BLOOD CHEMISTRY AS A DIAGNOSTIC AID IN FOCAL INFECTION[1]

RICHARD N. DENIORD

Buffalo, N. Y.

CONTENTS

I. INTRODUCTION

I am very grateful for the opportunity to meet you tonight, and to address you upon the subject of focal infection—a subject of vital importance to both medical and dental professions. This subject, while not new, is only beginning to come into its own. As has often happened in the past, the introduction of a new theory has brought about a division of the professions into several groups based on some of the apparently contradictory phenomena involved. It is my hope that blood chemistry, when properly utilized, will help to clear away some of these supposed paradoxes, and enable all of us to unite on a common basis and a more complete understanding.

At present our professions appear to be divided into three groups: the conservatives, who fail to accept the focal-infection theory either in whole or in part; the radicals, who jump to conclusions and in their enthusiasm are apt to overdo the matter of eradication of supposed foci; and, finally, the group (altogether too small) who realize that both conservatism and radicalism have their places.

[1] Read at the ninth annual meeting of the American Academy of Periodontology, Hotel Gibson, Cincinnati, December 6, 1922. See the related paper by McCall, and the ensuing discussion: *Journal of Dental Research*, 1922, iv; proceedings section, p. lxxi (this issue).

The chief object of this paper is to bring before you the fact that we now have a very definite means of diagnosing focal infection through blood chemistry, and thus settling many of the perplexing problems of chronic systemic disease. This does not mean that the chemical findings determine whether the focus is present in teeth, tonsils, or sinuses; the findings indicate only the presence or absence of foci *in the body*, and thus may justify what is frequently a prolonged and difficult search. I base this statement on my findings during the past seven years, on my own patients and on those referred to me for diagnosis. Very close coöperation of certain types of medical and dental specialists is necessary to localize definitely the focus or foci of infection that chemical study has proved to be present. The groups of specialists most generally called upon, to localize and eradicate such infection, include the laryngologist, the dental roentgenologist, the oral surgeon, and the internist; the general surgeon is sometimes needed as well.

In my opinion a focus of infection may best be defined as a circumscribed mass of nuclear degeneration, which may or may not be encysted. This may mean a chronic accumulation of pus, or it may mean simply a region exhibiting an abnormal degeneration of cellular elements. This mass may be enclosed in any of the cavities or tissues of the body. The tissues most commonly involved are the tonsils, including all lymphoid tissue in Waldeyer's ring; the teeth and periodontal tissues; the nasal accessory sinuses; the middle ear; the mastoid and lateral sinuses; in fact, all the cavities communicating with the mouth, nose, and naso-pharynx. I have arranged this classification in an order indicating the usual relative degrees of importance, namely, tonsils, teeth, and sinuses. The secondary results of focal infection in the body (and these constitute the patient's chief source of complaint) are indeed legion, but I will not burden you with allusions to them at this time.

The primary focus of infection must be regarded not only as the place of entrance for the bacteria, but also the place where the organisms acquire the peculiar properties necessary for infection. The location of such foci frequently offers one of the most difficult problems in medicine.

There are two distinct methods of approaching the study of focal infection, namely: bacteriological and chemical. It is not my intention to discuss the bacteriological phase, with its many interesting channels, the most noted chapter of which is Rosenow's work on the selective affinity of given strains of organisms for certain tissues. The organisms, or the toxins produced by these organisms, from one or more foci, give rise to the various clinical pictures so frequently seen in a certain class of patient. The bacteriological studies of Rosenow have proven conclusively that primary infection can exist about a tooth, and in the periodontal tissues, and is capable of giving rise to various secondary infections throughout the body. The relationship he has demonstrated between primary and secondary foci shows the importance of complete eradication of existing primary foci of infection.

II. ON THE PRODUCTION OF URIC ACID IN FOCI OF INFECTION: CAUSES OF HYPER-URIC-ACIDEMIA

In our chemical studies we have found a method of determining the existence of a focus or foci of infection in the body, thus providing a means of applying the focal-infection theory to the individual case. It is my desire to express myself as simply as possible, but it will be necessary to use some chemical terms that are more or less familiar to all of you. It is necessary, first, clearly to understand that the blood is a tissue in intimate contact with all other tissues, in order that we may appreciate its value in indicating the presence of infection in any portion of the body. The normal "chemical" constituents of the blood may be divided into the *organic salts*, of proteolytic origin; *inorganic salts*, ingested as such; *carbohydrates*, from starches and sugar; *lipoids*, from cholesterols and fats. At this time we will consider only the constituents of proteolytic origin, not that the others are unimportant but because they do not enter into the present discussion. The studies of these other factors are, however, of inestimable value as indicating the extent of changes, if any, in the general metabolism of the patient. These other substances should, therefore, always be included in any chemical studies of the blood, to ascertain whether their concentration is outside of normal limits.

