and offend valuable clients by running counter to their political views. I am proud to say that there are not a few who, regardless of self-interest and the absorbing claims of practice, do take their full share in political life, but the great bulk of the rank and file must content themselves with quiet work behind the scenes, talking, and defining and instructing, and eventually convincing; and then the M.P. will see that he had better join them, and he will bring his pressure to bear on his Government, and these in their turn will see that the time is ripe for action, that they will be backed up by public opinion outside, as well as by their supporters inside, and so the deed will be done.

Of course, scattered as we are, we could not do anything really practical without rallying points and centres of organisation and co-ordination, which knit our forces together, and enable us to march in compact mass to fight our social battles; and this we find ready made in our Association, which, by its Branches and Councils and Committees, and influential annual meetings, gives us just the binding force we need, and which has used its influence and power with great skill and discretion in shaping and helping legislation, instructing members of Parliament, and showing Governments that the time has come for carrying out useful measures of social reform, and that it would not be wise or even safe to resist any longer the popular demand; and finally, I think we should be a little more aggressive. By this I mean that we should not let the propagation of heresies and fallacies go on without effective public protest when active organisations send plausible emissaries about the country to denounce vaccination and vivisection, some well-instructed person should be there to explode their fallacies and refute their arguments, and we see with satisfaction how on some of these occasions a brave and clever doctor has turned the meeting round in his favour, so that those who came to curse remained to pray. Mr. Chaplin had some sensible observations of this point in his speech the other day. He said, "The Antivaccination League was a strong body, and there was nothing like it on the other side. If the people in England were in earnest in favour of vaccination, why did they not start a body to explode the fallacies of that small body of opponents who disseminated all manner of stuff in towns and villages, without there being anything to counteract it, so that it had a very bad effect on the poorer and less informed of the inhabitants."

In this connection you will probably remember that on the occasion at Woodside, when a distinguished pathologist and an able and respected journalist came to preach antivaccination at Woodside, they were met on the platform by Dr. Beveridge, who did not let them have it all their own way, and sent them home probably sadder if not wiser men.

Now, gentlemen, I must pull up my wanderings over the wide field of speculation and inquiry which stretches out before us. Many important questions concerning your interest, medical reform and others, are in the air, and will some day be sufficiently condensed for practical discussion. When they come before us we shall consider them on their merits, without precipitate zeal on the one hand, or overcaution on the other. In the end truth, as usual, will prevail, and good will have been done to ourselves, to the profession, and to the general public at large.

OBSERVATIONS ON GENERAL METABOLISM AND THE BLOOD IN GOUT.

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FROM his classical observations on acute gout, Sir A. Garrod, more than 50 years ago, arrived at the following conclusions: During the attack (1) the alkalinity of the blood is lowered; (2) the excretion of uric acid falls, this being associated with uric acid retention in the tissues, depending on a diminution of the excretory capacity of the kidneys; (3) the amount of uric acid in the blood is higher than in the interval. These three conclusions formed the basis of his theory of the causation of the phenomena of an attack of acute gout. Since that time very few detailed observations have been made on the subject, and these conclusions have been generally accepted almost up to the present day. Thus we find Sir W. Roberts¹

in 1897 writes: "The analyses of Sir A. Garrod indicate that in the early days of an attack the daily excretion of uric acid falls rather below the normal average." At the present time it is advisable that these conclusions should be tested in the light of observations made with more recent and accurate methods.

In 1898 the views as to the diminution of the alkalinity of the blood and on the increased amount of uric acid present in the blood during the acute attack were seriously called in question by Magnus Levy. This observer made an extended series of observations in 17 cases of gout, using the most modern and reliable methods, and in no case did he find evidence of a diminution in the alkalinity of the blood or of an increase in the amount of uric acid as compared with the interval between the attacks. Levy's observations on these points appear to be conclusive. Comparatively few observations seem to have been made on the second point—namely, the excretion of uric acid during the attack, and some of these recorded are rather limited in their scope. Pfeiffer,² Levy,³ and Badt⁴ have recorded a distinct increase in the uric acid excretions during the attack. On the other hand, Minkowski,⁵ in his most recent writing on the subject, adheres to the view that the excretion is diminished.

In the course of the past summer I had an opportunity of making an extended series of observations on a case of acute gout, and I directed my attention to this point among others. Before defining the objects of my investigations it is advisable to refer briefly to some of the unsolved questions and to certain views at present entertained regarding uric acid.

UNSOLVED QUESTIONS REGARDING URIC ACID.

Among the leading questions of importance from our present point of view the following may be cited: (1) What rôle does uric acid play in the development of an acute attack? (2) Is the deposit of urate of soda in the affected joint the cause or the result of the attack? (3) What is the relationship between the increased amount of uric acid in the blood and the local deposit? (4) In what form does the uric acid circulate in the blood in gout?

