says" We now know that the alkalinity of the blood is either normal or slightly increased . . . . . It is possible that uric acid may enter into combination with some other constituent of the blood than the alkaline salts. One of the most characteristic properties possessed by the blood is its uniformity of composition, and in no particular is this more marked than in the maintenance of its normal alkalinity."

Luff[3], from a series of investigations, found that the alkalinity of gouty blood is nearly one-third higher than that of normal blood. The increased alkalinity of the blood is due to a higher proportion of sodium carbonate or bicarbonate, and, since these substances accelerated the conversion of the soluble gelatinous biurate into the crystalline variety and therefore the precipitation of the latter, it is intelligible that such blood is prone to hasten and to augment the formation of gouty deposits — and to determine the gouty paroxysm.

(1) Treatise on Gout, p. 3.
(2) Med. Annual, 1903, p. 303.
(3) Lancet, March 31, 1900.

Chalmers Watson says [1] "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."

CRITICISM of other VIEWS.

As regards the views of the other authorities quoted, I am not qualified to contradict them, not having the equipment necessary to do so, but most of them seem to me to fall short, in some item or other, of a complete explanation of Gout. The views of Duckworth (especially in his neurosal theory), Woods Hutchinson, Chalmers Watson, and Walker Hall, fit in most completely with my clinical experiences of gout: I have found in their writings a confirmation of a series of facts which I have often observed without being able to experimentally demonstrate as they have been able in many instances to do .

If an excess of uric acid in the blood were the prime factor of Gout, why not have gouty symptoms in cases of pneumonia, in thymus feeding, and in leukaemia, in which latter at least the excess of uric acid has allowably been greater than in most cases of Gout? Granted that in gout there be renal inadequacy (a point not universally accepted) leading to accumulation of uric acid in the blood, while in leukaemia there is free

(1) Brit. Med. Journ., Jan. 21: 1903.

elimination (the amount of uric acid in the urine of leukaemia in the twenty-four hours varying from two to five grams[1]) the question naturally arises whether it can be definitely shown that owing to the (supposed) renal inadequacy in gout there results a greater accumulation of uric acid in the blood than there exists in leukaemia with free elimination? As far as my reading goes, this has never been done — on the other hand the actual amount of uric acid in the blood of the gouty is in many cases small, and rarely, if ever, reaches the amount often present in leukaemia. In leukaemia there is an enormous production of uric acid, which is not only voided in the urine, but may be deposited in the kidney to such an extent as to simulate renal calculi,[2] and Rose Bradford[3] mentions having seen uric acid coating the mucous membrane of the pelvis of the kidneys and along the centre length of the ureters to the bladder, and even with this there is often an excessive quantity in the blood.

If uric acid be the toxic agent it is represented to be, as in all poisons, the effects ought to be in direct proportion to the amount present in the blood, and I am not aware that it has been demonstrated, although suggested, that the uric acid in gouty blood is not the same as the uric acid in leukaemia. It has certainly been suggested by Garrod[4] that in gout the uric acid is

(1) A.E.Garrod, Brit. Med Journ., Sept. 24: 1904.
(2) Lauder Brunton, Clin. Journ., Dec. 7: 1898.
(3) Clin. Journ., June. 1: 1898.
(4) Brit. Med. Journ., Sept. 24: 1904.

at fault, and that the fraction which cannot be excreted lingers in the blood, and becomes deposited in the tissues, whereas even large quantities of uric acid merely in transit do not lead to the formation of deposits, but this is hypothetical.

Garrod's Uric acid theory of gout is based mainly on these three points :

1. Excess of uric acid in the blood — the amount being greatest before an attack and least immediately after one.

2. Defective excretion of uric acid by the kidneys, owing probably to functional derangement in the early, and certainly due to structural derangement in the later, stages of gout.

3. Deposition of urate of soda in the tissues.

The excess of uric acid in the blood is almost universally agreed upon, but Duckworth[1] admits that it is not always demonstrable even in cases of unequivocal uratic arthritis. Chalmers Watson[2] avers that the amount of urichaemia is not greater during the attack than in the intervening period.

Touching the second point — functional inadequa--cy of the kidneys to excrete uric acid is not clinically demonstrable, the normal limits, 0·2 to 1 gram in the twenty-four hours, being somewhat wide, and as Haig pointed out if the inadequacy existed, the urea excretion

(1) Treatise on Gout, p. 116.
(2) Brit. Med. Journ., Jan. 21: 1905.

would be likewise affected, which is not the case — a supposed failure of the kidney to excrete one particular metabolite would be new pathology.

The views of Ebstein and Critzman on this subject have already been given. Ebstein holds that primary gout may be either primary renal or primary articular: Critzman holds that primary renal mischief is always the cause of Gout, that with uric acid there can be no Gout without chronic nephritis. My clinical experience leads me strongly to dispute the theory that the kidneys are of necessity involved in gout even after repeated attacks. I have known several men with a strongly marked gouty diathesis manifested by well-marked attacks of gout live to be over eighty years old without any symptoms of chronic renal mischief. They are certainly endowed with a fine constitution, whereby doubtless the deleterious progress of the gouty processes were kept at bay.

CASES. The following are instances of patients with gouty diathesis who have lived to be over eighty years old — who suffered from attacks of acute gout, and who, nevertheless, did not suffer from chronic nephritis.

Case 1. U. B. died last year (1904) in Yorkshire, aged 99 years and 4 months, from cancer of the pylorus. Up to fifty years of age he was always, he said, considered rather a weakly man — he then came into a small fortune, and gave up his work as a hand-loom weaver. I knew him for ten years — there was a history of several attacks of gout in his earlier years, there were well-

marked tophi on his ears. He had one slight, but typical, attack of gout while under my observation, but suffered most from dyspepsia. Up to his 94th. year, he regularly, in good weather, walked to see his son(who was postmaster in my village) 2½ miles each way.

Case 2. B.A., Manufacturer, died, aet. 83, from old age. Marked gouty diathesis, evidenced by several acute attacks, mostly in his middle age. He was well known to me, but was attended by my brother, who writes — "there were no signs of chronic nephritis in this case."

Case 3. W. W., Manufacturer, under observation twelve years — during this time had two typical gouty seizures — suffered from gouty eczema — died, aet. 80 years and two months, from old age aggravated by Influenza.

Case 4. F.E., Master tailor, aet. 82 years — still alive. No acute attack from personal observation of thirteen years, but there is history of several attacks in the third and fourth decades of his life — suffers from gouty bronchitis.

Case 5. G.B., Master tailor, aet. 81 years, still alive — much the same history as in Case 4, but suffers from emphysema as well as bronchitis — getting feeble.

As has been said, in none of those cases were there any signs or symptoms of chronic nephritis — In cases 1, 4, and 5, my investigations as regards the presence or absence of chronic nephritis have been confirmed by my successor in Yorkshire, where all the cases occurred.

That great clinician, Jonathan Hutchinson, in a lecture which I had the privilege of hearing expressed the opinion that a decided gouty diathesis was, barring the haemorrhagic tendency almost as good as a certificate for long life, especially if the gouty subjects drank large quantities of weak tea to flush the system of impurities. What would Critzman and Haig say to this "dictum"?

Chalmers Watson[1] after experimental research finds "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."

I think that the renal inadequacy for the excretion of uric acid, functional in the early stages of gout according to Garrod, always organic according to Ebstein and Critzman, - which is invoked by those authorities as being a primary cause of gout, ought to be regarded if it exists, as the result of gout. If the primary cause, why do renal symptoms occur, as a rule, only as late events in gout, also why is it that so many subjects of chronic interstitial nephritis never exhibit unequivocal symptoms of gout?

West[2] refers to the statistics of Dickinson (Pathology and Treatment of Albuminuria, p. 149), as show-

(1) Brit. Med. Journ., Jan. 21: 1905.
(2) Practitioner, July, 1903; p. 37.

ing that out of sixty-nine fatal cases of granular kidney only sixteen were dependent on, or coincident with, gout, and to the statistics of Norman Moore, as showing that, out of twenty-six cases of granular kidney in women, only five had uratic deposits in the joints.