We have stated that focal infection is essentially a process leading to nuclear degeneration. This, in a word, means the production of nucleic acid. To elaborate somewhat: an infective process in a circumscribed tissue region results in a degeneration and possibly in a destruction of the cellular elements of the part, of the cellular elements of the blood, and of the bacteria themselves. All cells consist of protoplasm, a part of which is differentiated from the rest of the cell and constitutes the nucleus. One of the characteristic chemical substances found in cell nuclei is nucleic acid. The degeneration of cells and their nuclei gives rise to the liberation of "split" proteins and nucleic acid. The amount of nucleic acid produced depends on the number of existing foci, on the virulence of the infecting agent, and on the resistance of the host. We start, therefore, with nucleic acid and study its fate in the organism. This brings us to a consideration of the group of substances of which nucleic acid or its immediate forerunner, nucleoprotein, is a member, namely, the protein group. The metabolic end-products of this group are usually stated to be creatinin, urea, and uric acid; and it is from nucleoprotein or nucleic acid that uric acid is derived.

It will now be necessary to consider, for a moment, the chief avenue of elimination, namely the kidneys. We find that excretion, by the kidneys, of these various metabolic end-products occurs in the following order: first, creatinin, the most diffusible; then urea, intermediate; and uric acid, the least diffusible. For this reason these end-products have long been used as indices of renal permeability or function only. We find, however, that an exceedingly large number of individuals have an increased content of uric acid, with a normal or only moderately increased proportion of urea, in the blood. As further proof that such cases of hyper-uric-acidemia are not of renal origin, we find a normal urine with no fixation of the specific gravity, and no nocturia. The self-evident conclusion, from a series of such cases, is that the increased content of uric acid in the blood is not due to kidney damage, but rather to over-production of this end-product of nuclear degeneration.

Having thus briefly eliminated the kidney as the cause of hyper-uric-acidemia, we can therefore refrain from further mention of urea and creatinin. This brings us, then, to the point of our discussion,

namely, uric acid. We will consider briefly its two sources of origin, exogenous and endogenous. The exogenous sources are the foods rich in nucleic acid and commonly known as the purin group of foods. In this group are meats, legumes, and the edible glands of animals. It is impossible, however, for an individual to consume enough of these foods to produce a persistently high content of uric acid in the blood from this source alone. In other words, when renal function is normal, as indicated by the blood findings for urea and creatinin, the ingestion of food rich in purin bases merely produces a temporary increase in the uric acid in the blood, this uric acid being passed off through the kidneys in a short time. We can, therefore, further eliminate diet as a causative factor for a persistently high content of uric acid in the blood.

The endogenous uric acid arises from katabolism of body cells, and may be normal or abnormal. Such breaking down of cellular elements, when abnormal in amount, is found in a number of conditions, other than focal infections, such as primary anemias, leukemias, severe cachexias following large doses of x-ray or radium. It follows, then, that the conditions which may cause a hyper-uric-acidemia not or focal-infection origin can be eliminated with comparative ease.

III. THE PROPORTION OF URIC ACID IN THE BLOOD AS A DIAGNOSTIC INDEX OF THE EXISTENCE OF FOCAL INFECTION (AFTER EXCLUSION OF OTHER CAUSES OF HYPER-URIC-ACIDEMIA)

In cases in which examination makes it possible to eliminate the foregoing factors, it may be stated that a high content of uric acid in the blood is due to nuclear degeneration, which may be due to focal infection. In fact, if the aforementioned endogenous sources of uric acid are eliminated, such a high blood content must be due to focal infection. This finding makes the data of blood chemistry of inestimable value in the diagnosis of focal infection. We find, for instance, many evidences of infection in the mouth in regions where degeneration is not sufficiently pronounced to be macroscopic, and which have not reached the stage of definite abscess formations with well defined walled-off masses of pus. Such regions, however, invariably present microscopic evidence of inflammatory changes. The periodontal bone

may exhibit rarefaction or condensation, or may show only a change in the arrangement of the cancellous spaces. The variation of such regions, in density or structure, from the normal bone surrounding them may be so slight as readily to escape detection. To my mind, these regions are even more dangerous than those marked off by a layer of dense bone or pyogenic membrane, as they allow toxins to be absorbed freely into the circulation. These regions of diffuse rarefying osteitis and diffuse condensing osteitis, or those that exhibit alterations in the cancellation of the bone, produce virtually the same leukocytic infiltration, the same degeneration of tissue and blood elements, the same liberation of "split" proteins, as does a well defined abscess.