A final answer cannot yet be given to any of these questions, and it will probably not be forthcoming until we have a fuller knowledge of general and local metabolism in the tissues affected. With regard to the last-mentioned point, Sir Wm. Roberts concluded that uric acid is present in the blood in the form of a quadriurate of sodium, and the view has been generally accepted in this country, while numerous observations have been made on the solubility of this substance under varying conditions, and attempts made to draw deductions therefrom, applicable to the etiology and treatment of the disease. As, however, we know so little of the behaviour of the proteids and also of the acid and alkaline salts of the blood in their relation to uric acid, we must still regard that view as a hypothesis, and not a proven fact.

URIC ACID IN THE BLOOD AND TISSUES IN HEALTH.

Any views on the pathological relationships of uric acid should only be formulated after careful consideration of the physiology of that substance. Now as we are not yet in a position to give the complete history of its manner of formation or of its relation to other products of metabolism in health, it is obvious that care must be observed in drawing conclusions from pathological conditions, as these conclusions may have been drawn from inquiries which were really too narrow in their scope to be of any service. Physiologists are almost unanimous in regarding uric acid as a normal constituent of the blood, organs, and tissues of the body, the amount present being, however, exceedingly small. The relative amount present in the different organs is of importance. A series of observations made by the writer and recorded in the *BRITISH MEDICAL JOURNAL* of January 28th gave the following results: (1) The absolute amount in the liver was greater than in the kidneys and spleen; (2) the kidneys contained less than the spleen, both as regards absolute amount and percentage; (3) the spleen contained a higher percentage than the other two organs, this probably depending on its richness in nucleic-acid holding substance. Further reference will be made to this point later.

URIC ACID IN THE BLOOD AND TISSUES IN DISEASE.

A further point appealing for investigation is the examina-

tion of various pathological tissues and fluids. It is well known that an excess of uric acid exists in the blood in certain diseases which have no known relationship to gout, but it appeared to me advisable to make some detailed observations on the subject. The following are illustrative examples of results obtained :

A.—Fluids.

Disease.	Sex.	Age.	Fluid. a	H ₂ U.
1. Chronic Bright's disease ...	F.	60	Ozs. 10	Gram. 0.0068
2. Malignant disease ...	M.	55	30 b	0.0155
3. Aneurysm (aortic) ...	M.	40	19	0.0087
4. Ulcerative endocarditis ...	M.	30	26	0.0075
5. Lobar pneumonia ...	M.	22	10	Qualitative reaction.
6. " " ...	M.	40	16 17 c	0.0075 0.0095

Notes.—a This fluid was obtained at the post-mortem examination from the pleural cavity after removal of the thoracic viscera, and was usually diluted blood. b This was made up of 26 ozs. serous fluid and 4 ozs. diluted blood. c Two examinations were made from this case. The second one consisted of the examination of a thinner and more diluted fluid (17 ozs.) which oozed from the organs, and was examined eighteen hours after the previous fluid. The figures would indicate that there does not seem to be any loss of uric acid in the fluids after death, but rather the reverse.

B.—Tissues.

	Liver.	Spleen.	Kidney.	Lung.
Aneurysm ...	0.1064	—	—	—
Pneumonia ...	—	—	—	0.0130
" ...	0.1447	—	—	—
Granular contracted kidneys ...	0.0386	—	Qual. reaction	—
Leucocythæmia (weight of spleen 7½ lbs.)	—	0.0195*	—	—

* This observation is of interest in view of the fact that many investigators have failed to find uric acid in a leucocythæmic spleen. Scherer is, in fact, the only observer who has previously found it.

What conclusions are deducible from these figures? Looking especially at the former set, those dealing with the blood, we must bear in mind at least two points. In the first place the amount of blood examined was only a very small part of the total quantity in the body; and secondly, the figures indicate the uric acid present only at the particular time of examination. It seems clear, therefore, that there is no close relationship between excess of uric acid in the blood and gout. The degree of causal relationship is in general over estimated, and writers have failed to sufficiently observe that in gout the error in proteid metabolism which leads to an excess of uric acid in the blood may also induce the presence of other bodies more or less toxic which may be responsible for many of the symptoms of chronic or irregular gout. We have another point of evidence in favour of this, namely, the conditions in leucocythæmia. Here we find a very marked excess of uric acid in the blood, existing for a lengthened interval, without inducing any of the clinical manifestations of acute or chronic gout. This indicates that the nitrogen metabolism in the two diseases is markedly different.

LEUCOCYTOSIS AND URIC ACID EXCRETION.