On the other hand, Ord and Greenfield[1] found that in a series of patients who had uratic deposits in the great-toe joint two-thirds had granular kidney, and that in the remaining third the kidneys were not sound.

Norman Moore[2] in forty-nine cases of granular kidney in males found uratic deposits in twenty-two.

Pye-Smith[3] in ten cases of fatal gout found interstitial nephritis in eight cases.

Those statistics show that some patients may have gout and never develop granular kidney, and some have granular kidney and never develop gout: hence "the relationship, however close, is not constant or essential"[4] and hence Critzman's theory cannot be upheld.

To brand the kidneys as "functionally" inadequate to excrete uric acid when they are able to excrete urea, and when they clinically exhibit no symptoms of being otherwise than healthy, seems to me to be a case of begging the question.

Duckworth[5] believes that the excreting functions

(1) Trans. Internat. Med. Congress., London, 1881, p. 107.
(2) Trans. Internat. Med. Congress London, 1881, p. 292.
(3) Guy's Hosp. Rep., 1874.
(4) West. Practitioner, July, 1903; p. 37.
(5) Treatise on Gout, p. 39.

of the kidneys for uric acid and urea are separate and independent of each other. This requires proving.

The normal limits of uric acid excretion, 0·2 to 1 gram in the twenty-four hours, are, as I have already said, so wide, and in gout the personal factor is so marked, that it appears to me that it must be very difficult to say when the uric acid excretion is below normal, unless we could obtain a comparison of the habitual excretion of the patient before and after the attacks. This has been done by Chalmers Watson[1] who records that "the results of this investigation showed no disturbance in the uric acid elimination either before, during, or after the paroxysm."

Duckworth[2] by way of explanation of the supposed "special functional inactivity of the kidneys suggests that in gout those organs may be specially prone to be nervously impressed, but in view of Chalmers Watson's

(1) Brit. Med. Journ., Jan. 21: 1905.— Chalmers Watson's tables are:

Table iii. Case 1. Uric acid excretion in acute gout.

Acute attack.	Urea	$H_2\overline{U}$	$H_2\overline{U}$ — Urea Ratios.	Average of Days.
	Grams.	Grams.		
(last five days of severe 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

(2) Treatise on Gout, p.48.

Table IV. — Case 2.

Acute attack.	Urea.	$H_2\overline{U}$.	$H_2\overline{U}$ – 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	0·53	1 — 59	4

investigations the apparent corollary would be that the condition be first proved to exist, and only then tried to be explained!

Some upholders of Garrod's retention theory, having failed to satisfy themselves that the eliminating power of the kidneys was entirely, if at all, to blame for the excessive urichaemia in gout, have attempted to ascribe the condition to an error in the uric acid itself. Minkowski's and Von Noorden's theory has already been quoted. Sir Wm. Roberts's quadriurate theory was dispelled by the researches of Tunnicliffe and Rosenheim: it has also been suggested that the uric acid may not be in combination at all, but exists in the blood in a crystalline form: it has also been suggested that, although the bulk of uric acid in man is formed from nucleoproteids, a certain part has a synthetic origin, and that if the uric acid be at fault, the fault may be only in the synthetic portion.

Parkes, as already quoted, surmised that, although the kidneys were not inadequate to excrete uric acid, the uric acid was held back by some peculiar and unnatural combination in the blood or organs, and latterly Walker Hall[1] suggests that "the excess of urates in the blood stream may be possibly due to the presence of substances which hinder the separation of uric acid by the kidneys, although permitting its estimation by laboratory methods. Such substances may easily result from the abnormal metabolic processes which occur in gouty tissues, and which are formed continuously and quite apart from the incidental accession of toxins during the acute attacks."

The uric acid theory not proving sufficiently convincing to some minds, there has arisen a revulsion of feeling as regards uric acid in its causative relation to gout — a swing of the pendulum in the direction of regarding uric acid as being merely a secondary product.

Dr. Goodhart states his mind freely. "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."[2]

As regards the deposition of urate of sodium, all are agreed that in "frank" gout it does occur, and

(1) Brit. Med. Journ., Sept. 24: 1904.
(2) Lancet - Jan. 6: 1900.

in no other disease but Gout,[1] but Duckworth denies that it is always permament.[2]

Garrod believed the deposition to be the cause of the inflammation. Ord, as always quoted, denies this, and Duckworth says it all depends upon the amount of deposition.

In reference to the deposits of urates in the inflamed joints and tissues, Woods Hutchinson[3] regards them as being purely symptomatic in their character. "Firstly, the overwhelming balance of the injection experiments referred to shows clearly that the urates are either non-toxic or so feebly so as to be utterly incapable of accounting for the furious outburst of frank gout; secondly, that their deposit in the tissues by no means coincides with the acute attacks, but on the contrary is more apt to occur during the intervals; thirdly, that their formation and deposit in large masses and amounts may, and frequently do, occur without giving rise to any symptoms whatever, or even attracting the attention of the patient; and, fourthly, that they can be produced in abundance by the prolonged ingestion of a purely mineral poison (lead). In short, that they behave precisely like the reaction products of fibrous tissue stimulated by any slowly acting toxic substance.

(1) Woods Hutchinson's opinion makes it necessary for me to qualify this statement. In his article so often referred to by me, he says "This deposit (uratic) is not confined to true gout, but occurs in chronic plumbism, which is, in my judgment, not gout at all."

(2) Treatise on Gout, pp. 51 - 68.

(3) Lancet. Jan. 31: 1903.

ORIGIN of URIC ACID.

After all those years of experimental research and of discussion, it is not yet definitely decided where and whence uric acid is formed. Luff holds that uric acid is normally produced only in the kidneys. Haig holds that the liver is the chief site of formation. Ebstein is of opinion that in gouty people a large proportion of uric acid is formed in the muscles and possibly the medulla of bones.

It is said[1] that uric acid is derived by a process of disintegration from the nucleins, or materials of which the cell-nuclei consist, and that the spleen with its nuclein containing leucocytes is perhaps the main seat of uric acid formation. Woods Hutchinson[2], however, is of opinion that neither in the lymph nodes, the spleen, nor the thyroid (all of which might be considered as possibilities), is there, in all probability, a sufficiently rapid rate of disintegration going on to supply dead nuclei enough for the production of even the small normal amount of uric acid.

The constant disintegration of "the great brotherhood of leucocytes" which have undergone disintegration in the process of neutralising infectious toxins introduced into the body, in in Woods Hutchinson's opinion, the chief source of uric acid in gout and lithaemia[3]

Walker Hall[4] thinks that the probable sources

(1) Diagnostics of Internal Med., G.R.Butler, London and New York, 1904; p. 630. (2) Lancet, Jan. 31: 1903.

(3) Woods Hutchinson believes that uric acid in health is produced from two sources — the exogenous (Chittenden) from the nucleins and purin bases of the food —, the endogenous by nuclein katabolism in the tissues. The former provides most normally, the latter is alone increased in gout and lithaemia.

(4) Brit. Med. Journ., Sept. 24: 1904.

sources of uric acid are —

(1) Synthetic formation. (2) from the destruction of leucocytes. (3) from the breaking up of nucleo-proteids during cell processes.

Some years after starting general medical practice, I read in some journal an account of Gautier's researches on Auto-intoxication. It was, I believe, in 1885 that Gautier demonstrated that poisonous bodies to which he gave the name of leucomaines were formed from sound food during normal digestion and in large quantities and more virulent form if those digestive processes were interfered with.

Gautier pointed out that poisonous matters were being continuously formed by the decomposition of albumen in the intestinal canal during the process of digestion, and also in the blood and tissues by the metabolism which occurs during the functional activities of life. In short that the normal products of digestion are poisons of considerable power, and that if excessive formation of the products, or through both factors, they reach the circulation in any considerable quantity, alarming, or even dangerous symptoms occur.

Shortly after reading about Gautier's researches I was asked to visit a patient who had come from the south of England for a change of air.

The patient, F. S., aet. 35 years, draper's assistant, had been under medical treatment for six months for "diabetes" — symptoms first observed twelve months previous to my examination. He had taken medicine and had

been strictly dieted. While under treatment, patient was seized with acute pain and inflammation of the great toe joint — lasting one week — diagnosed as being of diabetic origin. After temporary improvement, patient became weaker and very despondent; and, finally being unable to work, he came North.

