THE SURFACE TENSION OF THE BLOOD SERUM IN HYPERTHYROIDISM

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The present communication is a report of an investigation of the surface tension of the blood serum in patients with severe thyroid intoxication. The general plan of the study has been as follows: Determinations of the surface tension were made upon samples of blood serum from untreated patients immediately upon admission to the hospital. Treatment with iodine (in the form of Lugol's solution) was then given in sufficient amount and over a sufficient period of time to allow an exhibition of its clinical effect, when the surface tension studies were repeated. Later the surface tension was again determined after surgical operation (double partial lobectomy of subtotal thyroidectomy) in order to observe any change resulting from the diminished activity of the thyroid gland due to its partial removal. In some cases iodine was continued for a short time after operation.

The direct reading tensiometer of Du Noüy (1) was used for making the surface tension determinations, and all the precautions recommended by him were carefully followed. The watch glasses used were of uniform size (diameter 8 cm.) and the same amount of serum, approximately 2 cc., used each time. The glassware used was boiled for two hours in a concentrated solution of sulphuric acid to which had been added 15 cc. saturated solution of potassium bichromate per liter. The watch glasses were washed not longer than two or three days before using and were flamed a short time before use in order to insure uniform spreading of the serum. The greatest care was taken throughout to avoid touching with the hands any glassware, including the collecting apparatus, centrifuge tubes and watch glasses.

The blood for the surface tension determinations was collected in

TABLE 1

Surface tension determinations

Subject	Date	Surface tension—serum			Remarks
		Initial reading	Reading after 2 hours	Drop	
		dynes per sq. cm.	*dynes per sq. cm.*	*dynes*	
Normal subjects					
E. G. N.	November 18, 1925	56.6	49.6	7.0	Staff
	November 27, 1925	56.8	49.7	7.1	
	January 7, 1926	57.1	49.6	7.5	
	January 8, 1926	56.7	49.6	7.1	
G. A. H.	November 18, 1925	56.6	49.7	6.9	Staff
	November 27, 1925	56.6	49.6	7.0	Staff
E. H.	November 18, 1925	56.8	49.4	7.4	Staff
	December 1, 1925	56.6	49.3	7.3	Staff
T. G.	November 18, 1925	57.1	49.8	7.3	Staff
A. S.	January 15, 1926	57.1	49.7	7.4	Student
H. P.	January 15, 1926	56.8	49.8	7.0	Student
C. W.	January 20, 1926	57.1	49.5	7.6	Student
I. T.	January 20, 1926	56.9	49.3	7.6	Student
S. W.	January 20, 1926	56.9	49.3	7.6	Student
L. W.	January 20, 1926	57.5	49.3	8.2	Student
E. T.	January 20, 1926	57.2	49.1	8.1	Student
W. S.	January 22, 1926	57.0	49.1	7.9	Student
J. B.	February 2, 1926	56.8	49.9	6.9	Student
E. C.	February 2, 1926	57.7	49.8	7.9	Student
Miscellaneous conditions					
G. C.	November 10, 1925	57.6	49.8	7.8	Incipient menopause; psychoneurosis
R. C.	November 10, 1925	57.1	49.4	7.7	Bronchial asthma, very mild reaction to ragweed and feathers
C. T.	November 10, 1925	56.6	49.5	7.1	Unexplained vertigo. Diagnosis: disease of vestibular apparatus following fracture of skull in 1921
F. P.	November 10, 1925	57.1	49.6	7.5	Pregnancy, second month (delivery normal)
P. L.	January 27, 1926	56.5	49.5	7.0	Hysteria
	February 2, 1926	56.7	49.5	7.2	

TABLE 1—*Concluded*

Subject	Date	Surface tension—serum			Remarks
		Initial reading	Reading after 2 hours	Drop	
Miscellaneous conditions—continued					
		dynes per sq. cm.	*dynes per sq. cm.*	*dynes*	
F. B.	February 2, 1926	56.9	49.4	7.5	Palsy
R. S.	January 14, 1926	57.5	49.5	8.0	Arthritis deformans
F. Mc.	January 14, 1926	57.0	49.9	7.1	Arthritis deformans
	January 21, 1926	57.1	49.9	7.2	Arthritis deformans
M. M.	December 24, 1925	56.9	49.2	7.7	Recovered coryza
G. C.	January 18, 1926	57.3	49.5	7.8	Convalescent pneumonia
C. J.	January 14, 1926	56.7	49.6	7.1	Scleroderma
	January 27, 1926	56.6	49.4	7.2	Scleroderma
O. N.	January 22, 1926	57.0	48.8	8.2	Scleroderma