Since Horbaczewski showed that uric acid could be formed by allowing blood to digest with splenic tissue under conditions admitting of free oxidation, and also by digesting nucleins and nucleic acid under the same conditions, a great deal of attention has been paid to these tissues which are rich in nucleins, and especially the leucocytes. Of late there has been a growing tendency to the opinion that there is a constant and definite relationship between the number of leucocytes in the blood and the excretion of uric acid and xanthin bases in the urine. Thus we find Ewart, in his recent work on gout, says: "An increased uric acid excretion goes

hand in hand with an increase in the number of leucocytes, whether physiological, as in infancy and childhood, and after ingestion of nucleins or pathological, as in leucocythæmia, pneumonia, etc." Such a view doubtless finds some support from the association of the leucocytosis and increase in uric acid excretion during digestion, and also from certain pathological states, but from many other stand-points lends itself to adverse criticism. I shall only refer to one of the points based on observations made by Milroy and Malcolm, and also Hale White and Hopkins. These observers investigated the excretion of urea (nitrogen) and P₂O₅ (the two end products of nuclear destruction) in leucocythæmia. In this disease there is a marked decrease in the phosphorus excretion, while the uric acid may or may not be increased in amount. When we bear in mind that the leucocytes in this disease may amount to 300,000 per c.cm., it is evident that there is no definite and constant relation between the excretion of uric acid in the urine and the number of leucocytes in the blood. Figures given by Milroy seem to be conclusive on this point:

	Leucocytes.	P ₂ O ₅ Excretion.	H ₂ U.
R. B. (a healthy man) ...	8,000	4.038	0.252
Leucocythæmia ...	330,000	0.915	0.202

These figures also corroborate the view that the general metabolism in the two conditions is essentially different.

URIC ACID AND NUCLEINS.

Since the publication of Horbaczewski's observations on the formation of uric acid from nuclein-holding tissues, numerous investigations have been made on the effect of the ingestion of nucleins, nucleic acid, and articles of diet rich in nucleins on the excretion of uric acid. So far these investigations have produced discordant results, some observers finding a decided increase, and others a decrease. The subject is a complicated one, and requires further elucidation. The influence of feeding with thymus gland was investigated in this case, with the results indicated.

PERSONAL OBSERVATIONS.

My recent investigations bear on the foregoing, the special points to which I directed my attention being: (1) The condition of general metabolism during the attack and in the interval, as evidenced by the total daily excretion of nitrogen in the form of urea and uric acid and of phosphorus in the form of P₂O₅; (2) a comparison of the ratios of the figures obtained; (3) the influence of the diet and drugs in use on the daily excretion of uric acid, etc.; (4) the state of the blood, as revealed by microscopic examination, enumeration of white blood corpuscles, and by stained films. (The preparation and examination of these films was kindly undertaken for me by Dr. H. S. Ballantyne, late Assistant to the Professor of Physiology.)

The following is a short note of the clinical aspects of the case:

Clinical History.—A. S., male, aged 41, a musician, was admitted to the Royal Edinburgh Infirmary on May 16th, 1899, under the care of Dr. Byrom Bramwell, complaining of "rheumatic gout" in his ankles, knees, and left elbow, of twelve years duration. The first attack, twelve years ago, affected the right great toe; the second, nine months later, the right wrist; a third, a year later, the right great toe, followed in a few days by a similar involvement of the left great toe; and thereafter he had an attack usually once a year. In the intervals the mobility of the joints was unimpaired. The present attack began about a fortnight before admission, and had been of a subacute character.

His father and mother are living, aged 75 and 76 respectively. His grandfather died at the age of 98. There is no history of gout or rheumatism in the direct or collateral lines. He has had syphilis and soft sore. He has always been a fairly large meat eater, and accustomed to take a moderate quantity of alcoholic liquor. He stated that his condition had been diagnosed as "gout" by Sir Alfred Garrod as well as by others.

On admission his weight was 11 st. 6 lbs., and his height 5 ft. 6 in. The affected joints were swollen, hot, and painful on movement. Marked pain existed on pressure over the right metatarsophalangeal joint, with distension of the superficial veins.

The condition was regarded as one of subacute gout, and the following dietetic and medicinal treatment was adopted.

Dietetic.—5.30 A.M. Milk, bread and butter. 9 A.M. Porridge, egg, bread and butter, coffee. 1.30 P.M. Fish or chicken, potatoes, occasionally green vegetables, milk pudding; or soup and fish or chicken with vegetables. 5.30 P.M. Bread and butter, egg, tea. 8.30 P.M. Milk, bread and butter.

Medicinal.—Pot. iodid., sod salicylas 33 gr. x. t. i. d.

