The existence of adenomata or hyperplastic tumours of the suprarenal bodies suggests the interesting speculation whether any symptoms can be correlated with this condition. Addison's disease and myxœdema have some analogies. Exophthalmic goitre is apparently due to altered structure and secretion of the thyroid gland. Is there any disease analogous to Graves's disease connected with the adrenals? The absence of any symptoms in association with adenoma or hyperplasia of the suprarenal bodies may be due to the fact that they nearly always show extreme fatty change, and so cannot be functionally active. Schäfer and Oliver⁴⁹ have quite recently shown that the cortex does not yield the active principle of suprarenal extract; hence hyperplasia of the cortex would not lead to any modification of the suprarenal secretion. A specimen of ganglionated neuroma has been described.⁵⁰ Dr. Payne⁵¹ has recorded a case of angioma of the suprarenal capsule; there were similar growths in the ovaries and many in the liver.

PRIMARY MALIGNANT GROWTHS.

Both carcinoma and sarcoma of the suprarenal capsules have been described, but generally the histological structure seems to be a vascular rather large-celled sarcoma. In some cases both organs have been the seat of primary malignant growths. The growth starting in the suprarenal body expands it, and may grow down the suprarenal vein or into the inferior vena cava.

By direct continuity the growth often invades the upper part of the kidney and, on the right side, the corresponding lobe of the liver. In some cases the growth may involve the pelvis of the kidney and give rise to hæmaturia. When the growth is extensive and invades the whole of the kidney, it is necessarily very difficult to say whether it began in the suprarenal or in the kidney. Secondary growths occur in the liver most frequently, but also in the lungs, kidneys, bones,⁵² and skin.

Dr. Dickinson⁵³ mentions that in a case of sarcoma of the suprarenal body, the colon did not form an anterior relation of the tumour, as is the case in renal tumours; and since reading this I have seen two cases in which the tumour appeared above the colon, which was somewhat displaced downwards. The soft vascular growths have a tendency to necrose, and so to become excavated into hæmorrhagic cysts; a specimen of a cystic sarcoma as large as a cricket ball is in the London Hospital Museum.

In young children excessive development of hair and of the genital organs has been noted in connection with suprarenal sarcoma.

H. Morris and Sutton speak of tumours of the suprarenal bodies which give rise to secondary growths as being analogous to those rare and interesting cases of bronchocele⁵⁴, which produce secondary growths in bone and elsewhere. Morris⁵⁵ described the growth in one of these cases as being composed of tissue like that on the medulla of the suprarenal body. It seems difficult to distinguish between such a tumour and a vascular large round-celled sarcoma.

Sutton⁵⁶ described an adenoma of the suprarenal body in a marmot giving rise to numerous secondary nodules on the liver, which on section presented a curious mottled appearance, and also to a single nodule in the spleen. Histologically the growth resembled suprarenal cortex, and was therefore not considered malignant. Abnormally low bodily temperature has been noticed in primary suprarenal sarcoma,⁵⁷ but the temperature in a rapidly growing sarcoma from the right suprarenal body⁵⁸ in a coloured girl aged 8 was on an average 100°.

Examples of renal sarcoma arising in suprarenal "rests" have been described. Not only is their structure much like that of primary suprarenal sarcoma, but they show a similar tendency to the formation of hæmorrhagic cysts and to undergo necrosis. Lubarsch⁵⁹ has found glycogen in eight cases, and regards this as indicating their embryonic origin. Schmorl⁶⁰ suggests that some of the primary neoplasms of the liver may similarly be due to proliferating changes in a suprarenal "rest."

SECONDARY GROWTHS IN THE SUPRARENAL BODIES.

In 1,050 *post-mortem* examinations carcinoma of various parts of the body occurred 63 times, and in 7 of these the suprarenal bodies contained secondary growths.

There were 24 cases of sarcoma, and of these only 2 cases showed metastatic growths in the suprarenal bodies.

Norman Moore,⁶¹ in 123 cases of new growth (102 carcinoma, 21 sarcoma) found secondary growths in the suprarenal bodies in 8. Three of these were carcinoma, 3 sarcoma, and 2 are described as endothelioma, the primary growth being in both cases in the heart.

