METABOLISM STUDIES BEFORE AND AFTER SPLENECTOMY IN A CASE OF PERNICIOUS ANEMIA *

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The present case is reported as a corollary to the other studies of metabolism before and after splenectomy reported from this laboratory.¹

In one of these² the literature concerning metabolism in anemia, before and after splenectomy, is thoroughly reviewed. Few references to the literature therefore will be given here. In brief the results of studies of metabolism before and after splenectomy for various types of anemia and in normal animals may be summarized as follows: (1) There is little or no change in the total nitrogen metabolism or in its partition, with the exception of a decrease in the uric acid excretion after splenectomy in certain cases. (2) A decrease in the elimination of iron occurs in certain cases after splenectomy. (3) A decrease in the output of urobilin and urobilinogen is noted in certain cases after splenectomy.

This decrease in the daily elimination of uric acid, iron and urobilin after splenectomy is apparently most marked in those cases in which before splenectomy there has been conspicuous evidence of increased hemolysis, indicated by abnormally high excretion of uric acid, iron and urobilin or by a lemon yellow color of the skin.

Robertson³ emphasizes the fact that cases which had shown a high urobilin excretion before splenectomy and in which after splenectomy the urobilin output exhibited only a transient reduction, or none at all, did not show as much improvement in other respects following the

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1. Austin, J. H., and Pearce, R. M.: The Influence of the Spleen on Iron Metabolism, *Jour. Exper. Med.*, 1914, xx, 122. Goldschmidt, S., Pepper, O. H. P., and Pearce, R. M.: Metabolism Studies Before and After Splenectomy in Congenital Hemolytic Icterus, *THE ARCHIVES INT. MED.*, 1915, xvi, 437. Goldschmidt, S., and Pearce, R. M.: Studies of Metabolism in the Dog Before and After Removal of the Spleen, *Jour. Exper. Med.*, 1915, xxii, 319.

2. See paper by S. Goldschmidt, O. H. P. Pepper, and R. M. Pearce, reference given in Footnote 1.

3. Robertson, O. H.: Urobilin in the Stool in Pernicious Anemia, as Influenced by Splenectomy, Transfusion and Salvarsan, *THE ARCHIVES INT. MED.*, 1915, xvi, 429.

operation as did those cases in which the urobilin output was permanently reduced after splenectomy. However, Lee, Vincent and Robertson⁴ state that in some cases of severe anemia which showed marked symptomatic improvement for several months after splenectomy there was throughout this postoperative period a continued high excretion of urobilin. The highest degrees of hemolysis over a prolonged period are probably to be found in congenital hemolytic icterus. In the study of this condition reported from this laboratory² the output of uric acid showed a decrease of 47 per cent. after operation, the iron in the feces decreased 40 per cent. and the excretion of urobilin plus urobilinogen after the splenectomy was only about one-ninth that before the operation. The excretion of these substances had been extremely high before the operation.

The case here reported was studied in contrast as a case of pernicious anemia with evidence of increased hemolysis. The study was limited to the total nitrogen, the uric acid, the iron and the urobilin and urobilinogen. Three periods were studied: one before transfusion and splenectomy, one two weeks after splenectomy, and the third two weeks later. During each period the patient was on a carefully controlled Folin metabolic diet, and the period was not commenced until the patient had reached an approximate nitrogen balance. The nitrogen of the food and urine was determined by the Kjeldahl-Gunning method, the uric acid according to Folin's permanganate method, the iron by Neumann's method and the urobilin and urobilinogen according to the method of Wilbur and Addis. Only negligible amounts of urobilin or urobilinogen were at any time found in the urine.

The history and findings in the case will be given briefly. The blood examinations are tabulated in Table 1 and the metabolic results in Table 2.

Clinical Notes.—The patient, a man, aged 40, had complained for two years of weakness, dizziness, dyspnea and edema. These symptoms were steadily becoming worse. In other respects his history is unimportant. The physical examination revealed nothing noteworthy other than the signs of intense anemia, associated with a lemon yellow pallor. The liver edge was just palpable. At operation the spleen was found to be about three times its normal size, weighing 340 gm. The pathologic examination of the spleen showed chronic diffuse and follicular hyperplastic splenitis, with passive congestion and excessive pigmentation. The Wassermann was negative. On account of a constant eosinophilia repeated careful examinations were made of the stools for ova or parasites, but with negative results. The other laboratory reports are unimportant. The patient improved gradually after the splenectomy and six months later was doing fairly arduous work, apparently in perfect health.

4. Lee, R. I., Vincent, B., and Robertson, O. H.: Immediate Results of Splenectomy in Pernicious Anemia, *Jour. Am. Med. Assn.*, 1915, lxx, 216.