This treatment was in operation prior to the date of my observations, and the diet was maintained till June 20th (see Table I). The drugs were stopped on June 13th, to enable observations to be made for a few days on the fixed diet, without drugs (see Tables I and II). The observations extended over twenty-four days. Every precaution was taken in the collection of the urine and in other details of importance in the inquiry. In this we were assisted by the patient, who took an intelligent interest in the observations. Daily notes were made at the bedside, and as these have some interest a few are appended on the table. Unfortunately for the patient, but fortunately for the purpose of the research a typical acute attack developed during the investigation.

This temperature chart should be studied along with the notes and figures in Table I. There is room for some difference of opinion as to the

arbitrary lines drawn between the 19th and 20th on Table I. Initial symptoms set in on June 17th, and a typical acute attack developed on the night of the 18th. On the morning of June 20th it was deemed advisable to administer some medicinal treatment (the drug treatment had been stopped on the 13th), and two 30-grain doses of salicylate of soda were given on that day—one at 12.15 P.M. and one at 5.30 P.M. Thereafter it was discontinued. The acute pain ceased within an hour of the first administration, but from his previous experience of the duration of acute attacks, patient felt quite uncertain as to the special influence of the drug. In connection with the figures on Table I it should be noted that the figures for June 19th include the urine voided up to 8 A.M. on the 20th.

Methods of Investigation.—The urine was collected at the same hour each morning, measured in cubic centimetre measure, and the specific gravity and reaction noted. The reaction was acid throughout. Periodic examinations were made for the presence of albumen.

For the Estimation of Uric Acid (Salkowski-Ludwig).—To 200 c.c.m. urine add 50 c.c.m. magnesia solution; make up to 300 c.c.m. with distilled water and filter quickly. Take 200 c.c.m. of the filtrate (equivalent to 133 of the original fluid), and test to see that all the phosphates have been removed, then precipitate the uric acid by the addition of 15 to 20 c.c.m. of a 3 per cent. silver nitrate solution, ammonia being added to keep the chlorides in solution. Allow the mixture to stand for half an hour in a dark place, when the uric acid is deposited in the form of a gelatinous precipitate of magnesium urate. Filter through a suction pump, and wash the filtrate with weak ammoniacal solution until chlorine free, then put the filter paper with the precipitate into a beaker with distilled water, acidify slightly with hydrochloric acid, and decompose the magnesium urate by passing through sulphuretted hydrogen, bring slowly to the boiling point and filter. The clear fluid thus obtained is evaporated on a water bath to a few c.c.m., when a few drops of hydrochloric acid are added to allow the uric acid to crystallise out. This is left over night then filtered, the precipitate being washed chlorine free (an allowance being made for wash water 0.5 mg. in 10 c.c.m.). Thereafter the nitrogen of the uric acid crystals was estimated preferably to weighing them.

For the estimation of nitrogen and P₂O₅. The Kjeldahl-Weibull method was employed: 20 c.c.m. of urine were run into a Kjeldahl flask, then 15 c.c.m. of H₂SO₄, 10 grams K₂SO₄, and a few crystals of CNSO₂ were added and the mixture incinerated in the usual way. The clear green fluid left after complete incineration was then made up to 250 c.c.m., with distilled

TABLE I.