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THE PATHOLOGY OF OEDEMA.¹

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THE subject of œdema has so frequently been discussed that it is only the introduction of some new information derived from experimental sources that can warrant its being made the subject of this lecture. The additional facts which I propose to bring forward before you to-day have been ascertained during the past two years from experiments made by me in the Pathological Laboratory of the University of Cambridge. If they be corroborated by other investigators they will materially alter our conceptions of to-day upon the pathology of œdema.

œdema has long been recognised by the medical profession. The other name—dropsy—by which it is known is evidence etymologically of the fact; and yet the pathological explanation of the condition was not questioned until the year 1680, when Richard Lower ligatured the inferior vena, and obtained œdema of both lower extremities. From this experiment he came to the conclusion that œdema depends upon an increase of pressure in the veins, which is transmitted to the capillaries, and which leads to an increased exudation of plasma from these vessels. This view, though it was not universally accepted by Lower's contemporaries, nevertheless held its own for 200 years, when the first formidable attack upon it was made by Ranvier in 1869. Ranvier repeated Lower's experiment, but with negative results; he therefore added to ligature of the inferior vena cava section of the sciatic nerve on one side. On this side he obtained œdema, whereas in the other limb, which was equally exposed to the effect of the venous obstruction, but which was free from the effects of nerve-section, no œdema appeared. Ranvier therefore ascribed œdema to vasomotor action. A few years later Cohnheim, who investigated the subject more thoroughly than any of his predecessors, stated it as his opinion that passive œdema was the result of two antagonistic pressures: venous obstruction and arterial pressure,

¹ The expense of some of the experiments referred to in this paper were in part defrayed by a grant from the British Medical Association.

which raised the pressure in the capillaries, and therefore led to increased exudation from them. The oedema obtained by Ranvier's method, he maintained, resulted from the fact that section of the nerve causes arterial dilatation, and consequently modifies the pressure unfavourably on one of the two sides of the capillaries. As the result of this criticism, Ranvier altered his position somewhat, and in 1881 he and Cornil wrote: "If in an animal in which one has tied a vein, the vasomotor nerves be cut, the arteries being dilated, a larger amount of blood reaches the part, and the tension becomes sufficient to lead to transudation of serum. This increased tension is the true cause of dropsy; if this tension be sufficient, independently of obliteration of the veins, oedema will occur. All kinds of oedema, except, perhaps, the oedema of cachexia, may be referred to the same cause." In 1892, at a discussion upon renal dropsy at the Royal Medical and Chirurgical Society, Sir George Johnson expressed his opinion that oedema is the result of an "active vital secretory process consequent on an accumulation of various morbid fluids and solids in the blood."

From the foregoing words it is seen that the explanations which have been given of oedema are of two kinds, mechanical and vital secretory. Many modifications have been introduced into the mechanical explanation, particularly those which cause the lymphatic vessels to enter into the question, but it is unnecessary to stop for their consideration at present.

Now oedema occurs under a variety of circumstances. There is the oedema which occurs as the result of too tight a ring or bandage; this variety, along with the oedema which occurs in cardiac disease, is usually spoken of as "passive oedema;" then there are "renal oedema," "inflammatory oedema," "cachectic oedema," "oedema of the lungs;" and all of these have been regarded as being dependent upon different causes, so that the number of explanations of oedema as a whole is legion. They agree in one point, however, they are all more or less mechanical with the exception of the "vital secretory" explanation. The mechanical explanation of oedema can best be considered in that variety which comes on after a period of passive congestion. In its simplest form it is represented by the tight ring or tight bandage.

It is essential, if the mechanical explanation be true, and if the vessel wall act like a filter, that the increased exudation should show itself in the tissues immediately after the pressure in the veins has been raised. It is beside the mark to say that oedema comes on "after some hours" or "next day." It is essential upon the mechanical explanation that it should come on at once. Since, however, it is impossible to detect minute quantities of oedema by the rough methods of measurement, pitting on pressure, etc., when investigating this question I made use of numerical values derived from the specific gravity of the blood and blood plasma, arterial and venous, and the specific gravity of the muscles and skin. It is obvious that if fluid leave the blood vessels of lower specific gravity than the blood and of lower specific gravity than the muscles and skin, the specific gravity of the blood must rise, and the specific gravity of the muscles and skin must fall. There is no need for me here to describe the methods I used, they can be found in detail elsewhere.* My results, however, have a direct bearing upon the subject we have in hand.