the morning after sixteen hours of complete fasting, by venapuncture without stasis. It was drawn directly into a 15 cc. centrifuge tube through an L-shaped glass capillary tube ground to fit on a platinum needle. After clotting it was centrifuged and the serum was poured into a watch glass, stirred, and a reading immediately made. After the reading, the watch glass containing the serum was covered by an inverted Petri dish and allowed to stand undisturbed for two hours, when a second reading was made to ascertain the time drop. In order to avoid disturbing the serum while standing, the watch glasses were placed on a revolving table similar to that described by Du Noüy.

All readings were made between 23° and 24°C. by placing the apparatus in a hood where the temperature could be regulated and air currents eliminated. A control reading of the surface tension of running tap water was made at the same time as that of the serum to be sure the instrument was accurately adjusted. Tap water was preferred to distilled water because of the extreme care needed for proper preparation of the latter. Undiluted serum was used because it required little handling and the chance of contamination was therefore

TABLE 2

Surface tension determinations in cases of hyperthyroid disease

Number	Subject Age Color Admission date	Date of determination	Surface tension—serum			Basal metabolic rate	Iodine therapy operation	Van den Bergh reaction—serum	(a) Clinical diagnosis (b) Surgical pathological report on material removed at operation
			Initial reading	Reading after 2 hours	Drop				
			dynes per sq. cm.						
1	Ada H. 35 C November 5	November 11, 1925	53.3	48.7	4.6		Died November 11, 1925	Sclerae jaundiced	(a) Hyperthyroidism and exophthalmic goiter Autopsy also showed endocarditis
2	Mary S. 46 W November 9	November 12, 1925 December 10, 1925 January 11, 1926	54.9 54.6 56.0	48.9 48.9 49.3	6.0 5.7 6.7	+57 +45	Before Lugol's 14 days Lugol's Operation December 10	Not done	(a) Hyperthyroidism and adenoma of thyroid (b) Mixed foetal and colloid adenomata (toxic)
3	Susan B. 47 W November 22	November 24, 1925 December 15, 1925	53.3 55.7	48.6 48.8	4.7 6.9	+23 +17	Before Lugol's Lugol's November 24 to December 5 Operation December 7	Sclerae jaundiced on admission	(a) Exophthalmic goiter (b) Exophthalmic hypertrophy of thyroid
4	Sue V. 23 W December 2	December 14, 1925 January 11, 1926 February 1, 1926	54.7 54.2 54.6	48.8 48.8 48.5	5.9 5.4 5.9	+25 + 9 +29	7 days Lugol's Lugol's December 7 to January 11 Operation December 24	Not done	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic hypertrophy of the thyroid
5	Wm. Z. 36 W December 9	December 14, 1925 December 23, 1925 January 5, 1926	54.6 54.8 56.0	48.5 48.8 49.0	6.1 6.0 7.0	+34 +22	Before Lugol's 9 days Lugol's Operation December 23	Not done	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter

6	Addie F.	December 15, 1925	56.6	50.0	6.6	+34	Lugol's October 15, to November 8	Not done	(a) Hyperthyroidism and exophthalmic goiter
	35 C	December 15, 1925	56.6	50.0	6.6	+34	Lugol's November 25 to December 11		(b) Exophthalmic goiter
	December 11	December 24, 1925	56.7	50.1	6.6	+18	Operation December 16		
7	Naomi W.	January 5, 1926	54.1	48.8	5.3	+30	Before Lugol's	Not done	(a) Hyperthyroidism and exophthalmic goiter
	22 W	January 12, 1926	53.8	48.6	5.2	+14	Lugol's January 10 to January 21		(b) Exophthalmic goiter
	December 30	February 3, 1926	55.8	49.0	6.8		Operation January 23		
8	John R.	January 21, 1926	55.4	48.6	6.8	+59	Before Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter
	49 W	January 30, 1926	55.4	48.5	6.9	+44	11 days Lugol's		(b) Exophthalmic goiter
	January 18	March 5, 1926	56.6	49.4	7.2	+ 3	Operation February 23		
9	Beulah W.	January 16, 1926	56.8	50.0	6.8	+16	Before Lugol's	Negative	(a) Hyperthyroidism
	22 W	January 29, 1926	57.1	50.1	7.0	+ 5	Lugol's January 24 to January 30		
	January 14						No operation		
10	Sue S.	January 30, 1926	55.4	48.8	6.6	+50	Before Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter
	29 S	February 10, 1926	55.7	48.9	6.8	+27	11 days Lugol's		(b) Exophthalmic goiter
	January 28	February 24, 1926	56.4	49.0	7.4		Operation February 12		
11	Ernest C.	February 3, 1926	55.5	48.8	6.7	+38	Before Lugol's	Negative	(a) Hyperthyroidism
	55 W	March 3, 1926	56.0	48.7	7.0	+13	30 days Lugol's		
	January 29						No operation		
12	Louise S.	February 16, 1926	54.6	48.6	5.8	+45	Before Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter
	22 W	February 27, 1926	55.1	48.8	6.4	+28	11 days Lugol's	(20 days after operation developed postoperative myxedema)	(b) Exophthalmic goiter
	February 11	March 23, 1926	56.2	49.0	7.2	− 5	20 days post-operative		
13	Gustava B.	February 22, 1926	54.8	48.8	6.0	+67	Before Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter
	39 W	March 10, 1926	55.0	48.6	6.4		Lugol's March 1 to March 23		(b) Exophthalmic goiter
	February 17	March 24, 1926	56.0	48.9	6.1	+17	Operation March 11		

TABLE 2—*Continued*

Number	Subject Age Color Admission date	Date of determination	Surface tension—serum			Basal metabolic rate	Iodine therapy operation	Van den Bergh reaction—serum	(a) Clinical diagnosis (b) Surgical pathological report on material removed at operation
			Initial reading	Reading after 2 hours	Drop				
			dynes per sq. cm.						
14	Zona C. 21 W March 2	March 15, 1926	55.6	49.2	6.4	+ 8	Before Lugol's No operation	Negative	(a) Hyperthyroidism
15	Joseph K. 38 W March 4	March 6, 1926 March 23, 1926 April 4, 1926	54.4 54.6 54.9	48.9 48.9 48.9	5.5 5.7 6.0	+73 +37 ± 0	Before Lugol's 15 days Lugol's Operation March 24	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
16	Ambrose W. 42 W March 5	March 8, 1926 March 14, 1926 March 28, 1926	54.3 55.0 55.9	49.1 49.3 49.0	5.2 5.7 6.9	+26 +14	Before Lugol's Lugol's March 8 to March 14 Operation March 23	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
17	Tollin T. 41 W March 9	March 12, 1926 March 26, 1926 April 29, 1926	56.0 56.5 57.1	48.9 49.2 49.2	7.1 7.3 7.9	+14 +28 	Before Lugol's Before Lugol's Operation April 16	Negative	(a) Hyperthroidism and exophthalmic goiter (b) Exophthalmic goiter
18	Gertrude Z. 19 W March 15	March 18, 1926 March 23, 1926 April 14, 1926	56.3 56.5 56.6	49.4 49.4 49.3	6.9 7.1 7.3	+34 ± 0	Before Lugol's Lugol's March 18 to March 31 Operation April 3	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Fetal and colloid adenoma of thyroid
20	Mary E. 29 W March 19	March 23, 1926 April 8, 1926 January 5, 1926	56.3 56.2 56.8	48.9 48.7 49.4	7.4 7.5 7.6	+65 +31 − 8	Before Lugol's 17 days Lugol's 9 months post-operative	Negative	(a) Hyperthroidism and exophthalmic goiter (b) Exophthalmic goiter