Period.	Diet.	Drug.	Date.	Total c.c.m. Urine.*	Specific Gravity.	Urea in Grams.	Uric Acid.	Total Nitrogen.	P ₂ O ₅ in Grams.	Uric Acid to Urea.	Uric Acid to P ₂ O ₅ .	Nitrogen to P ₂ O ₅ .
1	Mixed diet (q. v.)	Pot. iod. sod. salic. 33 gr. x. t. i. d.	May 31	1,380	1020	28.772	0.457	13.427	2.714	1 to 62	1 to 5.96	4.94 to 1
	"	"	June 1	1,180	1023	24.692	0.368	11.522	2.567	1 " 67	1 " 6.97	4.48 " 1
	"	"	" 2	990	1028	24.426	0.318	11.399	2.739	1 " 76	1 " 8.61	4.16 " 1
	"	"	" 3	1,425	1021	24.687	0.517	11.521	2.042	1 " 47	1 " 3.95	5.64 " 1
	"	"	" 4	1,540	1017	20.558	—	9.594	2.425	—	—	3.95 " 1
	"	"	" 5	1,335	1022	21.325	0.307	9.952	2.592	1 " 69	1 " 8.44	3.84 " 1
2	Mixed diet and thymus, 5½ ozs.	"	" 6	1,198	1026	22.281	0.419	10.398	2.935	1 " 53	1 " 7.00	3.54 " 1
	Mixed diet and thymus, 11 ozs.	"	" 7	1,468	1019	23.432	0.311	10.935	2.460	1 " 75	1 " 7.93	4.42 " 1
	Mixed diet and thymus, 9 ozs.	"	" 8	1,200	1023	19.890	—	9.282	3.320	—	—	2.79 " 1
	"	"	" 9	1,352	1016	19.062	0.336	8.896	2.591	1 " 56	1 " 7.71	3.43 " 1
3	Mixed diet	"	" 10	1,700	1017	20.781	0.327	9.698	2.620	1 " 63	1 " 8.01	3.70 " 1
	"	"	" 11	1,305	1018	19.665	0.319	9.317	2.425	1 " 62	1 " 7.60	3.88 " 1
	"	"	" 12	990	1020	17.522	0.332	8.177	2.161	1 " 52	1 " 5.50	3.78 " 1
	"	Drugs discontinued	" 13	1,645	1017	20.337	0.338	9.491	2.796	1 " 60	1 " 8.27	3.39 " 1
4	"	"	" 14	1,235	1018	18.893	0.491	8.817	2.624	1 " 38	1 " 5.34	3.36 " 1
	"	"	" 15	940	1020	16.354	0.435	7.632	2.075	1 " 37	1 " 4.77	3.67 " 1
	"	"	" 16	936	1020	17.830	0.452	8.321	2.560	1 " 39	1 " 5.67	3.24 " 1
5	"	"	" 17†	1,515	1017	24.542	0.513	11.453	1.893	1 " 47	1 " 3.69	6.05 " 1
	"	"	" 18	1,015	1024	22.380	0.682	10.444	1.860	1 " 32	1 " 2.72	5.61 " 1
	"	"	" 19	1,285	1020	30.261	0.768	14.122	1.745	1 " 39	1 " 2.27	8.09 " 1
6	Milk only from 12.15 P.M. on 20th	Sod. salic. gr. xx (bis in die)	" 20	1,440	1020	39.634	0.558	18.244	3.144	1 " 71	1 " 5.63	5.79 " 1
	"	—	" 21	775	1028	31.425	0.565	14.665	2.573	1 " 55	1 " 5.55	5.60 " 1
	"	—	" 22	815	1028	33.064	0.578	15.430	3.321	1 " 57	1 " 5.71	4.64 " 1
	"	—	" 23	1,170	1020	28.692	0.530	13.390	3.334	1 " 54	1 " 6.29	4.01 " 1

* There was practically no variation in the amount of fluid taken from day to day, the amount being small. † Acute attack—onset.

June 1st.—Woke up at 5 A.M. with severe pain in ball of left foot, the joint being swollen, red and painful on pressure. The tenderness remained for three or four days.

June 7th.—Feeling well. Still complains of pain in the left ankle on walking or standing.

June 9th.—More pain in the left ankle-joint, the outer part of which is swollen and tender. The superficial veins on the dorsum of the foot much distended.

June 10th.—The left ankle-joint easier. The right great-toe joint swollen and painful. The right fourth finger swollen and tender, and the seat of stinging pains.

June 13th.—Feels and looks very well. Has only very slight pain on deep pressure over the ankle-joint and toe-joint.

June 14th.—Not so well. Sharp pain in the right foot, the dorsum being swollen, tender, and red, with distended veins. Better on the following day.

June 16th.—Well again. No pain anywhere, and only traces of tenderness on deep pressure. Late at night began to complain of pains.

June 17th.—Pain, swelling, and tenderness on the inner aspect of both knee-joints, which became intensified on the 18th, when the ankles, the great-toe joints, the dorsum of the feet, and the left elbow-joint became involved. Complains also of "gouty" feeling in the hands and left forearm, which were tender on pressure. Condition intensified on 19th, patient unable to move. Tongue heavily coated and yellow. Radial tension increased.

June 20th.—The pains reached their maximum in the early morning. The worst and longest attack experienced. Diet on 20th included an egg, coffee, and bread and butter, but from the 21st onwards milk only. Sod. salicylate gr. xx given at 12.15 P.M., 5.30 P.M., and 8.30 P.M. The very acute pain disappeared on the afternoon of the 20th.