Too often has disappointment for both practitioner and patient followed a diagnosis that was incomplete rather than incorrect. Not only in the mouth, but also in other parts of the body, a definite diagnosis is hard to make. It is safe to say that the major part of the present scepticism regarding the reality of focal infection rests on this point. It is in this respect that chemical studies play so important a rôle. Such blood studies are also extremely valuable as a check on the thoroughness of eradication of the foci found, for, as long as any focus is present, the uric acid findings will not return to a normal level. This search for foci, let me repeat, is frequently most difficult and may require the most intimate form of team work of all concerned. Practice, however, based upon this method, has been most happy in its results. Patients invariably show such a measure of improvement as is to be expected from their history, and in accordance with the regenerative power of the tissues at the sites of the secondary infections.

IV. SUMMARY OF CONCLUSIONS

(1) Clinicians have at their disposal well established methods for the estimation of uric acid in blood.

(2) A persistently high uric-acid value for the blood is indicative of nuclear degeneration, which in turn may mean focal infection.

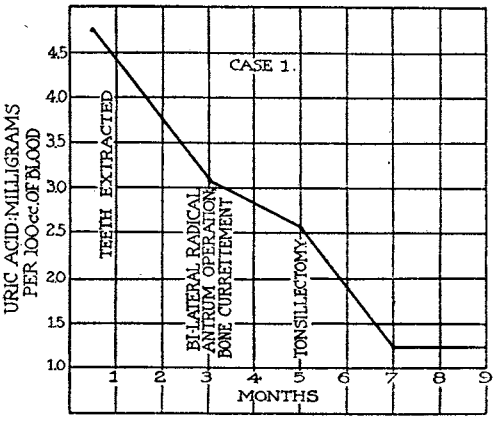
(3) Other factors productive of a high uric-acid value for the blood, aside from nuclear degeneration, are comparatively easy to determine, namely, leukemia, primary anemias, cachexias from whatever cause, and massive doses of x-ray or radium.

(4) Elimination of all foci of infection is followed, invariably, by a return to normal of the uric-acid value for the blood.

(5) Failure to eliminate all foci prevents return to a normal uric-acid value for the blood. The amounts of this substance, therefore, furnish a reliable index for the complete elimination of foci of infection.

V. CASE HISTORIES, WITH CHEMICAL DATA

The following brief case histories, and the accompanying graphs and collateral analytic data, give typical examples of the blood findings and the clinical parallels, selected from a series of 827 cases.



CASE 1. THE AUTHOR. PRONOUNCED ASTHENIA

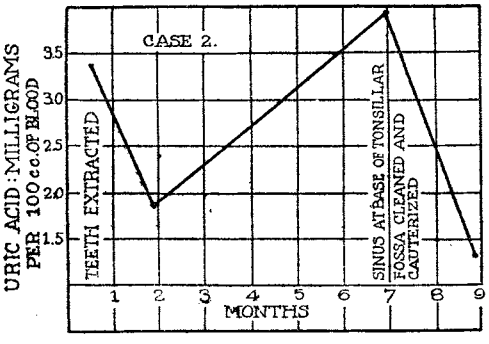
Case 1: Collateral analytic data[2]

	Milligrams per 100 cc. of blood First	Last
Urea	45	30
Urea N	21	14
Total non-protein N	42	28
Creatinin	0.4	0.2
Salt	500	500
Sugar	155	135
Cholesterol	210	175
Fatty acids	800	725
Total fats	1010	900
CO_2 combining power	47.2	49.0
Diastatic activity	31	21
Wassermann test	neg.	neg.
Plasma volume (%)	52	50
Corpuscle volume (%)	48	50

Case 1. The author. Pronounced asthenia. My own case was responsible for my initial interest in the causation of high blood content of uric acid. The physical symptoms could be summed up as indicating a pronounced asthenia. Extraction of several badly infected teeth brought some improvement and a decrease in the blood content of uric acid. A bi-lateral radical antrum operation brought about a still further improvement. The final return to the normal uric-acid level, and to the normal physical condition, was not secured until after tonsillectomy.

