Notes on Uric Acid in its relation to Disease.

The recent investigations of Dr. A. Neiz when taken in conjunction with those of Sir A. Faraday and others appear to show that in all probability Gout, Rheumatic Gout, Rheumatism, certain cases of Epilepsy, a large and well marked class of headache (Migraine) numerous forms of mental derangement varying from mere temporary depression and irritability up to melancholia and suicidal mania are to be regarded as a group of diseases that possess a common origin (Uric Acid) to which a very definite line of treatment may be applied with, in many cases, the very best results.

When we think how common, might I not say how increasingly common, are the diseases enumerated in this important group. When we reflect how widespread is their influence, and
and how vast is the number of the persons they affect. When we consider how they invade the houses both of the rich and of the poor when we note that their scope is from the most petty ailments up to the very gravest malady is it not well that every member of the profession, who can, should do his utmost by personal observation or otherwise to make clear his support to these investigations in order that a mass of facts may be accumulated, the weight of which shall warrant the issue of certain broad rules endorsed by an overwhelming majority of practitioners that shall serve to alleviate if not altogether cure the ailments so many of our fellow-men fall heir to.

This then must furnish any excuse for penning the following notes which though by some means altogether original are given by way of confirmation or in further of the facts that have been stated before they
the world of medicine by others for
more capable and conversant with
the subject than I am ever likely to
be. I believe my attention was
first called to this matter on account
of a headache which it has been
my misfortune to suffer from for
several years. This headache from
most of the characteristics described
by Neis in connection with what he
terms "Seric Acid" headache. This in
my case occipital, recurs at intervals
ranging from days to weeks or even
months lasts for several hours but
rarely ever continues a whole day.
Then it passes completely away and
not come on again until after the
tap of a certain more or less indistinct
period of time. Food is eaten well
as a rule even whilst the headache
is proceeding. The tongue is clean or
there is little or no disturbance of
the digestive functions beyond some
slight discomfort in the region of the
right hypochondrium if we except
the
the vomiting that usually terminates the attack. When it is at full play, the bowels act quite regularly; the temperature remains normal— if anything it is perhaps subnormal. Generally there is more or less chilling of the body; the feet more especially in the extremities. The pulse, however, is not slow, nor does it exhibit high tension. its tracing being decidedly diastolic.

These scarcely ever failed to cure such a headache in about an hour's time by taking a dose of from 10 to 20 minims of dilute nitric hydrochloric acid.

Before referring to the urine, the following 3 points require the method.

1. The apparatus I have used is for acidity. A solution of phenol for red, the hypobromite test with nitric acid. Haycraft process.

2. He assumed that 1:33 is the normal relation existing between the excreta and urine.

(3)
(3) My family history is a decidedly guilty one.

An examination of the urine passed immediately before the invasion of the headache has invariably shown a minus excretion of uric acid to the latter place whilst an examination of that passed during the time of the headache has exhibited an excretion in marked excess corresponding as I believe with a temporary excess of uric acid in the blood. The dose of acid has soon checked this excessive excretion.

For some considerable time it has been my custom to drink nothing in the way of stimulant except a few glasses of a light Spanish Clarke, or I have frequently noticed that when I have been dining out handsome glasses of champagne or Port wine in place of my usual beverage the next day my joints have been the subject of more or less arthritic pain sufficient severe to suggest to my mind what must be the history of those persons who frequently take
suffer from this distressing affection. These uncomfortable sensations have however been removed by moderate doses of Salicylic Acid and the urine passed during its administration has shown a plus excretion of the acid.

On two occasions during the last ten years I have been seriously troubled by an acute attack of dysentery in its nature apparently depending for its production upon a congested state of the liver for each occasion a large amount of blood has been passed by the bowel the temperature has been high. For some time prior to these illnesses my diet had been more than usually nitrogenous, the skin was itching about as a pig in cold water had been acting poorly but little exercise had been taken curiously enough each time the attack as far as I could judge was precipitated by one or two moderate doses of dilute nitric hydrochloric acid taken to relieve headache.
And it has occurred to me that in all probability these doses by suddenly raising the acidity of the blood and as Haig explains the uric acid in excess out of it into the liver already somewhat congested on account of the previous diet or weak action of the skin that this resulted in a sudden effort on the part of the bowel to relieve the undue pressure in its vessels causing thereby these unpleasant symptoms which I was called upon to bear.