I raised the pressure in the femoral vein of a dog to 50 mm. of mercury by means of an elastic bandage placed round the whole limb. Inasmuch as the normal pressure in that vein is about 3 or 4 mm. of mercury, if as much, the amount of obstruction produced was very considerable. At the same time, the pressure in the carotid was taken, and speaking generally, it was 100 mm. of mercury. It is obvious, therefore, that though impeded, there was a flow of blood through the limb. I kept the pressure in the femoral vein constant for an hour, and at the end of that time took the specific gravity of the blood, blood plasma, and tissues as mentioned. These I compared with values taken at the commencement of the experiment. The values were identical, and I provisionally concluded that increase of pressure in the femoral vein does not lead to exudation from the vessels, that is, venous obstruction does not cause oedema.

It was of course possible that though no changes were

found in the specific gravity of the blood and tissues exudation might have occurred, but might have been prevented from showing itself owing to an increased rate of flow through the lymphatics of the part. I therefore investigated the amount of lymph flow under normal conditions, and when there was increased pressure in the veins, and found that venous obstruction does not cause an increase in the amount of lymph flow.

This experiment corroborated my provisional conclusion, and I definitely decided that an increase of venous pressure in a limb for one hour does not cause oedema of that limb. It is impossible in the light of these facts to still hold to the explanation of oedema as being a purely mechanical filtrate from the blood vessels. Inasmuch too as the ligature by means of which I produced an increase of pressure in the femoral vein embraced the whole limb, any view which regards oedema as the result of an obstacle to the lymphatic flow is equally untenable. Section of the sciatic nerve, as in Ranvier's experiments, in no way modified the results given by my method. What then is the explanation of passive oedema? Upon a moment's consideration it will be seen that all forms of oedema coming under this heading are dependent upon anæmia of the part, by the word anæmia being understood not an absence of blood, for that is evidently not the case, but an insufficiency of blood, or an insufficient renewal of blood to meet the requirements of the tissues. In other words, passive oedema is always preceded by starvation of tissues, and it is to the importance of the tissues in determining oedema that I wish above all to direct attention. That anæmia of a part is of itself a cause of oedema is seen in cases of ligature of the main artery. Thus surgeons after ligature of the femoral artery for aneurysm or other cause occasionally see oedema of the leg, which obviously does not depend upon obstruction to the veins, and as obviously depends upon the cutting off of the normal blood supply to the limb. Supposing the case to go on favourably, the oedema disappears after the collateral circulation has become established. This explanation of oedema as the result of anæmia I have confirmed in the following way. By means of an Esmarch's bandage I rendered the limb of a dog bloodless, while at the same time of course most of the lymph was removed from the part. After keeping the limb thus anæmic for from two to three hours I removed the bandage, and now by means of the specific gravity method I found that oedema came on. The arterial blood rose in specific gravity, the blood in the femoral vein rose in such a way as to show that more fluid was being lost during the passage through the limb than normal; the muscles and skin fell in specific gravity. Starvation of the tissues therefore plays an important part in the causation of passive oedema.

In view, however, of the fact that venous obstruction is almost invariably followed by oedema, whereas anæmia of the part is not so definitely a cause, it was necessary to consider the effect of venous obstruction more closely. The difference in the two cases is the "venosity" of the blood. In simple anæmia a part is starved; with venous obstruction it is not only starved, it is being poisoned, partly by the metabolic products in the blood, partly by the metabolic products of its own life and activity, which are dammed back instead of being removed, as is usually the case. If, after a part has been starved, as in my experiments just mentioned, the pressure in the vein be raised by means of a ligature, this poisoning process is superadded to the starvation, and the amount of oedema becomes greater.

This point I confirmed in the following way. I exposed the sciatic nerve, rendered the limb anæmic with an Esmarch's bandage, and stimulated the nerve strongly for a quarter of an hour, allowed the products of metabolism to remain *in situ* for a further quarter of an hour, and then removed the bandage. The amount of oedema I obtained after an interval was far greater than that after three hours' anæmia alone, and I therefore came to the conclusion that the presence *in situ* of the metabolic products of functional activity plays a part in the causation of oedema even greater than that of simple starvation. This view is strengthened by certain experiments performed by Wooldridge to which reference will be made later.

Now, the methods by which I obtained oedema are so

* Phil. Trans. Roy. Soc., 1894.

clearly the same as processes which are of constant occurrence in the normal physiological condition of the body that it was necessary to see whether the pathological differed from the physiological process. Tissues are constantly requiring food and constantly forming metabolic products; do we under normal conditions find variations in the amount of lymph in the tissues in agreement with the varying requirements for nutriment?

