

TABLE I.  
Recovery of Acetone from Pure Acetone Solutions and Following the Oxidation of  $\beta$ -hydroxy-butyric Acid (Racemic).

Acetone		$\beta$ -hydroxy-butyric acid	
Present mg.	% recovered	Mg. % by Van Slyke method	% recovered
.0178	71.4	3.96	75.8
.0378	73.6	11.75	73.1
.0550	74.6	24.1	79.3
.0735	70.1	36.1	77.0
.0770	71.2	59.1	77.9
.0910	73.6		
.0960	76.0		
.1098	74.5		
.1543	76.6		
.1704	75.0		
.1931	74.9		
Aver.	73.9		76.6

Five cc. of 10% sodium hydroxide is used to wash the precipitate and decanted after centrifuging. Ten cc. of 20% hydrochloric acid is added and the tube connected by a ground glass joint to a distilling condenser, the delivery tip of which dips below the surface of an excess of iodine (.001 N) made alkaline with 5 cc. of 40% sodium hydroxide. After distillation of almost all the liquid in the special tube, the receiving flask solution is acidified with 50% sulfuric acid and the excess iodine titrated with thiosulfate. In Table I is shown the recovery of acetone from pure solutions (74%) and from the Denigè's-Van Slyke precipitate formed by the oxidation of  $\beta$ -hydroxy-butyric acid (76%). Recovery of these substances when added to ketone-free blood is essentially the same. Until more information as to the relative concentrations of the various acetone bodies in the blood in ketonemia is available we are expressing our results as acetone, and using the factor 1.33.

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Early Effect of Total Thyroidectomy in a Case of Polycythemia vera (Vaquez-Osler Syndrome).

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Up to the present time the etiology of polycythemia vera has not been clarified nor have the methods of treatment proposed met

with lasting success. It is generally agreed (Vaquez<sup>1</sup> and Osler<sup>2</sup>) that the hematopoietic tissues are primarily at fault. One group of workers look upon erythremia as a neoplasm of the bone marrow (Minot and Buckman<sup>3</sup>), another as an excessive response to agents formed in the liver, stomach (Marshall<sup>4</sup> and Morris<sup>5</sup>), and endocrine organs (Gunther,<sup>6</sup> Moehlig and Bates,<sup>7</sup> and others), and a third group visualizes the disease as an anoxemic response induced by subintimal and adventitial fibrosis in the arteries and arterioles of the bone marrow (Reznikoff, Foot and Bethea<sup>8</sup>).

In polycythemia the patho-physiological changes in the peripheral blood are characterized by an increase in the number of red blood cells per cmm., an increase in the hemoglobin, an increase in the volume of packed cells with a corresponding decrease in plasma volume (hematocrit reading) and an increase in the total circulating blood volume.

When one searches for a means of correcting this anomaly, the state of myxoedema presents itself. It has been shown (Minot,<sup>9</sup> Emery,<sup>10</sup> Mackenzie,<sup>11</sup> and Stone<sup>12</sup>) that anemia is a frequent if not constant finding in myxoedema; and there is abundant evidence (Tatum,<sup>13</sup> Lim,<sup>14</sup> and Kunde<sup>15</sup>) to indicate that the abolition of thyroid function would depress erythropoiesis. Myxoedema is also associated with a decreased blood volume (Thompson,<sup>16</sup> Goldbloom and Libin<sup>17</sup>). It seemed, therefore, a rational therapeutic procedure to subject a patient with polycythemia vera to a total thyroidectomy. This has been done and the results are here reported.

The patient's complaints were those usually encountered in this

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<sup>1</sup> Vaquez, M. H., *Comp. rend. Soc. de biol.*, 1892, **44**, 384.

<sup>2</sup> Osler, William, *Am. J. Med. Sc.*, 1903, **126**, 187.

<sup>3</sup> Minot, George R., Buchman, Thomas E., *Am. J. Med. Sc.*, 1923, **166**, 469.

<sup>4</sup> Marshall, L. H., *Am. J. Physiol.*, 1935, **114**, 194.

<sup>5</sup> Morris, R. S., Schiff, L., and Foulger, M., *J. Med.*, 1932, **13**, 318.

<sup>6</sup> Gunther, H., *Endocrinology*, 1930, **14**, 184.

<sup>7</sup> Moehlig, R. C., and Bates, G. S., *Arch. Int. Med.*, 1933, **51**, 207.

<sup>8</sup> Reznikoff, Paul, Foot, Nathan C., and Bethea, James M., *Am. J. Med. Sc.*, 1935, **189**, 753.

<sup>9</sup> Minot, George R., *Med. Clinics North America*, 1921, **4**, 1733.

<sup>10</sup> Emery, Jr., E. S., *Am. J. Med. Sc.*, 1923, **165**, 577.