[2] In these nine summaries, "first" signifies the initial finding; "last," the finding at the concluding examination. "N" signifies nitrogen. For references to the method of determining uric acid, used by the author, see Myers and Fine: *Journal of Biological Chemistry*, 1915 (xx); and Folin and Wu: *Ibid.*, 1919 (xxxviii).

Case 2. Mrs. F.: age 42. Chronic arthritis. The complaint was pain in the knees, shoulders and elbows, making it difficult for her to help herself; easy fatigue or asthenia. The tonsils had been removed and the throat appeared to be in good condition. Radiograms showed six infected teeth; their removal, with currettement, was followed by great improvement. This patient returned about one year later in greater discomfort than ever, with a higher uric-acid content in the blood than primarily. Investigation showed that the teeth and periodontal tissues were clear. Quite accidentally, in investigating the tonsillar fossa (which appeared clear), a sinus about three-fourths of an inch long was found, filled with purulent material (from which streptococcus viridans was isolated). This was cleaned out, cauterized and kept clean. Recovery quickly followed.



CASE 2. MRS. F.: AGE 42. CHRONIC ARTHRITIS

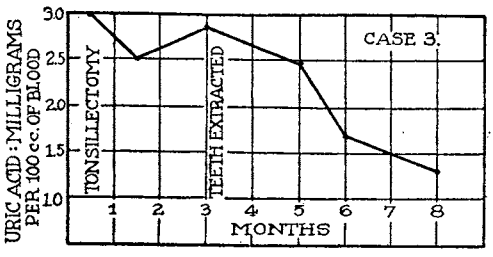
Case 2: Collateral analytic data

Milligrams per 100 cc. of blood

	First	*Last*
Urea	60	45
Urea N	28	21
Total non-protein N	56	42
Creatinin	0.6	0.4
Salt	510	500
Sugar	180	145
Cholesterol	260	220
Fatty acids	980	840
Total fats	1240	1060
CO_2 combining power	47.2	48.4
Diastatic activity	16	25
Wassermann test	neg.	neg.
Plasma volume (%)	58	54
Corpuscle volume (%)	42	46

Case 3. Miss B.: age 34; school teacher. Arthritis. She had been under the care of an orthopedist for two years and was getting progressively worse. Had pain in and some swelling of the ankles, knees and shoulders, so that she had not been able to teach for eighteen months. Some badly infected tonsils were removed, with very slight improvement. She had four definitely infected teeth but did not wish to lose them, as she had just had two fine removable bridges completed at considerable expense. She finally consented to extraction and currettement. Inside of two months there was complete recovery from all symptoms.

Case 4. Mr. H.: age 46. Typical gout. He had some kidney and cardiac complications. He regarded extraction of teeth as a fad, but consented to have three teeth taken out because of local discomfort. There

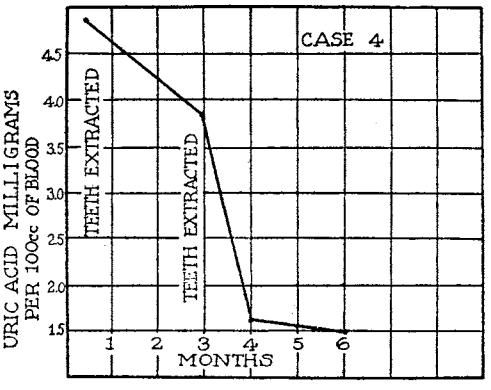


CASE 3. MISS B.: AGE 34. ARTHRITIS

Case 3: Collateral analytic data

	Milligrams per 100 cc. of blood First	Last
Urea	45	30
Urea N	21	14
Total non-protein N	42	28
Creatinin	0.45	0.3
Salt	460	480
Sugar	160	150
Cholesterol	210	190
Fatty acids	840	710
Total fats	1050	1000
CO_2 combining power	47.6	49.0
Diastatic activity.	20	24
Wassermann test.	neg.	neg.
Plasma volume (%)	50	50
Corpuscle volume (%)	50	50

was very slight improvement. After six months he was willing to proceed further and his oral condition was cleaned up. Recovery from the gouty symptoms was uneventful. His renal and cardiac conditions also improved somewhat, although they are still present.



