

the C:H:N ratio in the original material and in the KSCN cleavage product was almost identical: 7.5:10:1 versus 7.1:10:1. The brown precipitate formed during the HCl cleavage yielded C: 47.27, H: 5.32, ash: 2.90%.

The difficulty in calculating empirical formulas indicates we must further purify the material. For the original pigment the tentative formula is suggested: $(C_{15}H_{20}N_2O_9)_2Fe$.

Comment. The purplish-red color of the iron-pigment, the reversible color change with the pH and the type of the absorption spectrum³ strongly suggest that it belongs in the group of complex phenolic iron compounds. In such compounds a single ferric ion is complexly bound to a varying number of phenolic radicals.⁴ The data of the cleavage products indicate that during decomposition some phe-

nolic groups separate from the iron, whereas others do not. Thus in the supernatant fluid new compounds of smaller molecular weight are present with all the properties of the original pigment (including similar absorption spectra) but containing more iron.

Phenolic iron compounds, however, are less stable than the pigment of red hair. The latter's greater stability may be explained by assuming that the phenolic OH-group is attached to a heterocyclic ring containing nitrogen. The negative reactions for pyrrol and pyridine do not exclude such a possibility because substitutions on these rings modify their reactivity. At present, no definite statement can be made regarding the chemical structure of the iron-containing pigment of red hair.

Summary. A red iron pigment was isolated from human red hair. The presented data indicate that it may be a complex phenolic iron compound in which the phenolic OH group is attached to a heterocyclic ring containing nitrogen.

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Physiological Studies on Five Patients Following Ligation of the Inferior Vena Cava.

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The effects of ligation of the inferior vena cava of the experimental animal upon the circulation and functions of the parts drained by its tributaries have been studied by many.^{1,2} If the ligation is below the renal veins, there are no apparent serious results. The inferior vena cava has been ligated relatively frequently in man.^{3,4} It has

been noted that when the ligation is below the renal veins, there is little disturbance experienced by the patients. It is the purpose of this report to record briefly a few physiologic observations made on 5 patients in whom the inferior vena cava was ligated by Dr. C. G. Collins of the Department of Gynecology and Obstetrics of Tulane Medical School.

Methods. The patients were studied several days after operation when they were sufficiently well to be moved from Charity Hospital to a laboratory specially equipped for such observations. These people were too ill to be moved from the hospital to the laboratory for study before operation.

¹ Polkey, H. J., *Urol. and Cutan. Rev.*, 1929, **33**, 394.

² Whittenbergr, J. L., and Huggins, C., *Arch. Surg.*, 1940, **41**, 1334.

³ Krotski, J., *Chirurg.*, 1937, **9**, 425.

⁴ Ochsner, A., and DeBailey, M., *New England J. Med.*, 1941, **225**, 207.

All observations were conducted in an air-conditioned room with a temperature of $75^{\circ}\text{F} \pm 1^{\circ}$ and relative humidity of $50\% \pm 1\%$. The patients rested in bed for at least 30 minutes before any measurements were made. The room was constructed to reduce psychic disturbances to a minimum, being very much like one previously described.⁵ All observations except the venous pressure, were made essentially without the patient's knowledge except for small parts of the apparatus that were connected to her. All 5 patients were females.

The following measurements were made:

1. *The rate of water loss* from the skin of the right index finger tip, right second toe tip, right pretibial region and volar surface of the right forearm was determined quantitatively by a method previously described.⁶ The rate of water loss was determined first at a temperature and relative humidity of $75^{\circ}\text{F} \pm 1^{\circ}$ and $50\% \pm 1\%$ respectively. After measuring the rate of water loss under these environmental conditions for two 15-minute periods the temperature of the room was raised to $100^{\circ}\text{F} \pm 2^{\circ}$ and the relative humidity to $75\% \pm 2\%$. These levels were reached within 15 minutes and the rate of water loss was measured for 2 more 15-minute intervals. The room temperature and humidity were then returned to the original levels.

2. *The volume of pulsations* of the right index finger tip and right second toe tip were measured quantitatively by the plethysmographic method of Turner.⁷ These determinations were made after the subject had been resting another 30 minutes at the comfortable temperature and humidity of 75°F and 50% respectively.

3. *The venous pressure* in a vein of the dorsum of the foot and left antecubital area with the respective parts at the level of the heart was determined directly by a method previously described.⁸ The venous pressure

measurements were made after completing the other studies.

The above observations were made from 8 to 18 days after ligation of the inferior vena cava. In every instance, the patients were free from fever and other evidence of infection when the studies were performed. In 4 subjects the measurements were repeated at intervals indicated by Table I. Patient No. 1 could not be contacted for a follow-up study.

Results. The results are summarized in Table I.

The venous pressure was greatly elevated in the veins on the dorsum of the feet following ligation of the vena cava while the pressure in the antecubital veins remained normal. In no patient did the pressure return to normal, even as long as 10 months postoperatively.