It is to me a matter for regret that owing to my protracted condition the urine was not examined in either case as it is very likely it might have yielded interesting results.

The probable causation, however, of these attacks had led me to state a theory in connection with the probable production of Albuminuria in Adolescents.

This form of Albuminuria as is well known occurs in young persons especially males somewhat on a
end poorly nourished who suffer from headache, neuralgia, bodily mental languor, hysterical phenomena, disturbances of the functions of the stomach, liver, intestines. The albumen is regularly absent during the night but present during certain fixed hours during the day although the time of day is not the same in every patient.

Fisner (you need) describes ten such cases in which albumen was only present at a time 3 or 4 hours after the first meal in the morning as a rule as casts were found in the urine.

The albumen may be increased by the erect position, by mental or bodily exertion, by the ingestion of food rich may be made to disappear by keeping the patient in the recumbent position during the entire 24 hours.

If we examine the writings of Professor Semmola of Naples we find that he has stated after very careful
Careful experiment that whenever the dializable albumen in the blood exceeds 4 per 1000 then it will issue through the vessels of the kidney is found in the urine. He also says it is not only to be found in the renal secretion alone but is also found in the bile and the saliva.

Here then we have to deal with an albuminuria occurring in young individuals in whom there is no reason whatever to suspect any organic disease yet fact which are as far as we can see very fairly healthy.

Dismissing therefore the idea that we have to do with any organic disease as the cause of this effect we are naturally led to inquire what any mere temporary high pressure in the vessels would be sufficient to account for it.

When we look at this question we find that Dr. Samuel Bentzon (Dennies Dick J Red f. 24) states that experiments
seem to show that increased tension in the renal arteries does not produce Albuminuria except that the only change in circulation which will cause it is increased pressure in the renal veins. . . . . . . . Serious consequences of the previous, also occurs whenever the out ward flow of venous blood is obstructed either by a ligature on the renal veins, by the pressure of a tumour or of the pregnant uterus upon them or the Iena cava, by disease of the liver obstructing the Iena cava or by disease of the heart or lungs, such as tricuspid or mitral regurgitation or chronic Bronchitis or emphysema. . . . . . . .

the Albuminuria observed after varnishing the skin is probably due to the retention of some substance which acts as a poison.

I think when we come to inspect this statement of Dr. Drayton's in its entirety we must recognize that its plain meaning is that these temporary
high pressure in the vessels apart from organic disease will not cause albuminuria on the other hand it appears time to furnish very briefly the way of the probable mode of leading of paroxysmal albuminuria in the last sentence it is stated that the albuminuria which has been observed after varnishings the skin is in all probability due to the retention in the blood of some substance which acts as a poison.

If we suppose the poison here referred to the uric acid I think we shall at once perceive that the conditions under which the albuminuria we are considering occurs are just those in which we would expect to find an excessive excretion of this body the taking place in the urine, and indeed in all the cases that have knowledge of this has been chosen to be the case when the attack occurred.

The patients who are the subject of paroxysmal albuminuria very
generally complained of great chills, at the time of the attack, there is usually marked want of action on the part of the skin (which of course would be the case were its surface to be burned out), they suffer as we have seen from headache bodily or mental languor, disturbances of the functions of the stomach, liver, etc. The albumen is increased by mental or bodily exertion or by the injection of food of either has found it present at a time 3 or 4 hours after breakfast. Further, it may be made to disappear by keeping the patient in the recumbent position during the entire 24 hours. Nonetheless, that is after keeping them warm in bed was assisting in the skin action.

It seems to me, therefore, we have good reason to suppose that in all childhood boric acid acts in this way, in a manner exactly similar to that which it does when it produces headache, causing great chilliness and defective action of the skin spread over the entire.
entire surface of the body that this is directly followed by a large increase in the amount of dilatable albumen in the blood. The quantity of this substance having become so increased as to exceed the limit fixed by Semmel’s simplified out of the blood through the vessels of the kidney appears in the urine.