On examination I found the tongue dry, but not typically raw and "beefy" — patient complained of thirst and a nasty taste in his mouth, and of a feeling of distension most marked after meals. No physical signs of disease in chest or abdomen — muscular power enfeebled. Urine — pale, s.g. 1040, abundant precipitate with Fehling's solution verified by Moore's test; amount passed in twenty-four hours was eight pints, no diacetic reaction and no albumen. Patient was strictly dieting himself, and on the advice of his previous doctor took one or two pills of one grain of opium at bedtime. The sheaf of prescriptions he exhibited showed that he had gone through the gamut of "diabetic" drugs — opium, codeia, Salicylate of soda, Bromide of Potassium, etc., but he dolefully remarked that nothing of late had done him much good except the pills (opium), which induced otherwise unattainable sleep. I therefore, advised him to continue them until further orders, and prescribed a soda and gentian mixture and a seidlitz power every morning or alternate morning according to the state of the bowels.

One week later the patient's condition was

practically in statu quo, as there was nausea and constipation. I stopped the opium pills and prescribed two grains of calomel at bedtime and a seidlitz powder on the following morning.

Next morning — the medicine had acted well, just previous to my visit. On examining the stool, which was very offensive, I observed in it some segments of tape-worm. Here at last was something to treat! A few doses of male fern brought away the worm, including, as subsequent absence of signs showed, the head, although on careful examination of the motions I failed to discover it. The patient, on cross-examination, said he has noticed "these things" occasionally, but "didn't think they meant much" He had not mentioned the fact to his previous doctor.

After the evacuation of the tape-worm the amount of glycosuria slowly but steadily diminished, and so did the total quantity of urine passed. One month afterwards there was no trace of sugar, and the amount of urine passed daily was sixty ounces, the specific gravity was 1030, there was a preceptible uric acid deposit on settling. On testing for albumen (slight traces of which I had found two weeks previously in two specimens of urine submitted to me) with nitric acid a bluish ring developed at the point of contact. This at once suggested Indican, the presence of which was confirmed by the Hydrochloric acid and Chloride of Lime test — there was no albumen.

The patient, whose general condition had steadily improved, complained of a "distended" feeling after meals. I therefore prescribed a Bismuth, Soda, and Tincture of Nux Vomica Mixture, t.d.s.a.c., with two grains of Calomel at bedtime, and a full dose of Sulphate of soda on the following morning.

Two days afterwards the patient was seized with a typical attack of acute gout in his great toe joint, which under ordinary Colchicum and alkaline treatment, combined with gr. 1/6 of Calomel ter in die, subsided in about ten days.

The amount of Indican began to diminish on the fourth day after the gouty onset — after the second week there was only a mere trace.

The patient made a comparatively rapid recovery — gained flesh, looked well, and finally departed to the South to find some work. He wrote me about one year afterwards saying he felt very well and had had no recurrence of gout nor apparently of sugar as he passed what he termed "an ordinary amount" of urine. His landlady told me that she had heard a rumour that F.S. had died about two years afterwards of "inflammation," and that was the last I heard of a very interesting case.

POINTS in this CASE.

The points of the case seem to me to be:

1. That the case was not diabetes, but simply glycosuria.
2. That the glycosuria was largely due to the irritation of the tape worm.

3. That a morbid impulse from the coeliac plexus instigated by the irritation of the tape-worm, induced a reflex passive dilatation of the hepatic arterial system, which condition according to Duckworth is a prime factor in glycosuria.

4. That, as a result of hepatic disturbance, some toxins, including Indol, were produced in excess, or their poisonous properties not destroyed, and being absorbed.

5. that the gouty attack was produced — the first attack of pain in the great-toe being gouty in nature, although not recognised to be so.

Garrod held that glycosuria tends to check obvious gouty symptoms, the increased urinary flow carrying off uric acid and other solids. In the case of F.S., there was no appreciable amount of uric acid in the urine until the sugar disappeared and the amount of the urine decreased. It is quite probable that indican may have been present in the urine for a long time, but so diluted as not to be recognisable upon the addition of Nitric acid, but its well recognisable appearance in the urine just antecedent to the attack of gout is, to my mind, strongly suggestive of a toxic origin of the attack — there being in the case of F.S. no family history of gout.

S.A.K. — woollen manufacturer, aet. 42, consult- me for "chalky gout" in his finger joints. "The condition really was mild tophaceous gout — most marked on the right side. Father(dead)and uncle both gouty. The affected parts usually painless were on this occasion slightly swollen and painful — there was no history of "classic" gout in the great-toe — all the toe-joints were normal. Patient had been for two years gradually getting stouter — he worried much about business, and owned to an irascible temper. Tongue furred; patient complained of flatulence and irregularity of the bowels. Urine contained Indican and some urates — no sugar nor albumen.

I prescribed restricted diet, a rhubarb mixture, Calomel gr. 1 at bedtime for three nights, with Carlsbad water on the following mornings — a big drink of hot water every day at 11 a.m. and 4 p.m., and abstinence from business worries. The only local treatment advised was keeping the affected parts free from chills and cold water. Afterwards I prescribed an ordinary alkaline mixture, and gr. 1/6 of Calomel three times a day after meals.

Under this treatment at the end of a fortnight the patient had greatly improved — the fingers were quite painless — he went to Harrogate for three weeks, and returned feeling quite well — although the fingers were still "knotty."

He returned to business, and consulted me occasionally. On the second occasion I again found traces of Indican, which soon disappeared under Calomel gr. i

every second night. The gr. i doses were continued until the end of the first week — I then prescribed Calomel gr. 1/6 after meals, to be taken whenever flatulence was observed. From time to time afterwards I examined the urine, but never again found any traces of Indican — (on no occasion had I ever found any sugar or albumen). The patient took to golf and other outdoor exercise, and although he by no means led a life of dietetic abstinence, up to the time of my leaving Yorkshire he enjoyed very good health, and had had no recurrence of the pain in his finger joints, although the quiescent "chalky" condition remained in statu quo. S.A.K. is the nephew by marriage of Mrs. E.A. already referred to as having suffered from gouty cephalalgia. Curiously enough he is the only fair-haired gouty patient I have as yet come across.

Mrs. F.W., aet. 39, came under my care when I succeeded to my Leicestershire practice. She came of a tubercular stock on the paternal side, and had a large mass of enlarged cervical glands — dulness at right apex with sharp clicking râles — was subject to bouts of diarrhoea (evidently tubercular) and several attacks about every four or five weeks of "cramps", which my predecessor diagnosed as being hysterical. After carefully observing one of the seizures my diagnosis was remittent tetany due to the absorption of some intestinal toxins. The motions for a day or two prior to those "cramps" were abominably offensive. One day the urine on the addition

of nitric acid gave the reaction of Indican — the amount of which increased for three days, and on the fourth day the patient had a typical attack of gout in the great-toe, which attack ebbed and flowed for a fortnight — the indicanuria disappeared seven days after the onset of the gouty seizure.

The patient was treated with Potassii Citras and Vinum Colchici, but, after two days, the colchicum was omitted from the mixture owing to it causing epigastric pain and diarrhoea, which the substitution of Bismuth salicylas soon relieved. gr. 5 of Pulv. Ipecac. Co. were given when pain was very severe and locally a lotion of sod. carb. and Tinct. opii, and water mixed.

The patient was after gouty attack treated with various intestinal antiseptics. Bismuthi Salicylas, Salol, gr. 1/10 — 1/6 Calomel, Creasote (m.i. in capsules), and beta-naphthol, which lessened the frequency and intensity of the tetany attacks to three of four months' intervals, and two or three hours' duration, in contrast to the previous four or five weekly attacks lasting sometimes a whole day.

Gout and Tuberculosis are held to be antagonistic, and certainly my patient's general condition was temporarily improved after her gouty seizure; but, as time went on, her tubercular disease made steady progress, and, after rather a miserable existence of two years, she died of general exhaustion.