All patients developed edema postoperatively along with the increase in venous pressure. In the 5 persons the edema was worse when they were up and about and only one (Patient No. 3) was clinically free from edema during any time of observations. None of them developed any cyanosis, erythema, petechiæ, pallor, paresthesia, tenderness, or hyperesthesia. Except for edema of the legs below the knees, the patients were clinically well.

There were no significant disturbances in water loss under a comfortable room environment, or under a hot humid one. There was an increase in the rate of water loss from the skin in a normal fashion when the room was made hot and humid.

The volume of pulsations of the toe tips decreased markedly in all 5 patients following ligation of the inferior vena cava. Even the maximum volume of pulsation of the toe tips was less than the mean volume of pulsations in the normal toe tip, the former being 3.5 cmm per 5 cc of toe tip and the latter 4.0 cmm per 5 cc of toe tip. In patient No. 5 the volume of pulsations in the toe tip returned to normal by the time of the second observation, although the venous pressure was still abnormally high. There was no edema, however.

Discussion. Increase in venous pressure in the veins of the dorsum of the feet following ligation of the inferior vena cava is known to occur. The fact that the levels reached were

⁵ Neumann, C., Cohn, A. E., and Burch, G. E., *J. Clin. Invest.*, 1942, **21**, 651.

⁶ Neumann, C., Cohn, A. E., and Burch, G. E., *Am. J. Physiol.*, 1942, **132**, 748.

⁷ Turner, R. H., *J. Clin. Invest.*, 1937, **16**, 777.

⁸ Burch, G. E., and Sodeman, W. A., *J. Clin. Invest.*, 1939, **18**, 31.

TABLE I.
Venous Pressure, Rate of Water Loss from the Skin, and Volume of Pulsations of Peripheral Blood Vessels in Five Female Adults in Whom the Inferior Vena Cava Was Ligated Below the Renal Veins. Values in Normal Subjects Are Also Indicated.

Sub- ject	Date	Age	Color	Venous pressure, cm H ₂ O			Rate of water loss mm ³ /15 min/10 cm ²						Vol. of pulsations cc/5 cc part			
				Ante- cubital	Dorsum Rt. foot	Lt. foot	Rt. Ind. Fngr.		Rt. 2nd Toe		Rt. Leg		Rt. Forearm		Rt. Ind. Fngr. Tip	Rt. 2nd Toe Tip
							C.T.	H.H.T.	C.T.	H.H.T.	C.T.	H.H.T.	C.T.	H.H.T.		
(1)	4-11	21	W	12.2	24.8		50.2	149.0	18.8	39.5		11.2	63.0	3.5	0.3	1
(2)	5-20	31	C		36.0	50.0+	21.6	98.7	7.7	30.1	11.0	30.6		4.0	0.5	2
	6-24			10.6	35.6	36.6	15.5	69.0	10.2	25.2	10.0	31.2		11.2	1.2	
(3)	5-22	21	W	11.0	41.6	50.6	16.5	30.8	13.0	16.9		9.8	16.0	6.9	3.5	3
	to 3-9			14.0	20.0	22.0	20.7	53.5	9.8	23.7		4.6	12.6	2.1	0.8	
(4)	4-20	67	W	2.6	24.4		15.5	27.7	6.9	19.5	18.0	38.2		8.9	1.2	4
	6-30			10.6	30.6		17.4	31.8	6.1	12.8	6.6	28.0		10.3	2.7	
	11-7			5.0	30.0	30.0	24.7	28.0	13.5	17.6	10.0	27.2		10.1		
(5)	5-7	27	W	14.0	29.0									4.1	0.4	5
	6-1			12.6	25.6		13.7	24.5	12.1	19.3		10.8	23.6	7.5	6.0	
	11-10			10.0	17.0	18.0	21.7	56.3	12.3	30.9		13.6	29.8	9.9	5.6	
Mean			10.3	30.0	31.1	21.8	56.9	11.0	23.6	11.1	31.4	10.0	29.0	7.1	2.2	
Max.			14.0	41.6	50.6	50.2	149.0	18.8	39.5	18.0	38.2	13.6	63.0	10.3	6.0	
Min.			2.6	17.0	18.0	15.5	27.7	6.1	16.9	6.6	27.2	4.6	12.6	2.1	0.3	
Normal Values:																
Mean			8.0*	10.5†		23.2‡	47.9	12.5	31.1	8.3	32.1	4.4	25.9	6.9§	4.0¶	
Max.			14.0	11.0		41.3	52.1	15.7	48.7	13.6	37.6	8.4	37.8	12.4	11.5	
Min.			3.0	10.1		14.0	21.7	10.4	21.8	4.1	22.4	2.0	14.0	0.9	0.7	

a = Mean values calculated from the data obtained on the first observations.