21	Martha S. 53 W March 30	 April 20, 1926 May 6, 1926	 54.4 54.8	 48.8 48.8	 5.6 6.0	 +31 +10	 11 day Lugol's 10 days post-operative	Negative	(a) Adenoma of thyroid (b) Adenoma mixed fetal and colloid
22	Edna A. 26 W April 12	April 6, 1926 May 4, 1926 June 1, 1926	52.9 53.3 54.6	47.4 47.9 48.6	5.5 5.4 6.0	 +21 	Before Lugol's 18 days Lugol's 8 days post-operative	18 units (direct) 12 units 1 unit	(a) Adenoma of thyroid (b) Mixed adenoma
23	Lillian C. 22 W April 13	April 14, 1926 May 6, 1926 September 30, 1926	53.6 54.1 56.5	48.7 48.8 49.5	4.9 5.3 7.0	+73 +44 +11	Before Lugol's 19 days Lugol's 4 months post-operative	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
24	Anna B. 15 W September 23	September 28, 1926 October 5, 1926	55.9 56.3	49.8 49.7	6.1 6.6	+61 +32	Before Lugol's 7 days Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
25	Mary B. 27 W October 1	October 5, 1926	54.7	48.8	5.9	+55	3 days Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter with one encapsulated adenoma
26	Minnie H. 23 C October 25	November 2, 1926	55.1	49.0	6.1	+29	Before Lugol's No operation	Negative	(a) Hyperthyroidism
27	Wm. B. 38 W October 20	November 20, 1926	56.4	49.0	7.4	+32	Before Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
28	Jennie B 49 C November 2	November 4, 1926 November 23, 1926	53.7 54.5	49.5 49.4	4.2 5.1	+57 +32	Before Lugol's 13 days Lugol's	Trace Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goite
29	Henry B. 45 W November 15	November 16, 1926	54.3	49.5	4.8	+63	Treated before admission for blastomycosis probably with iodides	Negative	(a) Hyperthyroidisn and exophthalmic goiter (b) Exophthalmic goiter
30	Wm. C. 22 C November 30	December 3, 1926	53.6	48.8	4.8	+59	Before Lugol's	Trace	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter

TABLE 2—*Concluded*

Number	Subject Age Color Admission date	Date of determination	Surface tension—serum			Basal metabolic rate	Iodine therapy operation	Van den Bergh reaction—serum	(a) Clinical diagnosis (b) Surgical pathological report on material removed at operation
			Initial reading	Reading after 2 hours	Drop				
			dynes per sq. cm.						
31	Margaret K.	July 11, 1927	56.2	49.5	6.7	+54	Before Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter
	29 W	July 19, 1927	56.6	49.6	7.0	+13	6 days Lugol's		(b) Exophthalmic goiter
	July 6	July 31, 1927	56.8	49.6	7.2		10 days post-operative		
32	Mable S.	July 19, 1927	54.3	48.8	5.5	+100	Has received iodine 1 year	Negative	(a) Hyperthyroidism and toxic adenoma
	20 W					+101	before admission. Died		
	July 13						following operation		
33	Roxie M.	August 2, 1927	54.3	49.1	5.2		Before Lugol's	½ unit	(a) Hyperthyroidism and exophthalmic goiter
	29 W	August 9, 1927	55.3	49.0	6.3	+23	19 days Lugol's	Negative	(b) Exophthalmic goiter
	July 20	August 16, 1927	56.3	49.3	7.0	+22	12 days post-operative	Negative	
34	Effie D.	July 23, 1927	55.8	49.4	6.4	+48	Before Lugol's	Negative	(a) Hyperthyroidism and toxic adenoma
	37 C.	August 4, 1927	56.7	49.7	6.9	+25	10 days Lugol's		(b) Exophthalmic goiter
	July 15	August 19, 1927	56.5	49.4	7.1	+19	10 days post-operative		
35	Eliz. B.							Negative	(a) Hyperthyroidism and exophthalmic goiter
	40 W	July 30, 1927	54.8	48.8	6.0	+60	7 days Lugol's		(b) Exophthalmic goiter
	July 23	August 9, 1927	55.0	48.9	6.1	+16	8 days post-operative		
36	Cora W.	July 23, 1927	56.3	49.2	7.1	+11	Before Lugol's		(a) Mild hyperthyroidism
	35 C							Negative	
	July 19	August 2, 1927	56.8	49.4	7.4	+7	No operation		