Six months after the primary attack of gout, Mrs. F.W. had a very slight attack (only lasting one day) in the same great-toe — slight traces of Indican in the urine were detected.

The rationale of this case apparently is that the intestinal ulceration caused the production of indol and other toxins (not recognisable in the urine), which, when in excess, were absorbed and induced the gouty attacks, the vital tissue resistance being covered by the multiplication of growth of the Bacillus Tuberculosis in the lungs.

In neither the case of F.S. nor of Mrs. F.W. was there any family history (although I know the fallacies in tracing family histories are many) of gout — the gout must, therefore, in those two cases be regarded as being distinctly toxaemic.

In my own case the malady was variously diagnosed as being rheumatic, gouty, and influenzal, but the final diagnosis was gout. Some months afterwards slight ~~dysuria~~ glycosuria was observed, but soon disappeared. I periodically tested the urine and on one occasion found distinct traces of Indican, whereupon I promptly took Calomel, followed by Mist Sennae Co., and drank much hot water, with the result that I escaped everything except a few twinges of pain in my finger-joints. On another occasion, being very busy with confinement cases, etc., I stupidly ignored the danger signals — a distended and uncomfortable "sinking" sensation a few hours after meals, and distinct traces

of Indicanuria, and, as a result, had a sharp attack of gout, which laid me up for nearly three weeks.

AUTO - INTOXICATION. The doctrine of Auto-intoxication is a comparatively new pathological conception, but it is now no longer a theory, but a well-established fact, that the bodily organism can be poisoned by the products of its own metabolism, the metabolic processes having their seat in the several cells of the tissues and organs. The body is a great chemical laboratory, which is constantly dealing with a variety of chemical compounds, and the processes are of such a complex nature as to largely baffle the most refined methods of organic chemistry employed for their detection.

The passage of food from the mouth to the large intestine is one continual procession of chemical processes, in the mouth, stomach, small intestine, liver and pancreas — in addition we have through the whole intestine the complicating action of numberless bacteria, notably in the large intestine.

Following digestion we have the phenomena of absorption and assimilation, and finally a number of complex chemical processes which have their seat in the various cells of the body — oxidations, reductions, dissolutions, syntheses, and ultimately the chemical modifications preparatory to the elimination of the waste products, resulting in urea, uric acid, salts, etc.

The intestinal tract is one of the main channels of intoxication. We have occurring in the digestive tract (1) the processes of digestion; (2) fermentative processes due to the action of bacteria and of a twofold character — of the nature of fermentation and of the nature of putrefaction, i.e., carbohydrate and proteid decompositions resulting in the formation of butyric acid, acetic acid, formic acid, ammonia and ammonia compounds, phenyl, indol, skatol, etc. All those products are usually eliminated without producing abnormal reactions, if they accumulate they produce symptoms of autointoxication. The seat of carbohydrate decomposition due to the action of bacteria lies mainly in the stomach and small intestine. The seat of proteid or putrefactive decomposition lies mainly in the large intestine.

The intermediate products of proteid metabolism, about which we know very little, are normally absent from or are only sparingly represented in the excretions, but under pathological conditions, about which we also know very little, they may be produced and absorbed in excess. We have examples of those in creatin, cystin, oxalic acid, grape-sugar, etc. Under normal conditions those substances, if produced, undergo further changes (about which also we know little) — changes, it may be, of oxidation, reduction, or combination with other substances causing them to be inert. In this way their presence as toxic agents is but temporary, but circumstances may arise to make their presence felt.

GAUTIER and LEUCOMAINES. In this connection Gautier[1] differentiated a group of bodies — already referred to as leucomaines, which are alkaloidal products of physiological change, and therefore to be distinguished from ptomaines, which are produced by bacterial action in the course of putrefaction. Gautier divided the leucomaines into two broad groups — the uric acid group and the kreatinin group. The intermediate metabolic products are supposed, on the toxaemic theory of Gout, to enter the circulation and induce gout and its allied diabetes.

ARMSTRONG on TOXINS. Armstrong[2] enumerates the various toxins developed in the human body thus:

1. Alkaloids, divided into two groups:

(a) Ptomaines, formed from the action of bacteria, or of ferments, on the albuminoid substance of the dead tissues.

(b) Leucomaines, which are elaborated by the vital energy of the cells themselves.

2. The primary products of the albuminous decomposition of digestive ferments, such as peptones.

3. Acids — acetic, butyric, valeric, and sulphuric.

4. Ammonia and the ammonia compounds.

5. Leucin, tyrosin, indol, skatol, cresol, and phenol.

(1) Gautier, cited by Kauffmann, Archive de Physiol., Vol. viii, 1896.

(2) Brit. Med. Journ., July 31: 1897.

6. The salts of potash.

7. Bile acids.

8. Biliary colouring matters, especially bilirubin.

9. Various gases, of which sulphuretted hydrogen is probably the most toxic.

The remarkable regulating and self-defensive forces of the body, in health, protect us from the effects of those toxins, another saving factor is the antagonistic action of the poisons themselves. The skin, lungs, kidneys, liver, and intestine, all in their own way eliminate noxious matters. The kidneys are most important channels of elimination of toxic matters, and some authorities ascribe to them the power of acting directly on, and neutralising, a number of poisonous bodies. Bouchard[1] succeeded in finding seven toxic substances in normal urine —

BOUCHARD on TOXINS in NORMAL URINE.

1. A diuretic substance, which is probably urea.

2. A substance which produces salivation.

3. A narcotic substance.

4. A substance which contracts the pupil.

5. A heat-reducing substance.

6. An organic convulsive material.

7. An inorganic convulsive material, probably potass.

The intestines are valuable channels of elimination.

(1) Lectures on Auto-intoxication in Disease, translated by Thomas Oliver, M.A.,M.D.,F.R.C.P. Rebman, London, 1894. p. 182.

The liver has been happily described as a filter placed between the intestines and the heart: it affords protection against the poisonous products of intermediate metabolism, and neutralises and disposes of various poisons, organic and inorganic, and, in virtue of its biliary function, appears to have the power of preventing putrefactive processes occurring in the intestine.

ARMSTRONG on EXCESSIVE TOXIN FORMATION.

Armstrong[1] sums up the chief causes of excessive formation of those poisons as being —

(a) Defective action of the nervous system, leading to a failure of the processes of digestion, such as deficient or abnormal secretion of the various gastric and intestinal juices; or to torpidity of the muscular structures of the stomach and bowels, and a consequent loss of power to make the necessary movements. Then follows retention of food products, and consequent fermentation and putrefaction.

(b) The taking of food in too large a quantity, in wrong form; or, as is most common, in improper combination.

(c) Gastric dilatation.

(d) Duodenal dyspepsia and atony.

(e) Atony of the small and large intestines.

(1) Brit. Med. Journ. July 31: 1897.

INFLUENCE of the NERVOUS SYSTEM.

All those factors may be regarded as being in aetiological relationship to gout, and also as all resulting in a lesser or greater degree from some defective action of the nervous system. In his article on neuroses of the stomach. Clifford Allbutt[1] says "In the integration of animal function the proper activities of all our organs have been so completely reduced to the governance of the nervous system, that in a sense if may be said that their every act, their every disorder, whether in defect or in excess is a function of the nervous system . . . . . .

. . . . . To some extent, no doubt, the nervous system is the fly-wheel of the whole machine." {[1] System of Medicine. Vol. iii., p. 463.}

The experiments of various physiologists — notably Pawlow, Starling, and Bayliss, have shown that emotions of grief or anger may arrest the secretion of gastric juices. "The patient who swallows with dislike does not digest" says Bouchard.[2] {[2] Lectures on Auto-intoxication in Disease; p. 183.}

It is a matter of common experience that, within certain limits, perfect digestion largely depends upon the mental condition, morose or lively, of the individual at the time being: the most simple meal eaten in lonely solitude or under depressing circumstances often violently disagreeing, whereas a much more elaborate and less digestible meal, eaten under happier conditions or in congenial company, is easily digested. If depressing conditions may arrest the gastric secretion, it is only fair to infer that exhilaration may increase it.

