A NOTE ON THE EFFECT OF CERTAIN ANDROGENS UPON THE RED BLOOD CELL COUNT AND UPON THE GLUCOSE TOLERANCE*

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As experience with the clinical use of potent androgens accumulates, it becomes more apparent that many effects occur which are not limited to the masculinizing action of the drugs. Androgens are known to cause retention of water, sodium, chloride and nitrogen[1,2,3] and to increase body weight. They favor increased metabolic rate[4,5,6,7] and such an increase in basal metabolism usually is accompanied by weight gain and by relatively little shift in the blood pressure and pulse rate.

In reviewing blood counts done chiefly at random over a period of months or years during androgen therapy, we have become impressed by the increase in red cell count which occurs. Recently more systematic efforts have been made to follow the blood picture during androgen therapy for hypogonadism and a consistent rise in red cell count has been found. This seems especially definite following methyl testosterone therapy, due perhaps in some part to the fact that relatively large doses of this androgen have been used in our cases. A rise in hemoglobin and in hematocrit levels may be accompaniments.

Table 1 demonstrates changes in the basal metabolic rate, pulse rate, weight and the blood picture in a case of eunuchoidism treated over a long period of time. This patient developed severe hypogonadism following mumps at the age of 13 years and showed the typical clinical evidences of the disease. The patient was 32 years of age in 1932. The type and dose of androgen used is noted in the chart. The androtin mentioned as having been used from January 1933 to January 1938 was a urinary extract of relatively low potency. No significant increase in basal metabolism accompanied its use. The marked increase in weight is not considered to be due to the drug as it is not a consistent finding with the use of this extract in other cases. The basal metabolism rose during 1938 while the patient was receiving testosterone propionate, and fell to its pretreatment level or below between October 1939 and February 1940 during which time treatment was not given. The patient was given methyl testosterone orally during 1940 in the doses indicated. The metabolic rate rose approximately 25 per cent and had not fallen three weeks after cessation of the therapy. Thirty-six days after treatment was stopped, however, the basal metabolism was again low. The relatively slight change in pulse rate is shown. The gain in weight parallel-

*The testosterone propionate (Oreton) and the methyl testosterone (Oreton-M) used in these studies were donated through the courtesy of Dr. Max Gilbert and Dr. E. Schwenk of the Schering Corporation.

TABLE 1

Date	*Androgen Therapy in milligrams*	*Basal Metabolic Rate*	*Pulse*	*Weight*	*Red Blood Cells in Millions*	*Hemoglobin*	*Hematocrit in cc. per 100*
1932 Dec.		—24	72	160	4.16	74	39
1933 Jan.	Androtin						
Feb.		—28					
March					4.54	81	38
May					4.43	78	38
Aug.					4.01	75	34
1934 June					4.28	80	36
1935 Jan.					4.60	84	
Dec.		—27		192	4.40	91	
1937					4.20	72	
1938 Jan.	Testosterone propionate 5 mg. daily I.M.						
Mar. 1	25 mg. daily I.M.						
July 20	50 mg. daily I.M.						
Sept.					5.04	84	46
Sept. 20	25 mg. daily I.M.						
Oct. 3		—18					
Oct. 30	50 mg. daily I.M.						
Nov.					4.98	94	46
Dec. 6		—17	57	198			
1939 Feb. 8	50 mg. 3 times week I.M.						
Oct. 10	Therapy discontinued						
1940 Feb. 23	No therapy	—29	57	194			
Feb. 24	Methyl testosterone 50 mg. daily O.						
Mar. 27	100 mg. daily O.						
April 3	100 mg. daily O.	—15	69	197			
Aug.					5.31	94	48
Aug. 7	100 mg. daily O.	— 6	56	207			
Aug. 8	150 mg. daily O.						
Sept. 24	150 mg. daily O.	— 8	68	203	5.32	91	49
Nov. 6	100 mg. daily O.						
Nov. 12	Therapy discontinued	— 6	64	200	5.64	100	51
Dec. 3	No therapy	— 1	56	192	5.12	91	44
Dec. 16	No therapy				5.03	94	42
Dec. 18	No therapy	—22	76	190			
Dec. 23	No therapy	—18	58	190			