37	Elmer S. 31 W July 25	July 27, 1927 August 2, 1927 August 23, 1927	54.2 54.1 54.2	49.0 48.8 49.0	5.2 5.3 5.2	+100 +51 − 2	Before Lugol's 3 days Lugol's 10 days post-operative	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
38	May H. 27 W July 25	August 2, 1927	53.8	49.0	4.8	+60	Before Lugol's	Negative	
39	Alice K. 32 C July 26	July 27, 1927 August 9, 1927 August 19, 1927	53.7 54.0 54.6	49.3 49.2 49.1	4.4 4.8 5.5	+51 +23 +13	Before Lugol's 12 days Lugol's 9 days post-operative	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
40	Julia S. 42 W August 11	August 16, 1927 August 25, 1927 September 3, 1927	55.2 55.7 56.3	49.2 49.4 49.3	6.0 6.3 7.0	+46 +35 +34	Before Lugol's Before Lugol's 11 days Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
41	Hilda A. 22 C August 11	August 13, 1927 August 22, 1927 August 31, 1927	56.3 56.9 57.4	49.8 49.7 49.9	6.5 7.3 7.5	+31 + 4 + 2	Before Lugol's 7 days Lugol's 7 days post-operative	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
42	Milford P. 23 W July 23	July 26, 1926 August 6, 1927 August 29, 1927	54.3 55.0 55.4	48.8 48.9 49.3	5.5 5.9 6.0	+61 +13 − 2	Before Lugol's 11 days Lugol's 21 days post-operative	Negative	(a) Hyperthyroidism and exophthalmic goiter (b) Exophthalmic goiter
43	Eliza T. 42 C September 1	September 3, 1927	56.9	49.4	7.5	+61	Before Lugol's	Negative	(a) Adenoma of thyroid
44	Marie K. 35 W September 7	September 8, 1927	53.8	49.4	4.4	+58	Before Lugol's	Negative	(a) Hyperthyroidism and exophthalmic goiter

minimal. Serum was also preferred to plasma because of the danger of hemolysis when an anti-coagulant was used. Plasma was found to give a parallel but slightly higher reading than serum. This was true in the case of oxalated blood and also when coagulation was prevented by a highly purified sample of heparin, kindly supplied to us by Dr. W. H. Howell.

The surface tension of the blood serum of forty-four patients suffering with hyperthyroidism was determined in the above way and, for comparison, that of fourteen normal individuals and twelve persons with miscellaneous conditions. Table 1 gives the data obtained from the study of the controls, and table 2 the data obtained from that of the cases of thyroid intoxication.

DISCUSSION

From table 1 it will be seen that the initial surface tension in the normal cases varied between 56.6 and 57.7 dynes, and the two-hour time drop varied between 6.9 and 8.2 dynes. From table 2 it will be noted that thirty-nine out of forty-four cases of thyroid intoxication previous to treatment showed an initial surface tension reading of 56.5 dynes or less and that the time drop in thirty-eight of these cases was less than the minimal drop in the normal controls. These relationships are shown graphically in chart 1.

We consider that this data furnishes substantial evidence that during the period of thyroid intoxication a surface active substance is usually if not invariably present in the blood serum. Such a lowering of the surface tension in thyroid disease could be accounted for by the presence of bile acids in the serum. Since no convenient method was available at the time for the estimation of the bile salts the Van den Bergh reaction was carried out in all but seven of the cases to serve as an indirect indication of the presence of bile. Of the thirty-seven cases thus studied an amount of bilirubin above the normal limits, a "positive" Van den Bergh reaction, was found in the serum of four. Two of the cases with a "positive" Van den Bergh showed no jaundice clinically and only a trace of bilirubin in the serum. Serum from another case showed $\frac{1}{3}$ unit of bilirubin on admission but the Van den Bergh reaction was negative after nineteen days treatment with Lugol's solution. Nevertheless the lowered surface tension