water, and of this 150 c.cm. were taken for P_2O_5 , and 100 c.cm. for nitrogen. The nitrogen was estimated by the ordinary method, the ammonia being distilled over into a known quantity of $\frac{1}{2}$ normal oxalic acid solution, and titrated in the usual manner. The P_2O_5 was estimated as follows: The 150 c.cm. were made alkaline by ammonia, and then acidified by HNO_3 , and after cooling, ammonium molybdate solution was added, and the beaker allowed to stand in a warm place overnight. The fluid was then filtered, and the yellow precipitate washed with the filtrate on the filter paper, and finally washed with dilute HNO_3 . The filtrate was then tested with ammon. molybdate solution to see if all the phosphates were precipitated. The yellow precipitate was then dissolved in dilute ammonia, and a sufficient quantity of magnesia mixture added, and the mixture again allowed to remain overnight. The resulting precipitate of ammonium magnesium phosphate was then filtered, washed chlorine free, incinerated and weighed. The total P_2O_5 was calculated from the amount of magnesium pyrophosphate obtained. The urea was calculated from the total nitrogen. *Blood*: The points of special investigation were the leucocytes and the blood plates. The former were counted on three separate occasions: On June 7th, 9,000; on June 12th, 12,600; and on June 20th (at the height of the attack), 20,500. In some cases the films were fixed with heat (120° for 15 minutes), and in others with alcohol and ether for an hour. Some were stained with eosin (2 per cent. watery solution for 2 minutes), and hæmatoxylin (Hansen's solution 3 minutes), others with eosin and methylene blue. (Saturated watery solution for half a minute.) In those fixed with heat special attention was paid to the granular leucocytes.

The figures in Table I show the variations in excretion of each substance from day to day throughout the whole period of investigation. Table II gives the averages and ratios in the different periods of investigation.

TABLE II.

Period.			Urea.	Uric Acid.	Total Nit.	Total P_2O_5 .	Uric Acid to Urea.	Uric Acid to P_2O_5 .	Nitrogen to P_2O_5 .
No. 1	Mixed diet	Drugs	24.7	0.393	11.564	2.53	1:63	1:6.4	4:5
" 2	Mixed diet and thymus	"	21.1	0.355	9.877	2.82	1:69	1:7.4	3:4
" 3	Mixed diet	"	19.6	0.329	9.770	2.50	1:59	1:7.5	3:6
" 4	"	"	17.6	0.459	8.256	2.42	1:38	1:5.2	3:4
" 5	"	"	25.7	0.654	12.086	1.83	1:39	1:2.8	6:5
" 6	Milk diet	"	33.2	0.557	15.432	3.09	1:59	1:5.5	4:9

* Acute attack—earlier stages.

Blood A.—During the interval (June 7th) the number of leucocytes was slightly in excess of normal, and there were a few somewhat peculiar cells resembling myelocytes. The blood-plate masses were more irregular in size and shape than those in normal blood. *B.*—During the attack (June 20th) the films showed very marked leucocytosis. There were present a large number of the peculiar myelocyte-like cells previously referred to, these being rather more than half as numerous as the ordinary finely-granular oxyphil leucocytes. Each of these cells contained a large oval or horseshoe-shaped nucleus, poor in chromatin. The nucleus occupied about half of the total area of the cell. It did not stain uniformly, and it was usually situated to one side, coming right up to the cell outline, and occupying from a third to a half of the total circumference. In many of these cells the nucleus was almost round, with but one slight indentation; in others the indentation was pronounced. The whole cell, stained a pale blue, presented a degenerated appearance, and contrasted markedly with the ordinary leucocyte seen in the same film with its brilliant blue nucleus and bright red eosinophil granules. The special cells under description were also remarkable for their size, measuring about 15μ in diameter, a few being smaller, about 10μ . Some of them contained vacuoles in the cytoplasm. The general appearance of these cells suggested exhaustion in so far as the cytoplasm did not contain the typical fine oxyphil granules characteristic of the myelocyte. From the character of the nucleus and cytoplasm they were undoubtedly distinct from lymphocytes. The large lymphocytes were scarce, small lymphocytes were numerous. True eosinophil cells were also scarce. The main bulk of the leucocytes consisted of the ordinary finely-granular oxyphil leucocytes and the peculiar myelocyte cells described. *Blood Plates.*—Some of the blood plates were large (4μ in diameter), and often formed very irregular torn-looking masses. The red cells were apparently normal.

SUMMARY OF RESULTS.

Phenomena Observed during the Attack.— P_2O_5 : There are points of importance, both in relation to the total amount excreted and the ratio to the other substances, and especially uric acid. These points are well brought out in Table II. There is a very marked diminution in the excretion of P_2O_5

during the first three days of the attack, followed by an equally marked increase, the former period furnishing the lowest figure, the latter the highest figures of the whole series. It is interesting to note that the diminution in the P_2O_5 excretion was a progressive one for the three days in question. During the acute attack the ratios of P_2O_5 to the urea and uric acid differed very markedly from the ratios in the previous periods. These figures seem to indicate either a retention of P_2O_5 in the body or some alteration in metabolism leading to its diminished production. *Uric Acid*: The increase of uric acid excretion was very marked, and increasingly so during the first three days of the attack. The association with a diminution in the P_2O_5 excretion has already been referred to. The ratio of uric acid to urea was similar to that of the previous period, and is usually regarded as the normal. *Nitrogen*: The total nitrogen was increased during the early period of the attack, but very much more so in the later period—the patient being then on a less nitrogenous diet—there being no proportionate increase in the excretion of uric acid.