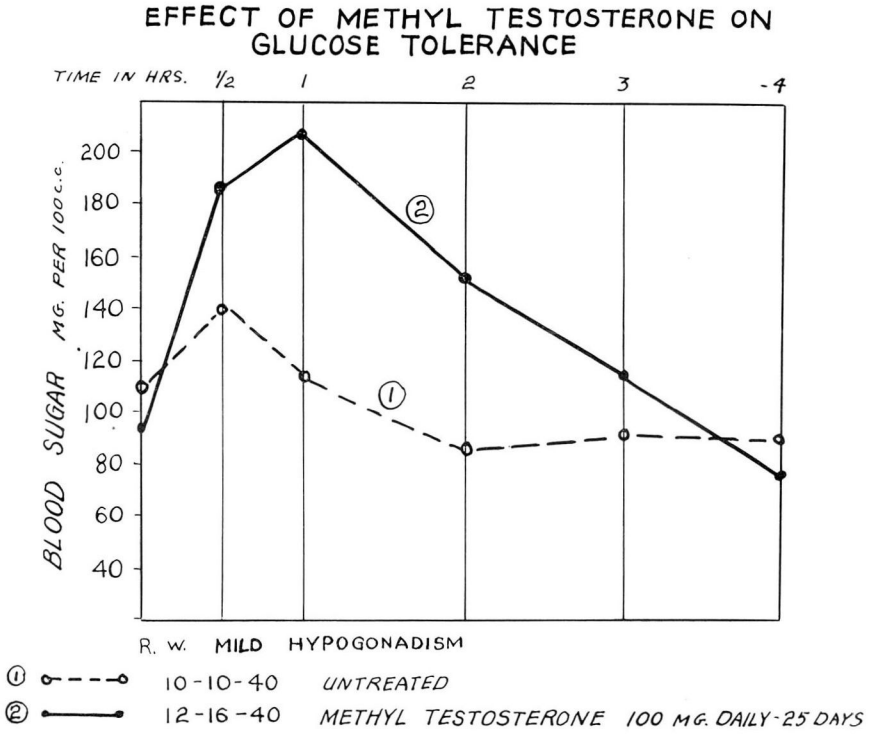

CHART I

ing the increase in the basal metabolic rate and the fall of ten to fifteen pounds on stopping treatment is typical of the effect of this drug.

This table is shown particularly to demonstrate the shift in blood count which occurred. That there should be an increase in red cell count due to androgens is not surprising if we recall that the red cell count of men is higher than that of women and children. Also, abnormally high red cell counts commonly are found in cases of adrenogenital syndrome, or Cushing's syndrome, in which there is an increase in masculinization or evidence of an excess of related steroids. This case was chosen as an example because the blood counts are spread over a long period of time, because they were all done with special care in the hematology research laboratory of Dr. Russell L. Haden and by the same technician (Miss Irene Smith) throughout. The patient was receiving relatively small doses of androgens between January 1933 and January 1938, but following January 1938 potent androgens in much larger dosages were used. Iron in various forms was prescribed from time to time prior to January 1938 but none since then. The length of time iron was used following each prescription is not shown in the records, and due to the infrequency of the blood counts the effect of the iron is not clearly apparent. The persistence of the tendency to anemia is obvious, how-

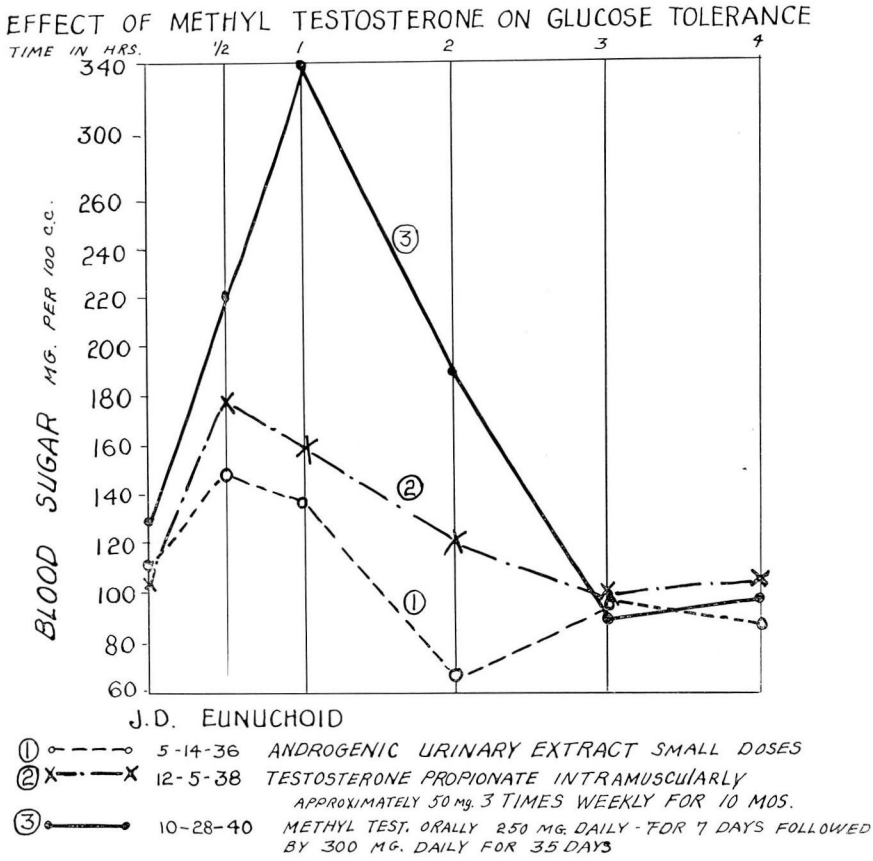

CHART II

ever. The following prescriptions for iron are shown in the records: August 1933, Blaud's mass, gr. XXX daily; October 1933, Blaud's mass, gr. XXX daily; June 1934, reduced iron; May 1937, Cupron (Ayerst, McKenna and Harrison) 3 capsules daily.