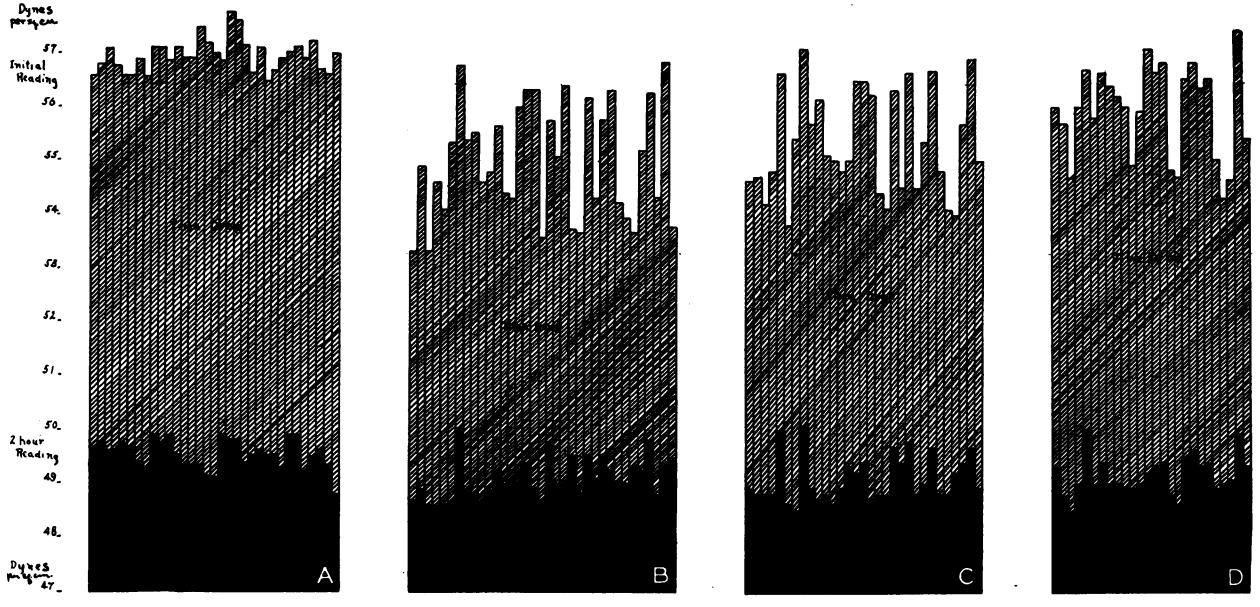

CHART 1. INDICATING THE INITIAL SURFACE TENSION READINGS AND THE TIME DROP IN CASES OF THYROID INTOXICATION TOGETHER WITH THE DETERMINATIONS MADE ON THE SERUM OF THE SAME PATIENTS AFTER IODINE TREATMENT AND AFTER SURGICAL OPERATION

The cross hatching represents the initial reading, the solid black represents the drop in surface tension in the same serum at the end of two hours.

A, normal subjects. Cases of hyperthyroidism: *B*, before treatment; *C*, after receiving Lugol's solution; *D*, after surgical operation.

of the serum still persisted at this time. Of the seven cases in which the Van den Bergh reaction was not made, two showed slight icteric discoloration of the sclerae on admission which had cleared up at the time that the surface tension studies were made. The other five cases showed no clinical evidence of jaundice. All of these observations are indicated in table 2. Aside from these exceptions none of the cases showed either clinical evidence of jaundice or an abnormal amount of bilirubin in the blood serum as indicated by the Van den Bergh reaction.

We have considered the possibility that the surface active substance which appears to be present may be an unsaturated compound, possibly an unsaturated fatty acid. This aspect is further dealt with in the following paper (4). Under such circumstances the administration of iodine, even in the rather small amounts of Lugol's solution which are effective therapeutically, might be sufficient to neutralize its effect. However, the fact that iodine administration has not markedly altered the low surface tension of the serum in this condition appears to indicate that such is not the explanation of its action. After partial thyroidectomy it also appears that the return of the surface tension of the serum to normal is very slow.

No previous report has been found of a lowering of the surface tension of the blood serum in thyroid disease. Adlersburg and Sugär (2) state that the surface tension of the urine is lowered in Basedow's Disease. While the present study was in progress a paper by Wilhelmj and Fleisher (3) appeared, in which they reported that after thyroidectomy in guinea pigs a gradual rise in the surface tension of the plasma occurred, so that in nineteen to twenty-two days the readings were definitely abnormal. They find that the time drop, after twenty minutes, was in general less in the plasma from the animals operated upon than in the plasma from normal controls. Essentially the same differences were found by them when readings were made after two hours as were found after an interval of twenty minutes. These authors also made a study of the effect of thyroxin and thyroid extract administration to guinea pigs. In most cases a definite decrease in the surface tension of the plasma was found, but little change on the average was detected in the time drop.

CONCLUSIONS

1. The surface tension of the blood serum is lower than normal in many cases of thyroid intoxication. This is associated with a diminished time drop at the end of two hours, when compared with that present in the serum of normal persons.

2. The administration of iodine in the form of Lugol's solution has an appreciable effect in increasing the lowered surface tension.

3. After operation involving the partial removal of the thyroid gland there is a tendency for the surface tension of the serum to rise even more than after iodine.

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