leukemias radium treatment is of no value. In some cases of chronic myelogenous leukemia, however, even when the general condition is very poor at the start, there may be marked temporary improvement. It must be understood, however, that the results should be regarded at the present time merely in the light of palliation and not as a cure. It is hoped, however, that future research will at least increase the duration of these remissions. It is suggested that the spleen be removed during the period of most marked improvement, at the height of a remission when the spleen is of normal size and the general condition of the patient excellent. Although the treatment must not be considered at the present time as curative, from the results obtained it is the best form of treatment now at our disposal.

The remissions last from months to years. In the case above detailed there was a remission of from six to eight months during which the patient was entirely free from symptoms of the disease. In other instances, remissions have lasted from two to three years, although there is always a tendency for the disease to relapse, and each recurrence responds less promptly and less completely to radium treatment. During the remissions, patients may feel entirely well and assume the usual duties connected with their work and social affairs. They are, however, very susceptible to intercurrent infections. A case of fatal pneumonia occurred at the height of the improvement in the remission. Rapid recurrence and death by small gradual or massive hemorrhages or from weakness may occur after benzol and x-ray treatment and also, as in the case above described, after a remission produced by radium. Indeed, such rapid termination is common in untreated cases.

Conclusions. I. Surface applications of radium in leukemia produce striking, indeed remarkable, improvement in (a) the blood picture which becomes almost normal, (b) in the size of the spleen and glands, which are reduced almost to normal, (c) in the general condition of the patient who from an emaciated and weak condition may become plump and strong. II. The duration of remission is variable, it may last from months to years. III. The results of radium treatment are *not* regarded as *curative*. It is believed to be, however, the safest as well as the most prompt palliative measure in cases of chronic leukemia whether *refractory* or not to benzol or x-ray treatment. From the results of radium therapy in leukemia it is believed to be the best form of treatment now at our disposal.

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A METABOLISM STUDY OF A CASE OF LEUKEMIA DURING RADIUM TREATMENT.*

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IN conjunction with a careful clinical study of a case of myelogenous leukemia treated by surface application of radium it was thought it might be of especial interest to study the metabolic output in the urine of the patient. In the literature there are numerous reports of the metabolism in leukemia cases, some without treatment, some during various treatments, among them the action of x-rays, but none, as far as the authors know, of the study of a case treated by surface application of radium.

Von Moraczewski¹ in a study of a case of chronic leukemia, concluded that leukemia is a nitrogen and phosphorus disease and found that almost all constituents, especially phosphorus and nitrogen, in the food, were retained abnormally, because of a lack of katabolism.

In "splenomedullary leucocythemia" Milroy and Malcolm² likewise observed an absolute diminution of phosphorus excretion. These observers also noted that the proportion of alloxuric nitrogen (uric acid and bases) to total nitrogen was increased. Later³ in "lymphatic leucocythemia" they found a marked diminution in the absolute amount of phosphorus excreted. In this case which they studied the uric acid and bases were hardly affected. In a case of "medullary leucocythemia," where the number of leucocytes was rapidly falling, the phosphorus excretion was found to have undergone no diminution, while the uric acid and the bases were diminished. White and Hopkins⁴ observed no relation between leucocytosis and the excretion of the products such as phosphorus and alloxuric bodies which result from katabolism of nuclein.

In complete balance experiments with cases of lymphatic and myelogenous leukemia Stejskal and Erben⁵ found in one chronic lymphatic case a marked nitrogen retention, indicating, according to them, diminished power of oxidation. In the case of myelogenous leukemia there was a slight retention of the nitrogen and phosphorus. Y. Henderson and Edwards⁶ in a case of lymphatic leukemia which they studied over a long period (6½ months), found that, notwithstanding, an enormous leucocytosis (175,000-380,000 per cu. mm., of 96% lymphocytes) and in spite of alternation of periods of great increase and marked diminution in the number of circulating corpuscles, the excretion of phosphorus and uric acid was at no time excessive. They believe leucocytosis to be due

* Clinical study of this case is reported by Dr. Thomas Ordway in a separate article.

not to general increase in nuclein metabolism but to failure in normal destructive metabolism. In the course of their study they observed two periods; in the first, nitrogen was subnormal, uric acid slightly above normal, and phosphorus distinctly subnormal; in the second period there was a distinct diminution of nitrogen, an increase of uric acid, and a further great reduction in phosphorus.