TABLE 1.—BLOOD EXAMINATIONS

Date	Hemo- globin, %	Erythro- cytes	Leuko- cytes*	Nucleated Erythrocytes	Reticu- lated Erythro- cytes, %	Remarks
3/28/15	26	1,150,000	4,600	Normoblasts + Megaloblasts +		Coagulation time, 4.5 min.
4/ 8/15	25	1,620,000	5,800	Megaloblasts +		
4/15/16	20	1,110,000	2,000	0	4	Hemolysis in NaCl: partial 0.425, com- plete 0.325
5/ 3/15	20	1,700,000	6,500	0	2	Left hospital for a month
6/ 5/15	28	1,300,000	4,300	Normoblasts +	1	Platelets less than 100,000
6/ 7/15						Transfusion 900 c.c.
6/ 8/15	40	1,810,000	3,800	0		
6/12/15						Splenectomy
6/15/15	37	1,420,000	16,600			
6/21/15	40	2,930,000	12,000	Normoblasts ++		
6/24/15						Severe hemorrhage from throat
6/24/15	27					After the hemorrhage
6/28/15	28	1,640,000	3,700	Normoblasts +		
7/ 9/15	31	1,630,000	6,300	0		
7/15/15	35	2,370,000	6,000	Normoblasts + Megaloblasts +		
7/22/15	48	2,030,000	8,100	Normoblasts +		
7/30/15	55	2,570,000	7,400	Normablasts +		
8/ 6/15	69	2,300,000	9,100	Normoblasts +	1	Howell-Jolly bodies +
8/16/15	48	3,200,000	8,300	0		
8/24/15	54	3,700,000	8,400	0		
8/29/15	70	3,580,000	9,400	0		
8/30/15						Discharged
1/ 8/16	83	4,400,000	10,500	Normoblast, occasional		Count by Dr. S. L. Freeman

* The differential counts of the leukocytes always showed a slight eosinophilia, but were otherwise normal. The erythrocytes showed the changes characteristic of severe anemia; these became less marked as the anemia disappeared.

TABLE 2.—EFFECT OF SPLENECTOMY ON ELIMINATION OF URIC ACID, IRON AND UROBLIN

Period	Date	Weight in Pounds	Nitrogen Intake, Gm.	Urine			Feces		Total Nitrogen Output, Gm.	Nitrogen Balance, Gm.	Uroblin and Urobilinogen
				Amount, C.c.	Total N, Gm.	Uric Acid, Mg.	Total N, Gm.	Iron, Mg.			
I	4/28/15	170½	16.7	1,550	14.8	762	1.46	17	16.26	+0.44	4/9/15 to 4/12/15, 18,300 per day
	4/29/15		17.6	1,820	16.2	824	1.46	17	17.66	—0.06	
	4/30/15		16.7	1,600	13.7	728	1.46	17	15.16	+1.54	
	5/ 1/15		17.2	1,680	14.5	788	1.46	17	15.96	+1.24	
	5/ 2/15	172½	16.6	2,200	16.2	832	1.46	17	17.66	—1.06	
	Average		16.96	1,770	15.08	791	1.46	17	16.54	+0.42	
	6/12/15	175	Splenectomy								
II	6/24/15		15.7	1,160	10.86	500	1.09	10	11.95	+3.75	6/25/15, 16,500 per day 6/28/15 to 7/2/15, 16,000 per day
	6/25/15		16.8	1,340	12.48	520	1.09	10	13.57	+3.23	
	6/26/15		17	1,600	14.76	740	1.09	10	15.85	+1.15	
	6/27/15		17.3	1,590	15.54	680	1.09	10	16.63	+0.67	
	Average		16.7	1,420	13.41	610	1.09	10	14.50	+2.20	
III	7/ 6/15	160½	17.2	1,000	14.2	680	1.97	..	16.17	+1.03	
	7/ 7/15		16.3	1,380	14.1	680	1.97	..	16.07	+0.23	
	7/ 8/15		16.6			...	1.97	..			
	7/ 9/15		17.2	1,210	13.44	500	1.97	..	15.41	+1.79	
	7/10/15		16.8	1,310	15.06	620	1.97	..	17.03	—0.23	
	7/11/15	162	16.4	1,290	14.82	640	1.97	..	16.79	—0.39	
	Average		16.75	1,360	14.82	624	1.97	..	16.29	+0.46	
	8/22/15	190				...		..			8/18/15 to 8/22/15, 2,300 per day

COMMENT

The figures of this study as given in the Tables show that but little change in the elimination of uric acid and iron took place as a result of the splenectomy. The direction of the changes is, however, in each instance, in accord with the more pronounced changes reported where the hemolytic factor was more marked.

In view of the fact that the nitrogen balance is practically identical in the first and third periods, it may be concluded that splenectomy in this case, as in other cases reported in the literature, is without effect on the total nitrogen balance. The distinct positive balance during the second period is of interest, but probably of no significance in relation to splenic function. The uric acid elimination before operation can not be said to be other than a high normal figure, and the lower postoperative figures are still within normal range; but when it is considered that the diet and régime in general was identical before and after operation, the lowered output after operation is definite and significant. The same can be said of the figures for the iron elimination.

In the combined urobilin and urobilinogen elimination a definite change is noted following the splenectomy. Two weeks after splenectomy the diminution in the urobilin output was negligible, the difference between 18,300 units per day and 16,000 being too slight to permit of significance being attached to it. Two months after splenectomy, however, at a time when the blood count showed a pronounced and most satisfactory improvement, the urobilin output had fallen to one seventh of its former figure and had reached a low normal elimination.

SUMMARY

In an adult with pernicious anemia of a moderately hemolytic type, splenectomy was followed by disappearance of the discoloration of the skin and by prompt and persistent improvement in the condition of the blood and general health. Metabolism studies before and after splenectomy gave the following results.

1. A slight positive nitrogen balance before splenectomy was followed by an increased nitrogen retention fourteen days after operation and a return to the preoperative balance after one month.
2. The output of uric acid, although never exceeding normal limits, showed a decrease of 22 per cent. after operation.
3. The output of iron through the feces, although never above normal, showed a decrease of 40 per cent. after operation.
4. The excretion of urobilinogen and urobilin in the feces before splenectomy was about three times the normal; two months after operation the output was about one seventh of that before splenectomy.