After the Acute Attack.—(Here we must bear in mind that 40 gr. of salicylate of soda were administered on the 20th.) The following points are to be noted: (1) A marked diminution in the excretion of uric acid compared with the first three days of the attack, while the total nitrogen was markedly increased. (2) The ratio of uric acid to urea became 1 to 59 instead of 1 to 39, as during the attack. (3) The decided rise in P_2O_5 excretion, which was almost twice as great as in the previous period. In the circumstances of the drug administration it is impossible to speak definitely from these figures, but they are in any case interesting in view of the ideas commonly expressed as to the effect of salicylate of soda, when given alone, in increasing the amount of uric acid excretion. The figures for June 20th in no way bear this out. It would seem as if, after the initial acute attack is over, the condition of metabolism is such as to induce an increased excretion of P_2O_5 and nitrogen without a corresponding increase in uric acid excretion.

The Blood: The point of greatest interest is the presence of the myelocytes in the blood both in the interval and during the attack, but very specially in the latter. I have not seen this referred to previously. Here I merely wish to draw attention to the histological characters of these cells as described, and to the alteration in the P_2O_5 excretion, and to indicate the possibility of there being a close connection between the two conditions. The condition of the blood plates was hardly such as might be expected if, as Balfour believes, thrombosis plays an all-important part in the development of the acute attack.

Remarks on the Observations of the Periods Preceding the Attack.—Here we are, in the first place, confronted with a difficulty, in so far as the patient had been taking, and continued to take, the two drugs in combination during the first three periods. In the fourth period only was no drug administered. The figures are, nevertheless, worthy of notice. The main points may be summarised: *Period 2*: Administration of nucleins in form of sweetbreads. Here the following points may be noted: (1) No increase in the nitrogen excretion, but a slight diminution; (2) no increase of uric acid excretion, but here also a slight diminution; (3) slight increase in the excretion of P_2O_5 , the rise on the 8th being very pronounced. These points are of interest if studied along with other observations made by previous observers on the effect of nucleins in varying conditions. *Period 3*: After nuclein period. Here we note a slight fall in the excretion of nitrogen and of uric acid, the P_2O_5 remaining the same as before the thymus administration. *Period 4*: After cessation of drugs. We note (1) the immediate and pronounced rise in the excretion of uric acid after cessation of the iodide and salicylate of soda; (2) the resulting alteration in the uric acid and urea ratio, this becoming practically, and for the first time, normal; (3) that the total nitrogen was not increased, but rather the reverse, the P_2O_5 being practically unaltered.

If we contrast Periods 4 and 5, we find that whereas the uric acid and urea ratio is the same, the uric acid and P_2O_5 shows a very striking alteration. This would seem to indicate that the cause of the acute attack must be sought in some other direction than in that of uric acid to urea ratio, on which so

much stress is laid by some writers, as the all-important factor in the genesis of gouty symptoms.

CONCLUDING REMARKS.

From the results here indicated as to the excretion of uric acid during the attack, in conjunction with the similar results referred to early in the paper, and from Levy's observations as to the alkalinity of the blood and the relative amount of uric acid present in the blood during the attack as compared to the interval, it would appear we must abandon the theory at present based on Garrod's original observations. In other words, the following points would appear to be established: (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 these points be accepted we must start *de novo* in search of the cause of the acute paroxysm. In this connection it would, I think, be well if much less attention were centred on the excretion of uric acid alone as the all-important factor in the disease, whether in its acute or chronic form. The results obtained by the line of investigations here followed suggest the advisability of more attention being devoted to the histochemical characters of the blood, the ratios of uric acid to other important products of metabolism, and, if opportunity be afforded, an examination of the bone marrow.

Since the foregoing was written, an interesting paper has been published by Bain⁶ on the excretion of uric acid and P_2O_5 in a case of gout. One of the concluding statements of that paper is "that the phosphoric acid varies directly with the uric acid excretion, the patient being on a fixed diet." It is I think doubtful if that conclusion can safely be arrived at from the record and figures given in his paper. The figures in this paper would rather tend to negative that conclusion, but much further investigation is necessary before any conclusion can be formulated. I may add that a more recent investigation of another case of gout has revealed the presence in the blood of the peculiar cells referred to, and tends also to indicate that the ratio between uric acid and phosphoric acid is not the constant one referred to by Bain.