Henderson and Edwards, by the changes in the amount and the proportion of urinary constituents during their own much more protracted observations, harmonize the conflicting observations of Milroy and Malcolm, Von Moraczewski, and White and Hopkins by showing that their apparent differences are probably due to the fact that these experimenters made their observations at different stages in the progress of the disease.

Symmers⁷ found the excretion of organic phosphorus in the urine pronounced in lymphatic leukemia.

In a case of myeloid leukemia treated by Roentgen rays Lossen and Morawitz⁸ found that the volume of urine was diminished, that the total nitrogen, uric acid and phosphorus excretions were lowered, and that the number of leucocytes was diminished (350,000-212,000). On continued treatment the uric acid content decreased, the nitrogen elimination remained the same and the phosphorus content increased. Königer⁹ in myeloid leukemia under the influence of Roentgen rays found that the uric acid excretion increases parallel with the retraction of the spleen and the breaking up of the leucocytes, and that the uric acid excretion is a positive measure of cell breakage, but not an index to the extent of the cell destruction. Ammonia and phosphates show at times an increase generally parallel with nitrogen increase and also with the betterment in the leukemic symptoms.

In a metabolism study of leukemia under the influence of Roentgen rays, Musser and Edsall¹⁰ found that the phosphorus metabolism is of particular interest. In conditions where leukemia symptoms are progressing, there is a constant construction of tissues that are rich in phosphorus and, hence, they believe there will be a retention, and since leukemia tissues contain large amounts of phosphorus the retention is relatively large. The excretion of nuclein products of disintegration of uric acid, purin bases, and phosphates is likely to be high, due to a large amount of nucleins in leukemia tissue. By the influence of Roentgen rays in three-day periods the nitrogen excretion increased about 70%, the uric acid about 60%, the purin bases about 260% and the phosphates about 200%. The authors explain this action of Roentgen rays as due to accelerating autolysis.

EXPERIMENTAL.

Since the clinical aspects of this case are discussed in a separate paper by Dr. Ordway,

no description of it is needed here other than to say that the patient was a woman, 30 years old, suffering from myelogenous leukemia. The spleen was greatly enlarged and the white count was 495,000 at the beginning of radium treatment.

The treatment consisted, briefly, in applying 50-60 millicuries of radium emanation (50-60 mg. of radium element) to small areas on the abdomen, which was marked off, indicating the outlines of the enlarged spleen. Each area was rayed for four hours during the first series and six hours during the second and third series of treatments. Each series of treatments required three to four days to cover the surface over the area of the enlarged spleen. Between each series of treatments about four to six weeks were allowed to intervene, the time being determined by the examination of the blood.

No attempt was made carefully to regulate the diet, although a record of food taken was kept and found to vary within narrow limits. The diet was practically purin free during and following the series of treatments. It consisted chiefly of bread, cereal, potatoes, milk, butter, eggs, fruit, and, occasionally, beef, chicken, and a few vegetables.

The urine was collected for 24-hour periods in thymolized bottles and brought to the laboratory for analysis immediately after the 24-hour period was up. At the beginning of the first series of treatments the urine was collected daily from November 6 to 13, inclusive, and after that date it was collected on an average of three times a week except during two periods of a week each when it was discarded because of menstruation.

Total nitrogen was estimated by the modified Kjeldahl method, urea by the urease method, ammonia by Folin's method, uric acid by Benedict's modification of Folin's colorimetric method, creatinin by Folin's method, phosphoric acid by titration with uranim acetate, and the acidity by Folin's method. The urine was at all times during the treatment free from albumen and sugar.

The results of the observations during and following the three series of radium treatments are given in the accompanying table with a report of the white and red blood count taken from Dr. Ordway's paper. Unfortunately, we were unable to obtain the urine several days before the series of treatments began so as to have a preliminary period to compare with the action of radium. However, the first day's sample of urine was partly collected during no radium treatment, as treatment was not begun until 6 p. m. and most likely radium had little effect in that sample of urine, the period of which was up at 8 a. m. the next morning. Also, in taking into consideration the results of a number of investigators, it is noted that the period during no effective treatment or increase in leukemia symptoms is characterized by re-