If we suppose still further that one of the results of the passage of albumen through the kidney is an irritation of its substance we can readily understand why it is when this irritation is repeated sufficiently often we get a Chronic interstitial nephritis established in persons whose family history on whose antecedents distinctly joint to Souf + Uric Acid.

To pass to another class of cases which seem the directly connected with Uric acid we may call them perhaps the hypochondriacal class.
met by numerous cases of irritability and depression which occur from time to time amongst people whose natural disposition is a bright and happy one. The individuals so affected are the very finest talents who know their best can confirm their statement, that they are not themselves being possessed for the time being of qualities quite foreign to their natural temperaments, which they are all the while quite unable to account for. Well do I know myself what these unhappy moments are, how great is the effort required not to give way on the very smallest provocation, an outburst of temper whose difficult it is to prevent becoming a nuisance a source of distress to those most closely united to me. Everything appears to conspire to all the brightest blaze found well ruffled up out of my life, if ever in cases exhibiting such
Symptoms as these we later test the urine of the patient, carefully separating that portion passed during the attack from that passed immediately before it, we shall, I think, soon discover that in many cases the irritation or the defecation of the person in question correspond to a period when urea acid is being excreted in excess in the urine or, in other words, when it is in all likelihood in excess in the blood.

It is somewhat interesting to note here what Dr. Böing says regarding the probable role of acid causation of suicide. He refers to those taking place in France in 1887 and says in a recent number of the Progrès Médicaux (1888, p. 165) it is stated that suicides are much more frequent in July than in any other month, the number for July being 790, the average for the other months 530 to 600. Thence on this he proceeds to remark, it occurred to him that suffering any
large amount of suicide is really due to the mental depression caused by ureic acid it would not be difficult to explain the preponderance of cases in July - for July is probably in France as in England the hottest month of the year. There would therefore be more activity of skin function, more elimination of acids in perspiration than in any other month. This would mean a low acidity of the urine, great increase of the normal alkalinity of the blood, urine, fluids, and which favour a large excretion of ureic acid via temporary excess in the blood.

Gout & Rheumatism - Few physicians are now sufficiently inclined to regard ureic acid as the cause of gout - especially because Sir R. Jones has shown (Jones & the late Jones 34 241/6 114 1732) that it is in excess in the blood during attacks, minus, or absent during the intervals, also that at the time.
time of an attack though uric acid is abundant in the blood, the daily excretion in the urine is often below the normal - the failure of this observer however to detect uric acid in the blood in rheumatism also the marked difference that exist in the manifestation of this disease from that of gout have rendered its etiology uncertain. Nevertheless the profuse acid perspirations which occur especially in its acute forms & the diet & drug treatment found to be efficacious in its cure appear to me to make it probable if not altogether establish the fact of its being caused by exactly the same poison which causes gout.

Epilepsy & Insanity - Beyond the effect of diet on certain epileptic patients the fact that Sir A. Sander (foot & then fort p. 459-61) has found uric acid to be in excess in the blood during attacks of epilepsy & also it shown if to be in excess in the urine in some
Some cases during these attacks have had but little opportunity for investigating the uric acid connection of either of these two diseases.

It is not at all difficult to imagine that just as an albuminuria which to begin with is purely functional temporary in its character may lead to renal disease which is chronic or permanent so diseased conditions of the brain or other organs may be produced by an irritation quite fleeting or transient provided it occur often enough in the cerebral or other tissues.