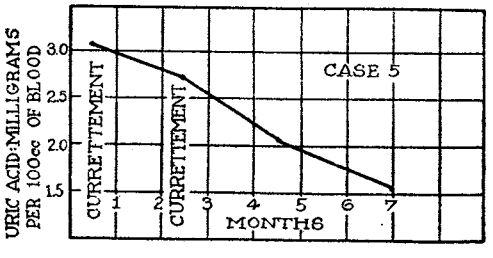
CASE 4. MR. H.: AGE 46. TYPICAL GOUT

Case 4: Collateral analytic data

	Milligrams per 100 cc. of blood First	Last
Urea	75	45
Urea N	35	21
Total non-protein N	70	42
Creatinin	0.6	0.3
Salt	540	490
Sugar	200	160
Cholesterol	230	175
Fatty acids	640	640
Total fats	870	815
CO_2 combining power	47.2	48.0
Diastatic activity.	10	18
Wassermann test.	neg.	neg.
Plasma volume (%)	60	52
Corpuscle volume (%)	40	48

Case 5. Mrs. L. W.: age 48. Diabetes mellitus and arthritis. The patient was in a general subnormal condition, with a very low carbohydrate tolerance. The tonsils had been removed some time previously. All her teeth had been removed. Radiograms, however, revealed several regions of infection in the bone and about two small roots. After currettement, another radiogram was taken and further currettement was done. There

was a slight improvement in her carbohydrate tolerance, although rigid diet is still necessary. The patient also completely recovered from the arthritic condition. Whether this was due to the improvement in her diabetic condition, or to the clearing up of focal infection, I am not prepared to say.

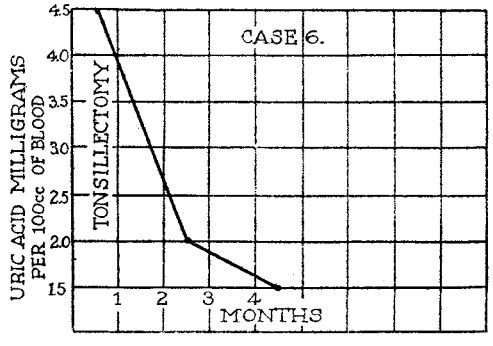


CASE 5. MRS. L. W.: AGE 48. DIABETES MELLITUS AND ARTHRITIS

Case 5: Collateral analytic data

Milligrams per 100 cc. of blood	*First*	*Last*
Urea	60	45
Urea N	28	21
Total non-protein N	56	42
Creatinin	0.3	0.22
Salt	480	485
Sugar	420	200
Cholesterol	240	200
Fatty acids	910	880
Total fats	1150	1080
CO_2 combining power	46.8	47.8
Diastatic activity.	12	18
Wassermann test.	neg.	neg.
Plasma volume (%)	56	50
Corpuscle volume (%)	44	50

Case 6. Miss B.: age 12. Chorea of two years' duration. The tonsils were found to be badly infected and removed. Recovery was uneventful.



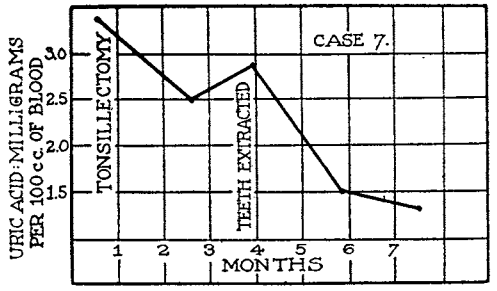
CASE 6. MISS B.: AGE 12. CHOREA OF TWO YEARS' DURATION

Case 6: Collateral analytic data

Milligrams per 100 cc. of blood	*First*	*Last*
Urea	30	30
Urea N	14	14
Total non-protein N	28	28
Creatinin	0.15	0.2
Salt	430	450
Sugar	140	135
Cholesterol	175	200
Fatty acids	625	600
Total fats	800	800
CO_2 combining power	48.0	48.8
Diastatic activity.	22	24
Wassermann test.	neg.	neg.
Plasma volume (%)	50	50
Corpuscle volume (%)	50	50

Case 7. Mr. J.: age 40. Asthma of six years' duration; not seasonal. This patient was not sensitive to any of the food proteins. Blood analysis showed focal infection. The tonsils were manifestly bad. Tonsillectomy

was followed by slight improvement. This patient would not immediately permit removal of the five teeth indicated on the radiograms. Later, there was recurrence of the symptoms. As the blood data still showed the presence of focal infection, he submitted himself to the oral surgeon. Recovery, to date.