<sup>11</sup> Mackenzie, G. M., *J. A. M. A.*, 1926, **136**, 462.

<sup>12</sup> Stone, C. T., *Ann. Int. Med.*, 1928, **11**, 215.

<sup>13</sup> Tatum, A. L., *J. Exp. Med.*, 1913, **17**, 636.

<sup>14</sup> Lim, R. K. S., Sarhar, B. B., and Jane, P. H., Brown, Graham, *J. Path. and Bact.*, 1922, **25**, 228.

<sup>15</sup> Kunde, M. M., *Am. J. Physiol.*, 1932, **99**, 469.

<sup>16</sup> Thompson, W. O., *J. Clinical Invest.*, 1925-26, **2**, 477.

<sup>17</sup> Goldbloom, A. Allen, Libin, Isaiah, *Arch. Int. Med.*, 1935, **55**, 484.

disease, headache, dizziness, fullness in the head, flushing of the face with cyanosis of lips, hands and feet, weakness, dyspnoea, nausea and occasional attacks of vomiting. The appearance of the patient, the engorgement of retinal veins, enlargement of the spleen, and the hematological studies completed the diagnosis.

The oxygen consumption values prior to thyroidectomy, as determined by breathing oxygen (Benedict-Roth apparatus) on 4 different days were plus 23, 22, 33, and 25%. On 3 other days using the Tissot gasometer and the gas analysis method values of plus 26, 22, and 35% were obtained. The cholesterol was 116 mg. %. Fifteen months after thyroidectomy the oxygen consumption gradually fell until it reached a value of minus 30%.

At this time the blood cholesterol was 250 mg. % and the clinical picture that of myxoedema.

The hematological changes which have occurred in the fifteen months period may be summarized as follows:

The hemoglobin values (gm. per 100 cc.) prior to thyroidectomy were 21, 21.5, and 19.0; and afterwards 20, 19, 19. The erythrocytes decreased from 8.25, 8.62 and 8.89 (millions) to 6.58, 6.32, and 6.50 (millions). The mean corpuscular volume values (Wintrobe) of 89, 92, 85.4 have not been changed significantly, but remain (94.2, 98.1, 95.3) at the upper limit of normal.

The mean corpuscular hemoglobin (mmgr.) has increased from a somewhat lower than normal value of 25.5, 24.8, 21.3 to a normal value of 30.4, 30.0, 29.2. With a reduction in the number of red cells there has occurred a return to normal of the hemoglobin load of the individual cells.

The mean corpuscular hemoglobin concentration, which is a function of the volume of packed cells has increased from 27.6, 26.1, 25.0% to 32.3, 30.0, 30.5%, but remains below the normal value, 35%. The white blood, the differential, and the reticulocyte counts have not been altered.

The volume changes have been most interesting and significant. The total plasma volume of 1927 cc. (1114 cc. per sq. meter surface) has increased to 2436 cc. (1350 cc. per sq. m.). If this is compared with an average normal value of 2090 cc. (1303 cc. per sq. m.) obtained in the case of 6 females in our laboratory, it will be seen that the plasma volume (per sq. m. surface) prior to thyroidectomy was somewhat below normal, but that it has now reached normal.

The hematocrit has dropped from 82% to 62%, but it has not as yet reached normal (44%). The blood volume has decreased

from 10706 cc. (6187 cc. per sq. m.) to 6447 cc. (3581 cc. per sq. m.). Since this is a function of the hematocrit the values would remain elevated until the hematocrit becomes normal.

The total circulating hemoglobin of 2194.73 gm. has been reduced to 1224.96 gm. This visualizes more clearly the effect of total thyroidectomy on erythropoiesis and hemoglobin formation than do hemoglobin concentration studies. It is probable that the patient's relief from symptoms is attributable to this reduction.

*Conclusions.* (1) All the alterations in the blood following a total thyroidectomy in a case of polycythemia vera are in the direction of normal. Normal values for total blood plasma, mean corpuscular hemoglobin ( $\gamma$ ,  $\gamma$ ) and mean corpuscular hemoglobin concentration have been attained. Although the concentration of hemoglobin per 100 cc. has remained unchanged the total circulating hemoglobin has been reduced to 56%. The other changes (hematocrit, total blood volume) are so striking as to be significant.

(2) The patient has been relieved of her former symptoms. Her present complaints are due solely to the myxoedema. No attempt has been made to control these as this would defeat the experimental objective.\*

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### Studies Relating to Time of Human Ovulation. II. During Lactation.

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It is a well known clinical fact that in the absence of any contraceptive measures, some women will become pregnant during their period of lactation while others will not. This has led to the conclusion that ovulation occurs in the former group but not in the latter. The frequency of ovulation in lactating women who are having catamenia at regular intervals is at present unknown. The following study was undertaken in order to shed some light on the subject.

A group of patients reporting to the postpartum clinic of the

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