At this point I may appropriately refer to an epileptic attack that my oldest boy had on April 13th (1847) which from every reason to believe was primarily caused by uric acid in excess in the blood. The child is 1 7/2 years old. He had whilst sleeping 4 convulsions the last of these happening when he was exactly 2 years of age. Since that time he has been very well till last winter
When gastro-intestinal attacks accompanied with a decided rise of temperature or more or less hepatic disturbance began to occur they continued at intervals of about 3 weeks or a month up to the present time. On the morning of the day mentioned the child complained as usual of discomfort in the epigastrium, the bowels were rather concluded. She had a temperature of about 103 - quite unexpectedly about midday she became convulsed and remained unconscious for about 1½ of an hour. This attack was followed by nothing more nor less than the result of a uric acid storm. In support of this view I give the following, rather imperfect account of the examination of the urine. I was unable to collect the urine passed after the convolution but that collected before indicates its probable character of high in the amount of uric acid if contained in proportion to the area exercised. I gave the following result.
Total area in 150 c.c. 46 grains

Uric Acid 1.7

Acidity 13.1

The relation of the uric acid is 1.65 - this therefore is a urine showing very high acidity for one would expect it to be very low in uric acid - Kaup's normal being 1-33 - this relation of acidity to uric is normally 1-6 - here it is only 1-3 a fraction.

Thus before a convulsion of this kind the uric acid is found low as at A., during the convulsion high as at B. after it sinks to normal as C.

Arterial tension. With regard to this matter I shall place upon which Waig lays great stress as being a probable index excess of uric acid in the blood. The rapid pulsations in my own radial artery + the diastolic tracing it yields at the same time that I am suffering from headaches.
There is also exertion taking place in my urine both to show that uric acid may be very frequent in excess quite apart from either of the conditions stated being placed such weight upon so that therefore though frequently present in such cases they cannot altogether be relied upon as a sure index to the real state of the case.

Having thus glanced very shortly at one of the other diseases associated with it in the group we are considering having come to the conclusion that they most likely all depend for their products upon a temporary excess, at least to begin with, of uric acid in the blood from time to time. Now first turn to that very shortly at the treatment found the useful in combating this excess by keeping others there to enable one or two cases as they own own experience of its use.

Dr. R. Querbach (Virchow Archiv 98, p. 572) has shown that vegetable & animal feeders differ considerably in their powers of preserving the alkaloid.
of the blood against acids formed in
their bodies, or introduced from withou
that even where, as in animal fele
man this power is greatest it may
be gradually diminished finally even
by continued excess of acid. If ther
we suppose with Kriez, that the Society
those who suffer from the diseases
associated with it, somewhat resemble
vegetable feeders in laboring less than
the normal amount of power of forming
ammonia, traces of acids prevent their
taking alkali from the blood then
there will eventually come a time
when on a diet highly acid in its
character the alkalinity of their blood
stone fluids will be so far overcome
that urates will be far less easily
soluble in them than in the normal blood.

Kriez moreover has found that
alkalies as soda or potash within certain
limits always increase the excretion
of uric acid whilst acids as citri citric
acetic acid always diminish it, and
driving it out of the blood into the liver.
Eleven points -

The treatment therefore may be said to solve itself into an enquiry into the conditions underlying a rise or diminution in the acidity of the blood to take place since upon this circumstance depend the retention or the excretion of uric acid.

We may for convenience group these conditions under 4 heads and look at each in succession. The four heads are:

Foods & Drinks - These may increase the acidity of the blood through fluids by:
(a) Stimulants: Nutritious Metabolism.
(b) Of the saliva they contain such as phosphates, sulphates, &c., which raise acidity.
(c) By their origination acid fermentative, alkaline.

Foods. Butcher's meat, cheese &c. may be taken as examples of foods which stimulate nutritive metabolism, increase acidity by the saliva they contain and
and sugar may be looked upon as a food that is apt to lead to fermentation.
Vegetables, fruit, and certain substances tend to increase on the other hand the blood's alkalinity.
Drinks. Beers and wines are for the most part strongly acid - for instance:

2 pints bottle of pale ale $\approx 14$ pints
2 pints $\approx 18$ pints
2 pints $\approx 25$ pints

And thus directly introduce acids into the system - they also may originate fermentation processes. Alkaline beverages such as soda water help act of course in the other direction. Tea acts injuriously by frequently causing dyspepsia.