C.T. = Comfortable temperature of room (75°F and 50% relative humidity).

H.H.T. = Hot and humid temperature of room (100°F and 75% relative humidity).

* Normal values from Burch, G. E., unpublished data.

† Normal values from McIntire, I. M., and Turner, A. H., *J. Clin. Invest.*, 1935, **14**, 16.

‡ Normal values for all rates of water loss from Burch, G. E., and Sodeman, W. A., *Am. J. Physiol.*, 1943, **138**, 603.

§ Normal values from Burch, G. E., Cohn, A. E., and Neumann, C., *Am. J. Physiol.*, 1942, **136**, 433.

¶ Inferior vena cava and both ovarian veins ligated on 3-19-42. Very slight pitting edema 3 weeks post-operatively. No edema on walking.

1 Thrombophlebitis of the left femoral vein extending into iliaes. Inferior vena cava, left femoral and both ovarian veins ligated on 5-2-42.

2 Marked edema of both legs, especially left on 5-20-42. On 6-24 little edema; more marked when up and about. Died Nov. '42, suddenly outside N.O. No autopsy obtained.

3 Inferior vena cava and both ovarian veins ligated on 4-30-42. Marked edema of right leg and moderate edema of left leg on 5-22. 3-9-43, fatigue. No edema or other symptoms.

4 Inferior vena cava ligated on 3-28-42. Marked bilateral edema, especially of the right leg on 4-20 and 6-30-42. 11-7-42, asymptomatic with pitting edema of both legs, particularly the right.

5 Inferior vena cava ligated on 4-25-42. Mild edema on 5-7-42 and no edema on 6-1-42. 11-10-42, edema only when up a long time.

not greater indicates a good collateral circulation around the ligated vena cava. To a large extent the level of the venous pressure reached is inversely related to the degree of collateral circulation. The pressure did not return to normal in any of the patients, even after approximately 10 months following operation. It is possible that in some instances the venous pressure will eventually reach normal.

Every patient developed edema of the legs and feet postoperatively and only one (Patient No. 3) became clinically free from edema during the period of study. The increases in venous pressure were sufficient to produce edema. Patient No. 3 was clinically free from edema even though the venous pressure was still elevated indicating adequate compensating phenomena.

The rate of water loss from the surface of the skin of the tip of the right second toe and the pretibial area was not changed materially by ligation of the inferior vena cava. There was a normal increase in rate of water loss when the patients' environment was made hot and humid. An increase in venous pressure for several days apparently does not significantly influence water loss through the skin. No observations were made immediately after ligations of the vena cava.

The effects of ligation of the inferior vena cava upon the volume of pulsations in the tip of the right second toe is in keeping with previous observations.^{9,10,11} It was found that an increase in venous pressure, produced by chemical irritation, ligation of the femoral vein, or by the influences of gravity, such as lowering the parts in man below heart level,¹¹ resulted in a marked decrease in the volume of pulsations of the distal blood vessels. The

relationships between the increase in venous pressure and volume of pulsations were studied in a mechanical model and were found to be inversely related functions.¹⁰ The effects of the decrease in the volume of pulsations in the peripheral blood vessels upon the efficiency of circulation, lymph flow, flow of intercellular fluids and the like remain unknown. Some studies indicated a decrease in the rate of lymph flow with a decrease in the volume of pulsations of blood vessels.¹²

Clinically these 5 patients compensated remarkably well following ligations of the inferior vena cava. The sudden death of patient No. 2, about 6 months following operation, may have been related to the ligation. The clinical history regarding her sudden death suggested hemorrhagic encephalitis following an intravenous injection of arsenic for lues as the cause. An autopsy could not be obtained.

Summary. The venous pressure, rate of water loss from the skin and volume of pulsations in the peripheral blood vessels were measured in 5 patients following ligation of the inferior vena cava below the level of the renal veins.

The venous pressure increased markedly in the veins of the dorsum of the foot. Edema developed immediately after operation and only one patient was edema-free approximately 10 months after operation. In no patient did the venous pressure in the veins of the foot return to normal up to 10 months postoperatively.

The rate of water loss from the skin of the tip of the right second toe and pretibial area was normal by the eighth postoperative day. There were no measurements earlier.

The volumes of pulsations of the peripheral blood vessels were decreased markedly by ligation of the inferior vena cava.

All patients showed a remarkably good compensation of the circulation following ligation.

⁹ DeBakey, M. E., Burch, G. E., and Ochsner, A., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **41**, 585.

¹⁰ Burch, G. E., DeBakey, M., and Sodeman, W. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **42**, 858.

¹¹ Turner, R. H., Burch, G. E., and Sodeman, W. A., *J. Clin. Invest.*, 1937, **16**, 789.

¹² Cressman, R. D., and Blalock, A., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **41**, 140.