It will be seen that there was a prompt decrease in red cell count, hemoglobin and a reduction in hematocrit levels following the withdrawal of therapy in November 1940. According to our knowledge of the effect of methyl testosterone upon water retention, it seems relatively sure that the weight loss which occurred between November 12 and December 18 was due chiefly to water loss. This, if it had been responsible for a shift in red cell count, should have tended to concentrate the blood and raise the hematocrit level. Thus, it appears the more likely that the high red cell count and high hematocrit level shown on November 13 represent an actual increase in red cell mass.

Another recently observed change which has followed the use of methyl testosterone is a decrease in tolerance for glucose. It is not

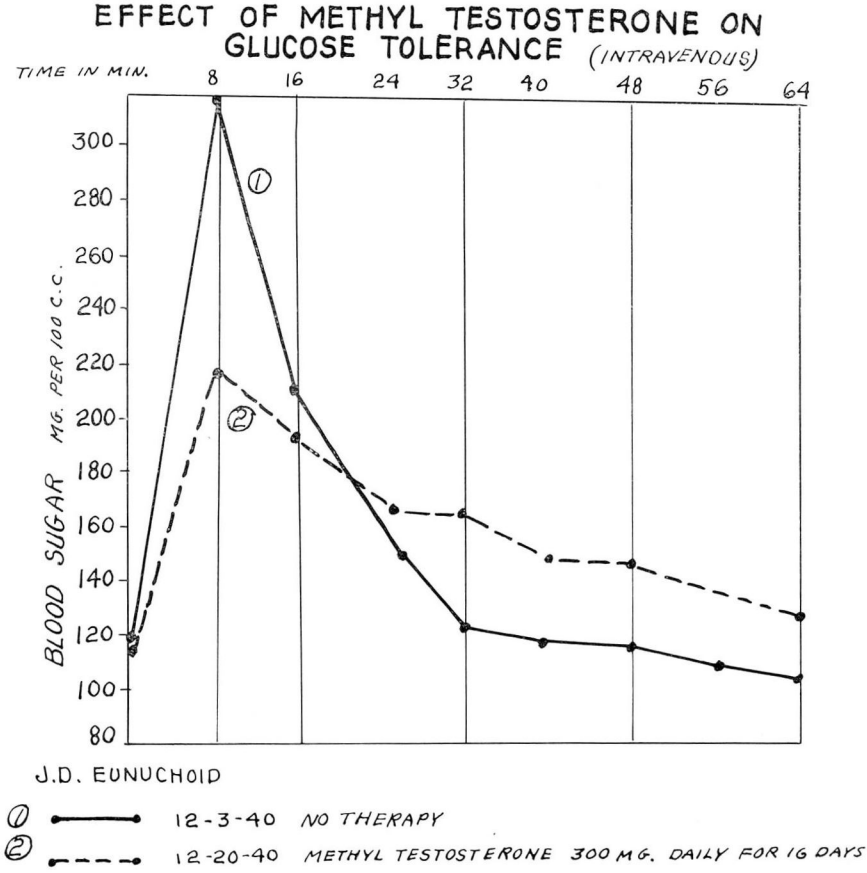

CHART III

apparent to us at this time how closely this may be related to other metabolic effects of the drug or whether it should be considered an evidence of deficiency on the part of the liver to store glucose. Liver function tests pertinent to this are being done. A decrease in tolerance following therapy or an increase in tolerance after withdrawal of therapy has been a consistent finding in 7 cases studied.

Seven glucose tolerance tests in two of the cases are shown here as examples of this change. Case W. is 19 years old and has mild hypogonadism. On November 10, 1940 prior to his using methyl testosterone a glucose tolerance test was done [labeled (1) on Chart I]. Blood sugars were estimated by Myer's[8] method, fasting, and at the intervals shown on the chart following the ingestion of 100 grams of glucose in 200 cc. of water.

The second curve, labeled (2) on Chart I, was the result of an identical

test following 100 mg. of methyl testosterone orally daily for 25 days. In Case J.D. the same type of change is shown (Chart II). The chart is self-explanatory.

In order to determine whether or not this change represented a shift in absorption rate, a glucose tolerance test was done by the intravenous method of Tunbridge and Allibone[9] (Chart III). Then therapy was stopped for seventeen days and the test repeated. "In the test described the blood sugar reading is shown to return to the preinjection level within 60 minutes in healthy young men."[9] Since the major portion of the curve is consistently higher during methyl testosterone therapy than it is following its withdrawal and since the blood sugar reading during treatment did not return to preinjection levels within sixty minutes, we assume that the shift in glucose tolerance is not due to changes in absorption and represents a failure of deposition. The fact should not be overlooked that the preceding oral glucose tolerance test was not normal and that the type of therapy which was the apparent cause of that shift had only been stopped for seventeen days before [curve (1) Chart III]. In short, if this should represent any change in liver function, judging from this test it had reverted to normal in seventeen days.

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