The neurotic or hypochondriac eats a simple meal which is not properly digested — toxins are produced in excess and are absorbed, and they poison some of those nerve centres, which we cannot at present definitely localise. As a result, their tonic or trophic influence over the various factors concerned in perfect digestion and assimilation is impaired, and thus a vicious cycle is established. The changes in the nerve centres are speculative, but the results are a matter of clinical experience.

ACTION of INTESTINAL TOXINS on NERVE CENTRES.

Intestinal toxins appear to have a marked partiality for the nerve centres, as is well instanced in the cramps and convulsions of children and in tetany. Daily storage of small quantities of noxious matter gradually deteriorate the nervous centres, producing giddiness, headache, insomnia, coma, melancholia, or hypochondriacal conditions.

Case of J.A.P.M. My friend Dr. M.D. Macleod, Medical Superintendent East Riding Lunatic Asylum, once mentioned to me a most interesting case of acute mental disturbance apparently solely induced by excessive faecal accumulation. On writing Dr. Macleod recently for detailed facts of the case, he answers — "Being convalescent from a severe illness, I have asked Dr. Archdale (assistant Medical officer) to reply to you. We have often discussed the

points, and are of one mind. He puts the points admirably." Dr. Archdale writes: J.A.P.M.—Private patient, aet. 27 years, theological student, quiet and of steady habits — no history of drink or venereal excess. Had always suffered from irregularity of the bowels. Family history of gout on father's side.

The mental state associated with toxaemia is usually that of confusion with hallucinations and outbursts of intense excitement, terror, or blind fury.

This case was typical in that respect, and, before admission, in his attempt to escape imaginary followers, the patient had rushed up a tree and thrown himself down a distance of forty feet. Constipation was most exaggerated, and as a result of aperients, copious motions came away involuntarily for about three weeks, the sphincters being paralysed for the time. The faecal matter was not weighed, but there must have been several stones. On admission there was black smoky urine, containing a little blood.

His mental state, urine, etc., quickly became normal when his bowels began to be moved. His bodily condition became fairly satisfactory, and the kidneys were apparently healthy. We did not notice any manifestations of gout in this patient, who was an inmate from 29th. May, 1903, to 4th. July, 1903. During his first week here he was very sore and much bruised, but he did not appear to suffer specially from his joints. We cannot say that

we have experienced much joint trouble in relation to constipation, though mental symptoms are always worse then. It is wonderful how much chronic cases are benefited by aperients given regularly, while we look on purging as a prime necessity in acute cases. Our patients are mostly agricultural, and we see very little gout."

Case of Mrs. G.H. The following case is of interest;—Mrs. G.H., aet. 39, came under my charge in April, 1899 — having suffered from "debility and biliousness", she was sent into my district for change of air. She suffered from obstinate constipation, headache, "sinking" feeling after meals, vague and indefinite general pains, and a general feeling of malaise. She had great mental depression — in fact was quite melancholic. She had never felt well since her last confinement three years previously. Teeth sound, tongue furred, no signs of organic disease in heart or lungs — slight tenderness over hepatic region, but no appreciable enlargement of liver. There was menorrhagia and intercostal pain (occasionally) on left side. The patient complained of occasional stiffness and throbbing pains in her finger joints — which appeared to be of gouty origin —; there was no visible enlargement of the joints when I saw them — there was no family history of gout.

The urine contained marked traces of Indican. Diagnosis — uterine disturbance — endometritis and sub-involution, associated with hepatic derangement and intest-

inal putrefaction. After preliminary treatment with Calomel and Saline aperients, the uterus was curetted, and pure acid carbolic applied to the endometrium. The after treatment consisted of tonics and aperients — two big drinks of hot water daily at 11 a.m. and 4 p.m. and gr. 1/6 Calomel (in tabloid form) after meals, whenever the "sinking" feeling was experienced. The indicanuria gradually lessened, and disappeared in three weeks time. I failed on any future ocassion to find any traces of Indicanuria .

The patient made a slow but steady recovery, and, at the end of her two months' holiday was visibly better — both in her bodily and her mental condition. She became quite cheerful — took long walks, developed a taste for gardening, and altogether was very different from what she was when I first saw her. She left for her home, promising to attend to the state of her bowels by means of occasional small doses of Calomel, saline aperients, and draughts of hot water before or between meals. When I last heard from her in Septr. 1900, she wrote that she was very well, and that she had only on one occasion since my attendance felt any twinges in her finger-joints. Unfortunately I have since lost sight of her.

Whether in this case the toxaemia was caused by the condition of the endometrium, or of the intestine, or by both, is difficult to say — probably the unhealthy condition of the endometrium combined with the menorrhagia caused "nerve poisoning", with consequent impairment

of hepatic function and excessive formation of intestinal toxins — probably there was a vicious cycle.

GOUT of the MENOPAUSE.

The more I see of the so-called "Gout of the Menopause" the more am I convinced that many of those cases are due to the unbalanced, probably irritative condition, of the nerve centres (evidenced by the "flushings" and other vaso-motor disturbances, mental irritability, etc.) reacting on the digestive functions and causing auto-intoxication. Vicious cycles often are produced owing to the unfortunate "tippling" in alcoholic liquors so often indulged in by women to tide them over this physiological Bay of Biscay, and when the systemic depuration of the catamenia has ceased to exist, gouty symptoms, commonly of irregular character, are very apt to ensue. There are almost invariably in those cases symptoms or signs of intestinal putrefaction, as evidenced by dyspeptic symptoms and the presence of Indicanuria, which I have found in fully 50% of those cases. Were my clinical methods of examining the urine in those cases, perhaps more delicate and were my time not so limited owing to the exigences of general practice, I would probably not only have found traces of Indicanuria in an even higher percentage of case, but also traces of other bodies — such as skatol, cresol, phenol, etc., in many of them.

It would savour of thrashing the proverbial

dead horse were I to attempt to prove that many of the cases of "Gout of the menopause" occurs in women in whom no definite family history of gout can be elicited, therefore, the gout in those cases must be distinctly toxaemic and due to auto-intoxication.

Dr. W. M. Ord at the Meeting of the British Medical Association at Belfast in 1884 pointed out —

1. That certain changes in nutrition take place in the joints through the influence of the nervous system.

2. That certain organs, especially the uterus and ovaries have the power through centripetal nervous influence, of producing considerable excitement in the spinal cord.

3. That in cases of debility and anaemia the reflex irritability of the spinal cord is greatly increased.

The concession of those points, combined with the theory of auto-intoxication would easily account for a great many, at least, of cases of Gout of the menopause.

INDICANURIA.

To revert to the subject of Indicanuria we know that it is present only to a small extent in normal urine. Indican is the indoxyl-sulphate of potassium, in which form it appears in the urine and is colourless. Indican is derived from Indol, a product formed in the intestine by the decomposition of the albumen under the influence of bacteria — indol when absorbed is oxidised,

forming indoxyl, which combines with the potassium sulphate to form indoxyl-sulphate of potassium or indican. Its presence in the urine is detected by the Jaffé — Senator test — to the urine add an equal quantity of fuming hydrochloric acid, and then add a concentrated solution of chloride of lime drop by drop, until the blue colour is fully developed. The blue colour is due to indigo which can be separated by shaking with chloroform, the indigo forming a blue layer at the bottom of the test-tube. Sometimes the addition of nitric acid alone developes a blue, violet, or blackish colour, due to the separation of indigo. It was this latter reaction, which in the case of F.S. already referred to, first opened my eyes, clinically to the presence of indican in the urine, and led me afterwards to recognise its importance as a sign of intestinal putrefaction — especially in the small intestine — notably in the duodenum. It may or may result from ordinary constipation, it is said, but when the constipation cause systemic disturbance I very frequently find traces of indicanuria. Indol is formed not only when albuminous substances are undergoing putrefaction in the intestine, but when they are rapidly decomposing in any part of the body, as in the putrid pus of septic peritonitis or in empyema — it is also present in the urine (as indican) in obstruction of the small intestine more often than of the large intestine and therefore the estimation of indican in the urine may have

considerable diagnostic value.

FREQUENCY of INDICANURIA in CASES of GOUT.