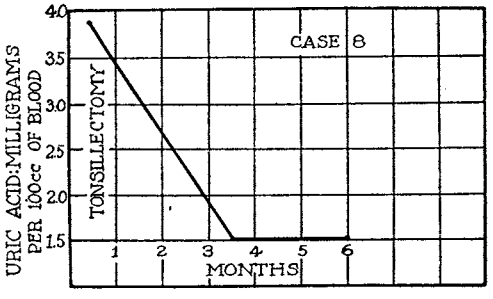


CASE 7. MR. J.: AGE 40. ASTHMA OF SIX YEARS' DURATION; NOT SEASONAL

Case 7: Collateral analytic data

	Milligrams per 100 cc. of blood First	Last
Urea	60	30
Urea N	28	14
Total non-protein N	56	28
Creatinin	0.42	0.31
Salt	490	485
Sugar	160	152
Cholesterol	180	200
Fatty acids	740	710
Total fats	920	910
CO_2 combining power	49.0	49.4
Diastatic activity	20	24
Wassermann test	neg.	neg.
Plasma volume (%)	54	50
Corpuscle volume (%)	46	50

Case 8. Miss E.: age 16. A 3-plus enlargement of the thyroid gland, bi-lateral; also some exophthalmos. There was no tremor but a tachycardia, and disturbance of menstruation, with a plus-12 basal metabolism. The tonsils were infected. Tonsillectomy was followed by slow recovery for six months, when she made complete recovery.

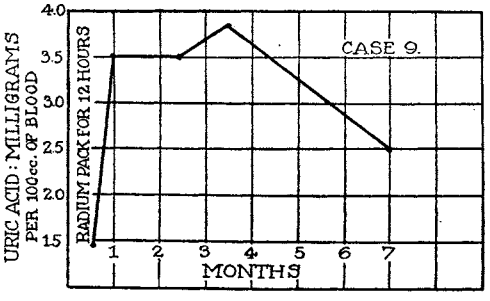


CASE 8. MISS E.: AGE 16. A 3-PLUS ENLARGEMENT OF THE THYROID GLAND, BILATERAL; ALSO SOME EXOPHTHALMOS

Case 8: Collateral analytic data

	Milligrams per 100 cc. of blood First	Last
Urea	30	30
Urea N	14	14
Total non-protein N	28	28
Creatinin	0.2	0.2
Salt	480	470
Sugar	135	140
Cholesterol	190	200
Fatty acids	820	700
Total fats	1010	900
CO_2 combining power	49.2	49.0
Diastatic activity	20	22
Wassermann test	neg.	neg.
Plasma volume (%)	48	50
Corpuscle volume (%)	52	50

Case 9. Mrs. Y.: age 58. The patient had a radium pack for a fibroid tumor. The rise in blood content of uric acid was followed by a partial return to normal. This case is shown simply to illustrate the effects of radium and x-rays on metabolism.

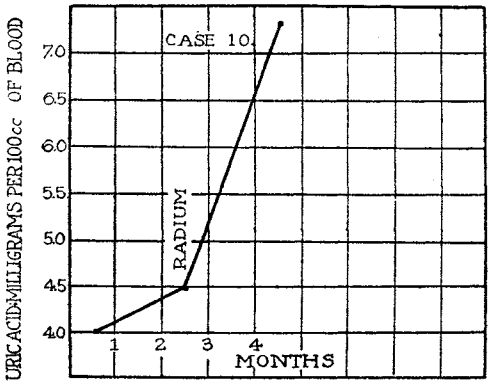


CASE 9. MRS. Y.: AGE 58. THE PATIENT HAD A RADIUM PACK FOR A FIBROID TUMOR

Case 9: Collateral analytic data

	Milligrams per 100 cc. of blood	
	First	*Last*
Urea	45	96
Urea N	21.0	44.8
Total non-protein N	42.0	89.6
Creatinin	0.42	0.7
Salt	490	500
Sugar	160	170
Cholesterol	190	200
Fatty acids	860	740
Total fats	1050	960
CO_2 combining power	48.8	46.8
Diastatic activity.	24	18
Wassermann test	neg.	neg.
Plasma volume (%)	52	58
Corpuscle volume (%)	48	42

Case 10. Mr. L.: age 32. Acute lymphatic leukemia. Uric acid content in the blood was high when first determined, and increased steadily. It rose still more rapidly after radium treatment. The case illustrates



CASE 10. MR. L.: AGE 32. ACUTE LYMPHATIC LEUKEMIA; TREATMENT WITH RADIUM

the effect of this condition on the amount of uric acid in the blood. This case, and case 9, illustrate conditions that have to be eliminated in arriving at a diagnosis of focal infection from the data for uric acid in the blood.

482 Franklin Street