Sir A. Garrod (Kempeian Lect. Brit. Med. Journ. Vol. 1783 p. 653) states that drinkers of light wines suffer least as these contain a small amount of alcohol - as unfermented matter can a considerable quantity of acid beget salts. Fresh fruits diminish acidity.
through the conversion of their alkaline salts into carbonates.

Tig's pertinently asks, why should the vegetable salts of the light wines be similarly converted?

Garrod further says the heavier wines, as those of Spain, others contain more alcohol, much unfermented malt, and almost devoid of vegetable salts, have great yeast-producing power. There again Tig remarks, from my point of view, wines, also Torter, may be all regarded as solutions containing a very small amount of albumenoid, a certain amount of alkali, or alkaline salts, a certain amount of acid free or combined. It is obvious that if the alkalies, or the vegetable salts, which can be converted into alkaline carbonates, predominate, the Genuine will act as doses of alkali, while if the acid, acid salts, incapable of conversion, predominate they will act as dosages. The expensive wines are found to be less harmful than cheap ones.
ones for one effect of keeping wine
is a loss of acidity by actinification
(see Dr. J. Blythes foods, composition &
analysis p. 439).

Alcohol itself apart from acid
probably raises acidity by stimulating
nitrogenous metabolism bodily activity
Drugs. Acids raise the acidity of
the blood lead brotenion of uric acid.
Alkalies, on the other hand, increase as
a rule the alkalinity of the blood from
the excretion of uric acid.

Salts of Potassium appear to
be especially as an alkaline test been
I have any special action upon the salts
of uric acid.

Bromides do not apparently affect
acidity one way or the other.

Uronic acid of ammonia raises
acidity greatly, hence leads to retention
of uric acid. Saccharates, phosphate, & Chlorides
as a rule do the same.

Opium raises acidity causes
retention of uric acid. I care, lead to
causes well being mental brightness
followed after a time by feelings of toxic due in all probability to direct action on the nerve centres.

Phosphate of Soda an a well known solvent of uric acid increases the excretion of uric acid in spite of the fact that it increases the acidity of the urine. This shows that only those substances that increase acidity work themselves aiding in the solution of uric acid cause its retention.

Pilocarpin, though of decided value in acute joint leads to intestinal irritation. This renders the experience of being uncertain but the hazard is small that it may do good through this very irritation which would diminish about the urinary acidity and promote excretion of uric acid.

Potassium, the nature of this drug has been shown by Dr. A. Farreol the extreme soluble yet the substance and retention of uric acid. This explains the reason of this in Brit. Med. Chirurgical Transactions
Iron would cause retention probably owing to the nature of these metals being insoluble.

Salicylates. The action of Salicylic acid and its salts upon the excretion of uric acid is very peculiar. Firstly stated this action is first to dissociate the excretion of uric acid from its general relation to acidity; that an increase of acidity while there is plenty of salicylic acid in the blood is not accompanied by any diminution of uric acid excretion. Second, it renders a large excess of uric acid when it occurs under a salicylate not accompanied by headache.

Action of the Skin. Still, Z. Arndt (Guttmann, p. 253) has pointed out that suppression of perspiration is followed by an increase in the urinary acidity. Hence exercise, warmth, or anything else which promotes skin action increases the alkalinity of the blood measured of uric acid.

Increased metabolism the result of disease, accident or old age acts intensely.
Imbue. The treatment by saying it is a good plan to weigh the patient before a change of diet is made that it must in each case be proportioned to the severity of the symptoms for it will certainly be of worth while for a patient who only suffers from occasional slight attacks of excessive uric acid excrescence accompanied by headache or other troubles, half white diet, an occasional dose of uric acid will relieve this symptom.

The following is a detailed sketch of a milk, fruit vegetable diet which he has found useful in curing this uric acid headache (uric acid headache) von which he has slept perfectly well for months.

**Breakfast:** Bread, butter, toast, butter, tea, milk, occasionally fruit.
- Tea, milk, a pint, half a slice of butter, one ounce.
- Lunch: Potatoes, butter, bread, butter, jam, fruit, milk, half a slice of butter, two ounces.