In gouty cases I have found indican present in appreciable extent in every other case, i.e., 50% (1) and always most appreciable prior to the attack and "tailing off" more or less, after the attack, with due care, in my experience it often entirely disappears if the patient attend to his nervous system by means of frequent holidays, and avoidance of business worries, and attend to his alimentary system by suitable diet and occasional doses of saline aperients — small doses of calomel, or beta-naphthol, and regular out door exercise, only to return if he kick over the traces and almost invariably in more appreciable quantities prior to an acute attack of the old enemy.

In order to correct or confirm my statistics I wrote Drs. Armstrong and Harburn of Buxton — who in partnership have a vast field for investigation — also asking if they had noted a visible increase of indican in the urine prior to acute seizures of gout.

Dr. Harburn (March 13: 1905). replied "I should say that we find indican in fully 90% of gouty cases. I think your experience of the greater amount of indican in the urine is the general rule, but I cannot give you quite definite information because in the vast majority of cases we see the patients after acute attacks."

(1) In 102 gouty patients I have found district traces of Indicanuria in 53 cases,

The 90% quite dwarfs my 50%, but in explanation I would say that, from personal observation, I know that Drs. Armstrong and Harburn either conduct, or personally supervise, an elaborate and systematic chemical examination of the urine of each of their patients, thereby determining the presence not only of Indican, but of many other toxins, whose presence in the urine though suspected cannot be verified by a general practitioner, inasmuch as the time necessary for the long complicated and delicate chemical processes in prohibitive.

In the case of J.A.P.M. page 73 it is probable that indican if sought for would have been found in the urine. The confirmed faecal retention would suggest to me (practising as I once did in the Huddersfield district — a district notorious for lead-poisoning) a possible element of lead-poisoning. In this case, however, the urine was not tested for lead.

PLUMBISM and GOUT.

Dr. Norman Porrit, now consulting Surgeon to the Huddersfield Infirmary in his Presidental address (delivered to the Huddersfield Medical society in Novr., 1891, and afterwards published in the Provincial Medical Journal in June, 1902) pointed out that there was pre-colickly stage of lead-poisoning (lead-poisoning from drinking the soft Huddersfield water). But though colic may be absent, though there be no wrist drop,

obstinate constipation, often so obstinate that the bowel seems paralysed is almost invariable, with the constipation there is usually associated some mental disturbances, usually depression. There may or may not be a blue line on the gums, and there may or may not be the anaemia — the saturnine cachexia, which Dr. Oliver in his Goulstorian lectures defined as pathognomionic of lead impregnation. There might only be a slight dirtiness of the complexion — very easily overlooked. The diagnosis of lead poisoning rests on the examination of the urine and drinking water.

Garrod's proportion of lead poisoning associated with gout was 25% — 33%.

Dr. Porritt in the address referred to says " "notwithstanding the resemblances between gout and plumbism my experience is that there is, comparatively speaking,not much gout in Huddersfield when the number of cases of gout is contrasted with the number of cases of plumbism the disproportion between them is remarkable. Unfortunately I have no figures that would place the question on an exact basis, but from my observation at the Infirmary and in general practice I should day that there have been twenty cases of plumbism to one of Gout . . . . . Dr. Oliver does not find that the workers in lead, who suffer from plumbism are often attacked by gout; and there can be no doubt that influences other than lead must be at work in developing gout, and that probably in the temperate and abstemious lead has no power whatever in inducing gout."

A study of Chap IX sect. 2 in Duckworth's "Treatise on Gout" shows that the opinions of many, if not most, of the authorities quoted fall in line with that of Dr. Porritt.

Quite lately (Feb., 1905) Dr. Porritt writes me— "The proportions given by Garrod seem to me very high indeed. It would be interesting to know how he arrived at them. He saw many cases of gout, and I suspect he has arrived at his figures by taking the number of his gouty cases who had plumbism. But this is most fallacious, and one can only arrive at a true result by getting a large number of cases of plumbism, and finding in what proportion of them gout occurs."

The Huddersfield district was so notorious for lead-poisoning in the most subtle form that the late Sir Andrew Clark (private communication to me) said that when a patient from the Huddersfield district consulted him for any malady whatever, he instinctively tested his urine for the presence of lead. Therefore, the quoted opinion of Dr. Norman Porritt, one of the most careful clinicians I know, — who has practised in the Huddersfield district for a quarter of a century is well worthy of notice.

It would appear that gout is not necessarily associated with plumbism and vice versa, unless the kidneys are organically defective prior to, or due to, the absorption of large quantities of lead and alcohol, and in many cases not even then (this is in accordance with

Critzman's views).

When gout does occur in plumbism I believe the gout is due to the deleterious action of lead on the nervous system and on general metabolism and to the invariable constipation associated with plumbism causing accumulation of intestinal toxins, which toxins are not excreted by the kidneys, which are more of less inadequate in those cases.

METCHNIKOFF'S THEORY of PHAGOCYTOSIS.

If Metchnikoff's theory of Phagocytosis be accepted, and it appears to me to be quite as feasible as the Alexine theory, although, perhaps, under varying circumstances both theories are correct, the leucocytes are the main tissue-guardians against the action of the various toxins to which the bodily economy is constantly exposed.

Whether in leucocytosis there is a total increase of leucocytes in the body — a hasty enrolment of raw recruits to reple the invaders, or whether the increase of the leucocytic army in the blood is due to the migration into the blood-vessels of cells from the intercellular spaces of the tissues — a calling out of the reserves — so to speak, is not yet known.

WOODS HUTCHINSON'S VIEWS.

Woods Hutchinson as already quoted defines Gout as being "a toxaemia of varying causation, usually of gastro-intestinal origin, accompanied by the formation

1. Lancet. Jan 31: 1903.

of an excess of urates, this excess of urates being due to due the breaking down of the leucocytes and fixed cells in the attempt to neutralise the poison -- in other words, being the measure of the resisting power of the body 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."

Using leucocytosis as an index of, and large factor in, the general resisting power of the body tissues Woods Hutchinson divides pateitns into three groups — the acytic, the hemicytic, and the hypercytic.

ACYTIC GROUP.

1. The Acytic in whom cellular resistance and leucocyte formation are markedly deficient. This group is apt to succumb readily to the invasion of any poison in food, air or otherwise, and are subject to tuberculosis, typhoid fever, and certain forms of chronic rheumatism.

HEMICYTIC GROUP.

2. The hemicytic or gouty group in which the leucocyte action is energetic but inadequate to prevent the toxins from producing an affect through a chronic and much modified one. The casualties on the side of the leucocytes and fixed cells appear in the urine as urates.

HYPERCYTIC GROUP.

3. The hypercytic in which the resisting power of the leucocytes is adquate to all emergencies — the

1. Ibid.

casualties being so slight that there is little or no increase in the amount of urates excreted.

Those three groups Woods Hutchinson admits are not constant in their boundaries; the hypercytic may, through some depression of the general vitality from various causes, if attacked by virulent toxins, readily fall into the hemicytic or even acytic class — the hemicyticmay,under certain circumstances, become acytic, but rarely hypercytic; while the poor acytic must usually be content to wallow in the mire, rarely becoming hemicytic and never hypercytic.

WOODS HUTCHINSON'S THEORY AMPLIFIED.

To amplify Woods Hutchinson's theory in military language — the entire body is the seat of war — the organising staff — the officers, are the various nerve-centres — the defensive fighting units are the leucocytes and fixed cells, which are controlled as to proper disposition against hostile attacks by the nervous afferent and efferent, representing the field-telegraphs, dispatch riders, etc. which continually communicate with head-quarters conveying messages backwards and forwards. Reinforcements constantly arrive from the spleen, blood glands and bone marrow — the toxins are the enemy of various units varying in ferocity — the battle-front extends all the legnth of the capillary system.

The kidneys, liver, intestine, skin, and lungs represent not only the sanitary department and the burial

parties who dispose of the dead but they also represent the parties who make prisoners of "undesirables" and promptly banish them from the country which is the seat of war. If the organising staff and the defensive units be at full strength and acting in perfect concert the enemy is destroyed or captured and quickly transported from the country, which is the seat of war.