Upon the question of anæmia the evidence has been given above. As the result of three hours' starvation the tissues become oedematous, though not to any marked extent. Further, in accordance with the well-recognised law that active congestion follows on anæmia, I found that active congestion occurred in my experiments. The object of this active congestion is obviously to supply the part with the food which has been denied, and it is the endeavour of the vascular system to meet the demands of the tissues. For a time it is insufficient, and the demand continuing, more and more fluid is poured into the part from the blood vessels. This extraordinary amount of fluid is beyond the powers of the lymphatics to remove, and therefore a portion remains in the tissues to constitute the oedema fluid, although a larger amount than normal may be flowing away by the lymphatics. By degrees, however, the increased demand of the tissues ceases, the outpouring from the blood vessels diminishes, the excessive amount of lymph in the part—the oedema fluid—is removed, and the tissues again return to a normal condition. The supply is excessive simply because the demand is excessive.

Upon the effect of the storage *in situ* of the products of functional activity on the causation of oedema the following experiment throws some light. Let the two gastrocnemii be removed from a frog with a length of nerve attached and be placed in a vessel of oil, and let one of the muscles be caused to contract until with a maximal induced current a minimal contraction occurs. If now the two gastrocnemii be removed from the oil simultaneously and be placed in normal saline solution for a minute or two, it will be found on removing them that the muscle which has been caused to contract is of lower specific gravity than its fellow. Functional activity of a muscle, therefore, is accompanied by changes which lead to an absorption of water. But the primary effect of functional activity upon metabolism is to cause an increased formation of waste products, and therefore we may conclude that the storage of waste products leads to an absorption of water. Whether this be a vital process or one depending upon the osmotic coefficient of the substances produced it is impossible as yet to say. If the experiment be performed in the body the same result is obtained with regard to the specific gravity. Now, functional activity is always accompanied by active congestion or active dilatation of the arteries; it is not unreasonable to suppose that one of the functions subserved by this increased supply of blood is to give a larger lymph supply to the part and therefore to remove the waste products formed.

It is seen, therefore, that normally tissues, when deprived of nutriment or when exercising their function, have a tendency to become oedematous, and one is therefore driven to the conclusion that the oedema of passive congestion is an excess of a normal process whereby the nutrition of the tissues and the removal of the waste products of their metabolism is carried out.

It is easy to see why normally tissues do not become "oedematous" in the pathological sense of the term. The reserve power of the heart and the degree of dilatation which the arteries can undergo is considerably greater than is usually called into play, and these two factors are able to meet any call that is likely to be made upon them, and, therefore, starvation and storage of waste products do not occur to any extent. On the other hand, when there is some failure of the central organ as in cardiac disease, or when there is an impediment to the circulation, as in the case of a tight ring or bandage, the action of which is prolonged, or when there is an insufficient supply of blood to meet the normal requirements of the tissue, as in ligation of the main artery of a limb, starvation or storage of waste products, or both together, are in excess of the powers of the circulation, and the tissues are in a constant condition of calling for more lymph. This is supplied in as large quantities as possible,

and the excess, owing to the limited capacity of the lymphatic system, remains in the tissues as oedema fluid.

It is worth notice in this context that oedema of the feet only occurs in heart disease after the heart has begun to fail. Whatever the lesion if compensation be effected there is no oedema, but when compensation fails oedema is invariable. The effect of rest, too, is easily explained on the view given above. Oedema in cases of heart disease frequently disappears as the result of rest alone, if the oedema be in an early stage. But rest in bed does away with the formation of waste products of functional activity, and, therefore, supply and demand are equalised by diminishing the demand. Later, rest in bed will not remove dropsy, for there still remains the formation of waste products as the result of the mere nutrition of the limb. Digitalis, strophanthus, strychnine, and iron are now of use; demand cannot be further reduced, therefore the supply must be increased. The drugs mentioned improve the condition of the heart muscle; supply again equalises demand, and again the dropsy disappears. But there comes a time when the heart can no longer be braced up, and when, aided to its utmost by drugs and by reduction to a minimum of the demand, it is nevertheless unable to meet the requirements of the tissues. Dropsy now never leaves the patient, but from causes that can easily be understood, it gets worse and worse until death closes the scene.