TABLE OF URINARY ANALYSES AND BLOOD COUNT

Date	Volume	Sp Gr	Total N	Urea N	Ammonia N	Creatinine N	Uric Acid	Total Acidity N/10 HCl	Total Phosphate P ₂ O ₅	Red blood cells	White blood cells
1915	cc.		gm	gm	gm	gm	gm	c.c.	gm		
Nov 6	First series of		Radium	Treatments							
	802	1.017	5.440	3.184	0.265	0.333	0.078	174	0.714	2,790,000	495,000
7	810	1.017	5.530	4.440	0.344	0.346	0.095	251	0.803		
8	900	1.017	6.280	4.549	0.376	0.381	0.187	256	0.847		
9	1030	1.016	7.084	5.373	0.405	0.379	0.189	334	1.086	2,930,000	446,000
10	1053	1.018	6.906	5.438	0.376	0.320	0.193	354	1.175		
11	1090	1.018	10.190	8.442	0.577	0.352	0.211	403	1.66		
12	1210	1.017	11.890	9.045	0.674	0.413	0.229	600	1.96		
13	1057	1.017	9.375	7.091	0.594	0.307	0.168	413	1.486	2,910,000	430,000
16	1040	1.014	8.508	5.325	0.728	0.305	0.206	330	1.114	3,090,000	406,000
18	1060	1.014	8.324	6.690	0.811	0.356	0.224	389	1.134	2,900,000	325,000
20	1088	1.012	6.276	5.118	0.584	0.341	0.158	256	1.351	2,980,000	264,000
22	1500	1.01	7.045	6.311	0.480	0.435	0.299	247	1.461		
27	1200	1.015	7.537	6.093	0.51	0.379	0.281	367	1.2	3,020,000	
Dec 8	920	1.016	8.528	6.428	0.698	0.364	0.189	383	1.452		
10	1175	1.016	9.220	7.633	0.698	0.309	0.283	358	1.21	3,680,000	332,000
18	Second series of		Radium	Treatments							
24	800	1.02	9.177	5.539	0.553	0.319	0.287	374	1.886	3,700,000	110,000
28	1275	1.016	10.941	9.509	0.663	0.439	0.262	475	3.89	3,720,000	72,000
Jan 4	1125	1.019	10.570	8.372	0.545	0.448	0.227	467	2.02	3,760,000	74,000
10	800	1.023	6.440	4.821	0.495	0.345	0.177	286	1.443		
12	950	1.022	7.626	4.852	0.418	0.377	0.182	256	1.215		
14	1040	1.018	6.938	5.194	0.427	0.411	0.196	289	1.920	3,920,000	630,000
17	900	1.025	8.256	6.184	0.385	0.406	0.249	292	1.323		
19	940	1.018	7.343	5.609	0.480	0.425	0.251	237	1.276		
22	1410	1.017	9.083	7.546	0.369	0.388	0.206		3.854		
26	1135	1.023	11.045	9.579	0.470	0.399	0.249	416	2.032		
27	Third series of		Radium	Treatments							
Feb 2	1000	1.02	9.430	8.338	0.605	0.326	0.161	350	2.604		
4	1220	1.021	11.450	9.774	0.694	0.437	0.169	448	3.35		
8	1020	1.024	10.320	8.669	0.206	0.430	0.210	416	2.134	4,100,000	17,800
10	1120	1.022	8.862			0.396	0.229		1.490		
12	1190	1.008	8.332				0.186		2.048		
17	1175	1.024	10.754	7.776	0.420	0.442	0.173	331	2.241		
19	1100	1.022	9.362	8.008	0.461	0.466	0.181	289	1.687		
22	1087	1.025	12.219				0.195	430	2.103	4,380,000	14,400
29	1100	1.024	11.860	9.317	1.532	0.414	0.281	434	2.363		
Mar 3	1210	1.024	12.439			0.204	0.294	320	1.247		

tention of nitrogen, phosphoric acid and uric acid.