In conclusion, I must express my indebtedness to Dr. Bramwell for kindly allowing me to investigate and record the case, to Dr. Ballantyne for the examination of the stained films, and to Dr. Milroy for valued assistance throughout the investigations.

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THE UNIMPORTANCE OF THE PRESENCE OF A TRACE OF ALBUMEN OR NUCLEO-ALBUMEN IN URINES OF EXTREMELY LOW SPECIFIC GRAVITY.

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I WILL at once explain that by "urines of extremely low specific gravity" I here refer to urines of practically the same specific gravity, when freshly passed, as ordinary tap water. The urinometer sinks to zero, but when the urine cools it may rise a degree or so. In the case of a "limpid urine" of this kind I believe that no conclusion of any value for diagnostic purposes can be drawn from the detection of a "very faint trace of albumen." The test for albumen which I have regularly employed in these cases is to boil the upper part of the column of the urine in a test tube and to add a few drops of acetic acid. When there is a faint but distinct cloudiness of the boiled portion (the two portions being compared with each other against a dark background) one may conclude, I think, that a trace of albumen or nucleo-albumen is present, for I do not see that the reaction can be due to anything else.

Some would even say that nucleo-albumen by itself cannot give rise to the reaction. Anyhow, the presence of such "a trace" is of very frequent if not of usual occurrence in urines of extremely low specific gravity.

I will take an illustrative case of ordinary occurrence. About midday a man hurries from his work in the City to an insurance office and is examined by the medical officer of the company. The applicant feels somewhat nervous; moreover, he may have had no time for lunch, and on the way to the insurance office takes perhaps a small glass of whisky and soda water with a sandwich. When he presents himself for examination the doctor probably finds the pulse rather frequent from excitement and hurry, the heart's action may be forcible, and there may be even a temporary systolic murmur, though possibly only of "cardio-pulmonary" nature. If in such a case I find the urine nearly colourless and the urinometer sink down to about zero, I almost expect to find a very faint trace of albumen (or nucleo-albumen) by employing the common and, as I believe, the most generally useful test, that is, the test which I have previously mentioned.

Has not this man got chronic interstitial nephritis? The urine is of extremely low specific gravity, and apparently contains the very faintest trace of albumen; the heart's action is somewhat violent. Moreover, if the specific gravity of the urine were higher, the "trace" might become a regular "cloud." In many such cases the breath of the person under examination has a faint but distinct smell, as if he had just had some alcoholic drink; but very little alcohol will produce this smell in some people, especially if taken on an empty stomach. I maintain that no positive conclusion of any diagnostic value can be drawn from the examination of the urine in such cases, not even that alcoholic drinks are frequently indulged in.

It seems, in fact, that in healthy persons, under certain more or less temporary conditions, a urine is passed containing hardly any of the ordinary solid constituents, but a faint trace of albumen or nucleo-albumen. In some very different cases, when the urine is of high specific gravity and loaded with urates, a trace of albumen may be discovered, which disappears when, by alteration of diet, etc., the urine becomes of lower specific gravity, and free from precipitate on cooling. These two classes of urine may be contrasted with each other. In the latter class the kidneys, when overworked (from a variety of causes) allow a trace of albumen to pass together with large quantities of urea and uric acid salts. In the former case, under some temporary influence, a large quantity of urine is passed, containing a faint trace of albumen, or nucleo-albumen, but hardly any urea or urates or other solid constituents.

INJURIES PRODUCED BY A SIX-POUNDER HOTCHKISS SHELL.

By MAJOR J. R. DODD, F.R.C.S., R.A.M.C.

(Communicated by the DIRECTOR-GENERAL, Army Medical Department.)

R. B., a workman in the Royal Laboratory, Woolwich Arsenal, was admitted to the Arsenal Hospital at 3 P.M. on September 14th, 1899, suffering from the effects of the explosion of a six-pounder quickfiring Hotchkiss shell. He was engaged in removing the shells from the cases in some old ammunition which had been returned into the arsenal unused, when one of the cartridges exploded in the extracting machine from some unexplained cause. He was found to be suffering from the following injuries:

The right eye was burned, and the surface of the globe abraded and blackened, but there was considerable power of vision. The left eye was collapsed and absolutely destroyed, evidently by lodgment of a large foreign body. There was an incised wound about 3 inches long extending from the middle of Poupart's ligament on the left side towards the umbilicus. From this protruded about 2 feet of small intestines and a small amount of omentum, and in the intestines were two penetrating wounds, each about 1 inch long, and each about 1 inch from the mesenteric attachment. The semi-solid contents of the gut were escaping from both wounds.

In the middle of the right thigh, opposite the apex of