The distribution of dropsy in cardiac disease, however, is so characteristic, that it has long been regarded as a strong support of the mechanical explanation of oedema which on other grounds we have already found to be untenable. It is necessary to see in what way an explanation can be given of the fact that cardiac dropsy shows itself first in the neighbourhood of the ankles.

It is obvious in the case of cardiac failure that all parts must suffer proportionately if not equally. To this point we shall return later, but it is clear that all parts must suffer. Why, then, should oedema show itself first in the feet and not in the hands? The effect of gravity in the case of the foot is double. In the first place it aids the arterial flow, and in the second place it impedes to an equal extent the venous flow. The effect of gravity in the case of the hand is precisely similar. Gravity, therefore, does not produce any effect upon the rate of flow through the hand and foot. It increases, however, the pressure on the blood in the capillaries, and there is a difference between the two cases, for the lower limbs are more frequently in a vertical position than the arms, and therefore the capillaries in the foot have to bear the effect of gravity more than those of the hand.

It has been said above that increase of venous pressure for one hour does not lead to an increase in the amount of lymph secreted. This is true for the normal condition of the limb, but after a modification has been introduced, leading to starvation or storage of waste products, this law does not hold good. On the contrary, when there is active congestion, that is, when oedema is about to come on, the amount of lymph secreted per unit of time varies directly with the pressure in the femoral vein, rising when the pressure in the vein is raised, falling when that pressure is again allowed to fall to the normal. Given, therefore, that the pressure on the capillary wall is greater normally in the foot than in the hand and that in active congestion lymph flow varies directly with venous pressure, it is easy to understand that oedema is bound to show itself first in the foot. Whether lymph flow varies with venous pressure in the degree of active congestion that occurs in every-day life I am unable to say; with considerable degrees of starvation and of storage of waste products it occurs to a marked extent.

In what way the demands of the tissues are made known to the blood vessels it is impossible to say. The active dilatation of the arteries in active congestion seems to be brought about by means of some peripheral mechanism which is largely independent of the vasomotor system, for section of the sciatic nerve, as in Ranvier's experiment, which leads to a dilatation of the blood vessels that cannot be distinguished but by its results from that of active congestion, does not lead to oedema or an increase in the amount of lymph flow—at all events, until after some hours has elapsed. It has been thought by some to be dependent upon the carbonic

acid which is formed as the result of metabolism, but of this there is no proof, and indeed there are certain facts against this view. At present the *modus operandi* of what is an undoubted fact is quite unknown.

It is obvious that many other forms of oedema are open to explanation in the same way as that given above. In the oedema of chlorosis it is evident that there is a chronic starvation of the tissues, at all events of oxygen; while the constipation which is usually present may possibly enter in some way into the question. It is also possible, in view of the fact that anæmia is frequently accompanied by a pulse of high tension, as shown, independently, by Archibald Garrod and Dickinson, that a renal element may play a subordinate part.

Cachectic dropsy manifestly depends upon starvation of the tissues. To take three typical examples. Dropsy of the ankles occurs at the end of cases of pulmonary tuberculosis, of malignant disease, and of malaria. In tuberculosis the heart is always small and ill-nourished; in malignant disease the blood supply is largely diverted for the growth of a tissue which is physiologically outside the body; in malaria there is a great destruction of corpuscles. In all these cases, therefore, there is ample explanation for starvation of the tissues, and the effect of starvation has already been considered. Oedema of the lungs is a subject of more uncertainty. The lung tissue obtains its nutriment through the bronchial arteries, which are small in comparison with the area they have to supply. Whether the lungs obtain food from the blood of the pulmonary artery it is impossible to say, though such a source seems improbable. Having regard, however, to the fact that in cardiac disease oedema of the lungs is a sign of cardiac failure as much as is oedema of the ankles, we may provisionally regard oedema of the lungs as the result of a failure in nutrition of the lung tissue. The subject, however, is so fraught with difficulties from an experimental point of view that the solution given must not be regarded as more than a possible one.

(To be continued.)

REMARKS ON THE CHEMICAL PATHOLOGY, SYMPTOMS, AND TREATMENT OF URIC ACID GRAVEL.

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EXPERIMENTAL medicine has during the last two decades been especially turned towards bacteriology, and consequently the important branch of pathology embraced in the word "metabolism" has received but scant attention. In spite of this, as regards the question of uric acid formation so much has been done in this direction that it may be said our views are entirely different from what they were a quarter of a century ago, and we are now able to treat patients suffering from uric acid disease on new scientific instead of old empirical principles.