**Afternoon tea:** Tea with milk, bread, and milk.

**Dinner:** Soup without any stock (lentil), beans with lots of milk, a good bit of butter.
make a soup which few would believe contained no stock. The same may be done with peas, potatoes, lentils, or tomatoes. Fried or otherwise prepared at least one other vegetable with butter or milk from the next course—then puddings, bread or stewed fruit—followed by bread and butter dessert, or fruit salad. But at least ten per cent of several kinds of fresh or dried fruit eaten in considerable quantity.

Soda to the extent of at least 10 ounces is taken with dinners mixed with the fruit or vegetables or alone. Any other liquid the time to be eaten is the either plain water or some simple aerated water such as Salubrine.

On such a diet not only is the formation of urea or uric acid small but the uric acid in all passed out of the body at once along with the urea that corresponds to it. For there is no high acidity to cause its retention in the liver, spleen, joints or other tissues.

Having thus briefly reviewed the treatment I now pass on to make a few remarks.
remarks as to my own experience of its use.

The experiments I have made upon the urine and the results I have obtained whilst treating myself and other patients who suffer from uric acid diathesis so absolutely confirm Hahn's general statement that acids raise the acidity of the blood thereby cause retention of uric acid while alkalies diminish the acidity of the blood increase its alkaline reserve and favour the excretion of uric acid.

Salts of Potassium. Although the examination I have made of the urine of patients who have been taking this drug in no way tend to support Hahn's sal

Salts of Potassium. Although the examination I have made of the urine of patients who have been taking this drug in no way tend to support Hahn's
got I am unable to agree with the general conclusion that it acts merely as an alterant because I have too frequently had to use the evacuation marked cessation in the arthritic pains of forty patients that has directly followed its administration when other alkalies have apparently failed to produce any relief.

Iron I think unquestionably
harmful in this class of disease can
examination of the urine clearly indicate
that the drug causes retention of
urine.

Salicylates have proved best
exactly as being has shown receiving
an excessive excretion of uric acid
during their administration is in my
own case unaccompanied by headache.

In the matter quoted with my
diabetic pulse require more attention
how than they allow himself, but I
can bear witnesses to the great diminution
that has taken place in my headache.

The great freedom I have had from
mental depression ever since instead
my daily consumption of butcher meat
with drinking light claret in place of
beer or the heavier wines - the same
observations hold true in the cases of
the patients have had who gave the
fair trial - beer believe would be
much less harmful if sweetened with less
sugar or more rye. I have also been
surprised to find how much less liable
the livers of young children whose family history is a uric acid one are especially 
during the cold months of the year when 
sweet is only given to them three times 
a week instead of every day.

I can further testify to the great 
value of a non-nitrogenous diet in cases 
of gout where the cause of the crystals 
seems to have a uric acid origin.

In conclusion I would cite 
the writings of Dr. A. Brög that I have 
read regarding gout in connection with 
this disease.

1. Some Clinical Features of the Uric Acid Kidney 
   (St. Bartholomew's Hospital Reports, 1873)
2. Excretion of Uric Acid in a Case of Gout 
   (St. Bartholomew's Hospital Reports, 1874)
3. The relation of a certain form of kidney to the 
excretion of uric acid. 
   (London Medical Clinical Transactions, 1874)
4. Influence of Salicylic acid and salts on the 
excretion of uric acid. 
   (London Medical Clinical Transactions, 1874)
5. Effect in health of use of some drugs which cause 
   retention of uric acid. 
   (London Medical Clinical Transactions, 1874)
6. Mental depression the excretion of
ume Acid
(The Practitioner Jul 41. No. 5)

7. Variations in the excretion of uric
acid produced by administration of
salicylic acid (Journal of Physiology Jul 8. No. 374)

8. Beitrag zu der Beziehung zwischen
wenigen Formen von Epilepsie und
der Ausscheidung von Harnsäure
(Neurologisches Centralblatt 1888. No. 5)

9. The Formation and excretion of uric Acid
(John Bale & Sons, London. 1888)

10. On uric Acid + Arterial tension
(Arch. Int. J. 6. 9. 1889)

J. Craig Brodie

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