Examining the table of analyses it is noted that the volume of urine increased 50% in the first seven days from the beginning of treatment. The total nitrogen, urea nitrogen, and ammonia nitrogen excretions likewise showed remarkable increases in the first seven days. The total nitrogen increased about 115%, urea nitrogen 140%, and ammonia nitrogen 150%. The uric acid nitrogen increased less than any of the other nitrogen excretions, only about 28%. We would expect the uric acid to increase considerably more since the tissue which is disintegrated is rich in nuclein material and should be among the products of disintegration. It may be that the uric acid is broken down further, due to radium having a disintegrating action on uric acid as it does in vitro. According to Sarvonat¹¹, radium emanation decomposes uric acid; oxalic acid is found among the products of decomposition. Another theory why uric acid may not be increased so much is that

of Gudzent and Lowenthal¹². They found that radium emanation has a pronounced influence on purin metabolism. The action being due to activation of those ferments which are responsible for building up or for cleavage of uric acid according to which ferment action predominates. In the above instance in which we would expect the uric acid to increase considerably it may be possible that the cleavage ferment is activated and in which case it would break up the uric acid.

Coincident with the increase of the nitrogen constituents, the total acidity and phosphates show a very decided increase; the former is increased by about 235% and the latter 174%. The total acidity was parallel, to a certain extent, with the excretion of the total phosphates.

After the seventh day of the first series of treatments all of the excretory products show a slight drop. However, these excretory products, in spite of this drop, are at a higher level at the time of the next series of treatments than at the beginning of the first series.

Charts showing results of Urinary Analyses and Blood Count.

In the second series of treatments which began December 18 we were unfortunate in not getting any samples of urine for several days on account of the menstrual period. However, it seems that the same effect occurs as in the first series—an increased excretion. The total phosphates reaching in this series on the tenth day an increase of 445% over the excretion for the first day of the experiment. The high level of excretion seems to occur about the tenth day compared to the seventh day in the first series. There is in this series a slight drop in the excretions after the tenth day and then later a rise so that at the beginning of the third series of treatments the excretions are again at a higher level. It may be that the radium action is still effective at this date or that there is very little or no retention of products at this stage of the disease.

The third series of treatments began January 27. Since excretions were high just before the treatment began there does not appear a decided increase in any of the constituents except the phosphates on the eighth day after the beginning of the third series.

It is interesting to note in the first series of radium treatment that the increase in the excretory products in the urine begins immediately and reaches a maximum in about seven days while the drop in white blood count is more gradual in that time. The greatest drop in the number of leucocytes occurred between the twelfth to fifteenth day after treatment.

It is also very striking that throughout the series of treatments the uric acid excretion is not excessive at any time, which might be expected to run more or less parallel with phosphorus excretion.

The charts showing the results of the urinary analyses and blood count also aid in showing the changes brought about by the radium treatment and are more or less self-explanatory.

CONCLUSIONS.

The excretions of total nitrogen, urea, ammonia and phosphates are enormously increased immediately after the action of radium.

The uric acid output is only slightly increased compared to the other nitrogenous constituents.

Surface applications of radium over the spleen accelerates the disintegration of nuclein tissue, resulting in the above increases. The uric acid which would be expected to be formed by disintegration of nuclein is probably broken up further so that it is not increased.

The phosphates show the most remarkable results, increasing as high as 400%, at times, over the excretions at the beginning of treatment.

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Book Reviews.

A Reference Hand Book of the Medical Sciences.

Third edition, completely revised and rewritten. Edited by THOMAS LATHROP STEDMAN, A.M., M.D., complete in 8 volumes. Volume VII. New York: Wm. Wood & Company. 1917.

This seventh volume of the third edition of the familiar handbook originally edited by Dr. Albert H. Buck and embracing the entire range of scientific and practical medicine and allied science, includes the subjects alphabetically from Pacchioni to Storax. It is the work of over one hundred contributors, including many familiar names of distinction in the United States and Canada. The volume is well illustrated with numerous chromo-lithographs and with 469 half tones and wood engravings. The series to which it belongs is a valuable adjunct as a work of reference in the library of every physician.

Care of Patients Undergoing Gynecologic and Abdominal Procedures, Before, During and After Operation. By E. E. MONTGOMERY, A.M., M.D., LL.D., F.A.C.S. Illustrated. Philadelphia and London: W. B. Saunders Company. 1916.

The little book gives to the intern an excellent view of some gynecological procedures. It is especially to be recommended to the novice to whom, at the beginning of his work in the hospital, everything is "unusual." It helps him to find himself and his place more quickly, particularly in hospitals where the house-officer is expected to absorb information and grow in knowledge without much instruction from his superiors. It is clear, compact and sound.