As it would take up too much time to discuss the entire uric acid diathesis, I will merely call attention to that form known under the name of uric acid sand or gravel, and leave the question of its concretions with gout entirely out of the question.

Our first step in an inquiry into the causation of uric acid gravel is as regards the formation of uric acid in the organism. Until quite recently uric acid was regarded as one of the normal products resulting from the breaking down of proteids in the processes of metabolism. Sir William Roberts regarded it in man as a vestigial feature of some ancestral form. Chemists had succeeded by a process of oxidation and hydration in converting uric acid in the test tube through the transitional stages of alloxan, parabanic acid, oxaluric acid, and oxalic acid into the final products of urea and carbonic acid. Physiologists considered that proteids passed through the stage of uric acid in the animal body before being converted into urea by oxidation. If, then, uric acid is under normal circumstances oxidised in the animal body into urea and carbonic acid, one might expect that in diseases

in which oxidation is hindered there would be an increase in the uric acid eliminated into the urine. Contrary to this expectation, Senator, as early as 1868, failed to find any increase in the uric acid in the urine when the respiratory processes were artificially interfered with, and Naunyn and Reiss equally obtained negative results when tissue oxidation was retarded by venesection. Further, pathology shows us that in simple anæmia there is no increased elimination of uric acid.

Bunge explains the failure of the oxidation theory by calling attention to the fact that in birds in whom respiration is most active the bulk of the nitrogen is eliminated as uric acid. While Frerichs, Wöhler, Zabelin, and others had previously shown that when uric acid was given, either by the mouth or intravenously, it appeared in the urine as urea, and no increase of uric acid could be recognised. Haig has lately pointed out that this is probably due to precipitation of uric acid in the organs, and if it is given while the blood is kept alkaline there is really an increased elimination of uric acid in the urine. It thus follows that, experimentally, we have no evidence that uric acid is converted into urea in the organism.

The researches of Horbaczewski, Kossel, etc., have led to the view that uric acid is not derived from the metabolism of the general proteids which yield urea, but from nuclein derived from the nucleo-albumin of the cells. Horbaczewski showed that when splenic pulp is mixed with blood and kept for some time at the temperature of the body it yields xanthin bases; and that when the same process is carried out in the presence of an abundant supply of oxygen instead of xanthin bases uric acid is formed.

The constituent of the spleen which yielded these xanthin bases was found to be nuclein. Other observers, in addition, found that all the tissues of the body that contain nuclein are in like manner capable of yielding uric acid.

Horbaczewski further showed that feeding animals with nuclein, or injecting it subcutaneously, causes an increase in the elimination of uric acid, not only in animals, but also in man. This last statement has been contradicted by Stadthagen in the case of dogs, in whose urine he says he found, if anything, the amount of uric acid decreased, and, on the other hand, the urea markedly increased.

These contradictory statements have likewise been made, as already stated, as regards the effects of feeding with uric acid, and we must leave them for the present for further investigation.

We can now turn to observations made on man to see if we find this nuclein view of uric acid formation supported.

Marès examined the urine as to the quantity of uric acid excreted from time to time, and found that, after a meal, it rose rapidly, so that in two to five hours it had reached double or even three times what it was during fasting; it then slowly fell for the first thirteen hours after food, and then remained constant until fresh food was taken. He found the rise was greatest after animal less after vegetable diet. Urea, on the other hand, does not begin to be increased in quantity until some time after food, and only reaches its maximum nine or more hours after the meal, and then still more gradually falls. It is known that after a large meal, especially of animal food, a great increase of leucocytes takes place in the blood, and at the time that they are being destroyed and their nuclein liberated it appears that there is this increase in the amount of uric acid eliminated in the urine.

As early as in the year 1868 Bartels showed that in leucocythæmia four times the normal amount of uric acid was eliminated with the urine in twenty-four hours. Schultzen, Ebstein, and others have confirmed the statement that the quantity of uric acid is always markedly increased in this disease.

Fleischer and Penzoldt, on comparing the quantity of uric acid passed by a leucocythæmic patient with that of a healthy patient on the same diet, found that while the first was more than double the amount of uric acid eliminated by the healthy man, the quantity of urea excreted was the same in both cases. This fact of the urea remaining the same shows that the nitrogenous matter taken as proteids in the food was equally eliminated in both cases, while the excess of leucocytes in the blood of the one caused an excessive break-