If from any reason the organising staff (the nerve centres) are incompetent through illness, overwork, or from incapacity, hereditary or otherwise, for the duties entrusted to them, the rank and file, deprived of their accustomed leaders, get demoralised, the enemy effects an inroad and a "regrettable incident" occurs.

If, on the other hand, although the officers be competent the rank and file from insufficient or improper food or insufficiency of numbers lose their morale and fail to repel, destroy, or capture, the invaders, the enemy seizes the whole position, destroys the defensive force in large numbers — even the organising staff (the nerve centres) being among the wounded.

The enemy naturally capture the positions in the extended front where the defence is weakest, hence the joints and other parts of the body where the circulation is most feeble bear the brunt of the attack and the heaps of dead (represented by the uratic deposits) testify to the ferocity and success of the onslaught — isolated places where the defenders have "died to a man" are represented by the tophi. According to Woods Hutchin-

son in"hemicytics" or gouty people the cellular resisting power is fair, but not adequate to all emergencies, thus the constitution and vehemence of the attacking forces, the site of attack, the measure of resistance and the disposal, adequate or otherwise of the casualties on both sides, determine the acute or chronic aspect of gout, whether articular or abarticular, and its effect on the bodily economy, the presence or absence of uratic deposits and all the so-called protean aspects of gout in the glycosuria, albuminuria, oxaluria, indicanuria asthma, eczema, etc., so often associated with the malady.

In this way Duckworth's neurosal and Woods Hutchinson's leucocytosal theories can be amalgamated into a very plausible theory as to the nature and causation of gout.

If the controlling nerve centres can, so to speak, keep the digestive and assimilative organs up to the mark, the leucocytes and fixed cells can without many casualties capture or destroy the toxins, which are quickly eliminated by the various emunctory organs. If through want of proper nervous central or from excess or deficiency of food or any disturbing local lesion the digestive organs are incompetent, toxins are produced in excess, their poisonous properties are not neutralised and a general toxaemia results. The condition of the nerve centres reacts on the condition of the digestive and assimilative organs and vice versa, and ~~their~~ thus vicious cycles are produced.

The "primordial vice of nutrition" of M. Rendu and the "inherited tissue peculiarity" of Jonathan Hutchinson as applied to gout may thus be construed into "a deficiently antagonstic or neutralising power, hereditary or acquired, of the leucocytes and fixed cells of the body towards certain, usually gastro-intestinal, toxins."

WALKER HALL'S OBJECTION to the VIEWS of WOODS HUTCHINSON.

Characteristic of the inevitable discussion which always rages round every new theory regarding the aetiology of gout, is the disclaimer of Walker Hall[1], who denies that the leucocytosis invoked by Woods Hutchinson can account for the total output of endogenous purins and uric acid. (Purin, C_5N_4, is the name given by Emil Fischer to the nucleus which uric acid contains.)

Walker Hall holds that synthetic formation to a lesser extent and the breaking up of nucleo-proteids during cell processes to a greater extent, are more important factors of their production in gout.

AUTHOR'S VIEWS.

I would point out that Woods Hutchinson imputes the formation of the excess of urates not only to the breaking down of the leucocytes, but also of the fixed cells, leucocytes being used as an index of, and large factor in, the general resisting-power. He also quotes Magnus Levy as showing that uric acid is only one

(1) Brit. Med. Journ., Sept. 24: 1904.

of the various products of destructive tissue metabolism excreted at this time, as it is always accompanied by large amounts of other nitrogenous extractives in the urine. Woods Hutchinson also refers to the marked increase of phosphoric acid in the urine during a gouty attack. "What does this mean? Simply, that, as all nucleins are composed of a phosphoric acid element, nucleic acid, $C_{40}H_{59}N_{14}O_{22}P_2O_5$, united with a purin or adenin base, we have here the other moiety of the nuclei of the cells which have been destroyed in the toxic process."(1) He adds " We might as justly blame phosphoric acid for the attack as uric acid. Both are symptoms."

I think the views of Wood Hutchinson and Walker Hall can be partially, at least, reconciled by a consideration of the far-reaching effects of a war on the country on whose soil it is fought.

The amount of casualties cannot be altogether relegated to the fighting line. As the result of internecine war, all the economics industries of the land suffer: starvation, poverty, crime, and insurrection, are apt to ensue — there is the "moral and intellectual damage" to be considered as well as the actual casualties of the fighting lines, and all this perversion and wastage, in the case of gout, can be summed up as the production in excess of uric acid and other metabolites.

This is perhaps very broad pathology, but it probably sums up as much as we actually know concerning that most elusive problem, the aetiology of gout and its

(1) Lancet, Jan.31: 1903.

relation to uric acid.

EPITOME of WOODS HUTCHINSON'S VIEWS on GOUT.

The conclusions of Woods Hutchinson, to which I have so frequently referred, can be thus summarised —

1. That between the production of urea and uric acid there is no connection (they practically being as distinct from each other as the urine from the faeces), and that therefore marked limitation of animal or nitrogenous foods, as such, in gout is irrational.

2. That of the two sources of uric acid formation in the human body, exogenous and endogenous, the latter, due to the destructive metabolism of the nucleins in the body-tissues, is alone increased in gout and lithaemia.

3. Gout and lithaemia are mere symptom names for certain chronic toxaemic processes, miscellaneous in origin, which are characterised by the production of uric acid and urates.

4. The "gouty diathesis" is the expression of an inadequate resisting-power of the body to oppose the entrance of any poison, whatever its character or source.

5. That uric acid, equally with phosphoric acid, is an index as it were of the degree of damage done by such poisons; hence the use of lithia and other "solvents" is irrational, since these products are not the essence of the disease.

6, That diet in gout should be regulated solely with

a view to the diminution of intestinal fermentation and putrefaction.

7. That the limitation of animal foods is indicated, because they are the most appetising, and the most liable to be indulged in to excess, but starches and sugars are also often at fault.

8. Since uric acid is not toxic or only feebly so, it is not rational to prohibit foods rich in nucleins or similar bodies, except in so far as they tend to increase the attractiveness of the diet and thus lead to overfeeding.

9. The role of the liver in gout is a negative one, being inability to perform its chief normal function as a "poison filter," and to absorb or to transform into harmless excreting substances the excess of toxins brought to it by the portal vein.

10. The drugs formed by value in gout owe their efficacy chiefly to their power of checking intestinal putrefaction or of preventing the absorption or promoting the elimination of its products.

AUTHOR'S VIEWS.

Those views of Woods Hutchinson, which almost exactly are in accord with my clinical experience of gout, appear to me much more feasible than those of Garrod. Garrod ascribed all the disasters of gout to uric acid, a substance the birthplace of which has been as much disputed as that of Homer, a substance whose companions or associates in its daily walk are after years

and years of investigation and discussion still the subject of controversy — a substance which has been variously reputed as being very virulent, and quite harmless, or under varying, hitherto undefinable, circumstances, sometimes the one and sometimes the other!

If Woods Hutchinson's theory be accepted, the position of uric acid, from being a very Napoleon of organic wickedness, must tumble down to the mean level of being mere the débris of dead cell-nuclei, which have no more causative relation to Gout than have the heaps of dead littered over a battlefield to the clash of battle raging round them!

Why do the toxins in gout show such a marked preference for the joints and their surroundings? For the same reason, probably, as do the poisons of rheumatism, gonorrhoea, syphilis, tuberculosis, pyaemia, scarlet-fever, influenza, Malta fever, etc., because the joints and bones are the points of the poorest blood-supply, of slowest circulation, and of feeblest metabolism in the entire body — as well as being very liable to injuries. The agonising pains of gout may be associated to a toxic neuritis.

What is the particular toxin in gout, we do not know — judging from the analogy of acute rheumatism and rheumatoid arthritis, to which gout is supposed to bear some affinity, the day will come when the specific bacillus or micrococcus will be isolated. Woods Hutchinson, as already quoted believes that the formation and

introduction of the toxins 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.

Walker Hall[1] contends that "gout cannot be regarded as a state of simple malnutrition; it is rather a condition of insufficient cellular resistance against the absorption of intestinal poisons or auto-toxines, characterised by the production of imperfectly formed metabolites, which act upon some tissues as irritants, and in others excite degenerative changes that permit uratic infiltration."

Chalmers Watson[2] believes that there is an infective element in gout — "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."

AUTHOR'S CONCLUSIONS.

The conclusions I have, after a broad study of the whole subject from its many standpoints, come to, are the following:—

1. That gout is due to a toxin.

2. That as Gout can be induced in most people under suitable provocation, the toxin must be due to one of the bacilli normally found in the digestive canal, more

(1) Practitioner, July, 1903.
(2) Brit. Med.Journ. Jan. 21: 1905.

especially as acute gouty symptoms so often rapidly follow the ingestion of some special article of diet.

3. That as toxins are presumably present in the gastro-intestinal canals of people who never develope any gout, and as gout is such a definite disease with such definite symptoms, the gout-producing toxin must be due to a definite bacillus sufficiently potent to overcome and destroy the cellular defensive army of the body — the intensity of the gouty symptoms depending on the measure of the resistance offered.

When the Golden Age dawns in which by means of inoculation, — prophylactic or curative, the world at large is rendered immune to the pangs of gout in its protean aspects, then, perhaps, may be realised Haig's dream[1] —"a glorious development, both of mind and body, to which in the past we have been strangers. And when the change has been made and become general, future generations will look back on our present records of sorrow, suffering, and degradation, with amazement."

(1) Practitioner, July, 1903.

THE PRINCIPLES of TREATMENT of GOUT.

As gout in my experience is manifestly associated with intestinal putrefaction, treatment, dietetic and otherwise, should aim at the diminution of that condition — at the same time, of course, it is necessary that the various "systems" in the body be got into an as well-working condition as possible, always remembering that the condition of any of the systems is affected by that of the others. In particular it must be recognised how the condition of any of the other systems reacts on the nervous system, and vice versa.

Duckworth[1] says " an implanted neurosis is, as it were, the representation of a morbid physiognomy for the cerebro-spinal axis. A neurosis, then, is a peculiar disposition or tendency on the part of the nervous system or some definite tract of it towards morbid evolution or manifestations of nerve-functions."

This neurosis may be hereditary or acquired through undue mental labour, worry or habitual or prolonged excess. An old saying was —

Wine is the father of gout,
Feasting is the mother,
Venus is the midwife.

My experience is that all gouty people have unstable gastro-intestinal secretions — idiosyncrasy is a most marked feature in those subject to gout. Some years.

(1) Treatise on Gout, p. 21.

ago I compiled a detailed list of articles of diet which I had found both to agree and disagree with my gouty patients, and to summarise the list, it comprised practically every known article of diet, including milk and white fish! In no disease is it more important to remember the personal factor — as Moxon well put it, "it is quite as important to know what kind of a patient the disease has got, as to know what sort of a disease the patient has got."

The influence of the nervous system on gout is sometimes remarkable — fright or sudden shock, joyful or otherwise, having often been known both to cause and to cure a gouty attack. A Yorkshire manufacturer, a patient of mine, who was subject to gout, would invariably, when he felt out of sorts, from any cause, order all the blinds on that side of his house, which commanded a view of his mill to be pulled down. If unable to leave home, he gazed through his other windows on a pastoral scene, took some Calomel and Black Draught, and often escaped gouty attacks. The sight of the mill-chimney was, according to my patient, quite sufficient to bring on an acute attack.

Instances where an accident has induced an attack of gout (sometimes long expected by the doctor) could be multiplied ad infinitum, as well as cases induced by spasmodic and excessive outdoor exercise frequently followed by an excessive meal.

When I was surgeon on the Union-Castle Line, on one occasion a passenger presented himself at Southampton,

and asked me if he would be seasick. He had apparently taken some preventive measures, and, as the sea was quite calm and the boat large and steady, my prognosis was favourable. However, before we were many hours out at sea, this passenger got violently sea-sick, and on recovery told me he knew he would be ill, as his father was "just the same" under similar circumstances. On nearing Madeira, my patient said he was sure he would have an attack of gout, because his father had had one at Maderia. Sure enough acute podagra ensued, but, before reaching Cape Town, my patient was up and about, taking a much more rosy view of life than previously. He had been very morbidly introspective, and inclined to mope in corners, even when able to move about.

I met him again two trips afterwards on the homeward journey; he had turned out to be quite a jolly little man with a hitherto undiscovered vein of humour. He said he could now eat things which he dare not attempt before. All went well until, three days out of Las Palmas, a passenger threw himself overboard, and was drowned. This caused great consternation on board, and in less than two hours my neurotic patient was laid up with acute podagra!

In my own case I once aborted an exceedingly painful attack of gout in the thumb by going to Bradford (22 miles distance) on a very disagreeable night, and witnessing the ludicrous antics of Eric Thorne as Hilarius in "La Poupée" — certainly the therapeutical value

of laughter is a promising field for research!

My system, by which for the last seven years I have kept myself perfectly free from gouty attacks is —

1. Keeping up the general health by eating and drinking only what I find to agree with me — always regarding moderation.

2. Regular outdoor exercise — walking, riding, bicycling, golf, etc., and frequent short holidays.

3. A big drink (about one pint) of hot water or Salutaris water twice a day — 3 hours after, or 1 hour before, meals.

4. Testing the urine every week for indican.

5. If indican present in appreciable amount taking gr. i Calomel for three nights, followed in the morning by Sod. Sulphas; — by restricting the diet, and by going to the nearest theatre or other place of amusement.

6. If unable to get away to a theatre or for a holiday, I have found great benefit from the combined liver and spinal mustard bran pack, twice or three times a week. This is two poultices made of mustard bran — one being applied over the stomach and liver, and the other to the nape of the neck and down the spine to between the shoulders — keep on fifteen or twenty minutes, and then sponge skin underneath with warm water. This double pack stimulates the liver, and that portion of the nervous system presumably connected with the process of digestion — it has always acted like a charm in my case in relieving the feeling of depression associated

with occipital headache, which, in years gone by were the almost invariable prodromata of gouty seizures.

I have derived the greatest benefit in my cases of subacute and chronic gout from the judicious use of Calomel in one grain doses occasionally, and in one-sixth of a grain doses more frequently, with sulphate or phosphate of soda in the early morning, and a draught of hot water or Salutaris twice a day — as before mentioned — Calomel must, of course be given with discretion: anyone who would recklessly prescribe Calomel or any other mercurial without due regard to the condition of the kidneys, would be as little worthy of trust as a physician, as Lucrezia Borgia would be as a cook!

When for any reason Calomel cannot be given, I use creasote, betanaphthol, Guaiacum, charcoal, or some other intestinal antiseptics.

In acute cases of gout, like everyone else I use the alkaline and colchicum treatment. Exactly how Colichum acts no one definitely knows, but no one doubts its power, although some like Alexander Trallianus of old think it ought to be restricted to patients who have no time to be ill!

Some practical men, especially the type of practical men described by Beaconsfield as practising the errors of their predecessors, may despise the theory that a central neurosis associated with intestinal putrefaction is the essential cause exciting or predisposing, of Gout.

Like the people of old, they want a sign, and to them the uric acid theory of Garrod may appear a much more solid fact than the theory that some changes in the nerve centres, about which we know little, associated with the formation and absorption of gastro-intestinal toxins, about which we know less, are the cause of Gout.

My facts are that, after reading the results of Gautier's researches (years before I read Woods Hutchinson's theory) and treating my subacute and chronic cases of gout with intestinal antiseptics, I have had far better results than I had previously, and several of my medical confrères, after trying the system, can subscribe to my opinion.

After all, results are, for us, better than any theory, even if we express ourselves in the heterodox language of the late Dr. Milner Fothergill.(1)

"The student is taught too exclusively at present to look at disease from a dead-house point of view. To make a diagnosis which would be corroborated in the dead-house, that is the great matter! Yes, so it is at a medical school; but in practice for yourself, remember that a living, grateful patient, who has got well under your care, is worth far, far more to you than

(1) Aids to National Therapeutics, p. 121.

any amount of accurate diagnosis, which, so far as other persons and their opinions are concerned, is as voiceless to further your interests as the tombstones in the churchyard which mark your failures."