Studies in Edema: Cholesterol and Its Relation to Protein Nitrogen in Edema Fluid

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The only study of cholesterol in edema fluid has been that of Chauffard *et al.* in 1911 on four patients (*4*). We report here 16 cases and include the correlation of cholesterol with the protein nitrogen content of edema fluid.

Material and Methods. The patients studied fell into two classes (clinical details in Table 1): (a) those with edema originating from congestive heart failure, and (b) those with edema of an obstructive origin, either venous or lymphatic.

Edema fluid was obtained by inserting an 18-gauge needle subcutaneously into the extremity and letting the fluid drip into a test tube. Venous blood was drawn simultaneously.

Total cholesterol and cholesterol esters were determined in serum and edema fluid by Bloor's method (*1, 2*). Nitrogen determinations were performed by the micro-Kjeldahl method (*7*).

Results. Results are presented in Table 1.

Discussion and Conclusions. The average edema fluid cholesterol of 14.6 mg % in congestive heart failure is in sharp contrast to the average of 175.2 mg % in lymphatic obstruction. This may serve to differentiate these fluids.

Chauffard *et al.* reported cholesterol values (method not specified) in edema fluid from two patients with Bright's disease, (5.0 and 3.0 mg %) and two with cardiac edema (1.3 and 4.5 mg %). Protein nitrogen was not investigated.

TABLE 1

CHOLESTEROL AND PROTEIN NITROGEN IN EDEMA FLUID AND SERUM

Patient	Clinical			Type of edema*	Total cholesterol			Protein nitrogen† mg %		Cholesterol ester mg %	
	Age	Sex	Diagnosis*		Edema mg %	Serum mg %	$\frac{E}{S} \times 100$	Edema	Serum	Edema	Serum
S.P.	80	M	Anemia	C.H.F.	19.4	161.0	12.1				
R.I.	62	F	ACVD HCVD	C.H.F.	27.1	524.0	5.2	46.4	754.0	8.0	418.0
A.E.	57	F	ACVD HCVD	C.H.F.	25.0	244.0	10.2	87.0	1034.0		
A.L.	52	F	ACVD HCVD	C.H.F.	7.8	302.0	2.6	45.7	1002.0		
M.W.	54	F	ACVD RHD	C.H.F.	6.1	187.0	3.3	44.6	1058.0	0.0	117.0
A.B.	50	F	RHD	C.H.F.	2.4	163.0	1.5	27.6	940.0	1.0	131.0
T.T.	60	F	Ca. Uterus	V.O.	30.0	215.0	14.0				
L.K.	61	M	Ca. Colon	V.O.	9.6	364.0	2.6				
V.G.	44	M	Chiari	V.O.	12.3	277.0	4.5	89.8	958.0	0.0	111.5
H.A.	75	M	Ca. Rectum	L.O.	162.0	213.0	77.4				
M.P.	51	F	Ca. Breast	L.O.	151.5	332.0	45.7	580.0	1170.0	92.5	245.5
L.J.	71	F	Ca. Breast	L.O.	212.0	421.0	50.2	712.0	1284.0		
M.D.	44	M	L.S.	Stasis	21.0	245.0	8.6				
M.J.	24	F	K.-W.	Hypoproteinemia	18.8	552.0	3.4				
M.G.	62	F	Ca. Breast	C.H.F.(?)‡	7.2	382.0	1.9	25.8	830.0	0.0	166.0
T.L.	62	F	Ca. Colon	C.H.F.(?)‡	15.2	442.0	3.4	42.8	866.0	12.8	336.0

* ACVD arteriosclerotic cardiovascular disease; HCVD hypertensive cardiovascular disease; RHD rheumatic heart disease; Ca. cancer of; L.S. lateral sclerosis; C.H.F. congestive heart failure; V.O. venous obstruction; L.O. lymphatic obstruction; K.-W. Kimmelstiel-Wilson's syndrome.

† Total nitrogen mg % minus 30 mg % nonprotein nitrogen.

‡ Not included in average values for congestive heart failure.

The total cholesterol in edema fluid is related to the protein nitrogen content (coefficient of correlation, $r = 0.99$). The average total cholesterol/protein nitrogen ratio in edema fluid is 0.26 ± 0.14. This relationship of cholesterol to protein nitrogen in edema fluid confirms that found in other pathological body fluids (*3, 5, 6*).

In summary, cholesterol content of edema fluid in patients with congestive heart failure averaged 14.6 mg % (average edema fluid/serum cholesterol ratio was 6%). In edema fluid originating from venous obstruction, the average cholesterol content was 17.3 mg % (average

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edema fluid/serum cholesterol ratio was 7%). Where lymphatic obstruction was the predominant factor in edema formation, the cholesterol content averaged 175.2 mg % (average edema fluid/serum cholesterol ratio was 58%). The average total cholesterol/protein nitrogen ratio in edema fluid is 0.26 ± 0.14.

References

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The Urea Complexes of Unsaturated Fatty Acids

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The phenomenon of urea complex formation with aliphatic straight chain compounds was discovered in 1940 by F. Bengen.[1] He showed that normal aliphatic compounds form complexes with urea by addition, whereas branched and cyclic compounds do not, thus allowing the separation of straight chain compounds from the others by complex formation. Bengen and Schlenk, in a preliminary report emphasizing that the complexes formed are of a type so far unknown (*1*), recently summarized research in this field during the intervening years. Zimmerschied *et al.* called attention to, confirmed, and extended the observations in the original patent application (*3, 4*). Schlenk reports in detail on the formation of urea complexes in relation to the shape of the organic molecule, their composition, their crystal structure, and their energy of formation (*2*).

These reports emphasize that to form urea complexes, straight chain molecules are required. It was of interest to learn what influence the *shape* of unbranched molecules has upon the urea addition. For this study the unsaturated fatty acids of the C_{18} series were chosen because the double bonds alter the shape of the molecules. In general, it was found that the unsaturated fatty acids form urea addition complexes also. The degree of unsaturation, the position of the double bonds, and *cis-trans* isomerism do not markedly influence the composition of the complexes, 14.0–14.5 moles urea per mole C_{18} acid.

A remarkable property of the complexes of the unsaturated acids is their resistance to autoxidation. This is illustrated in Fig. 1. In another experiment with larger quantities, the autoxidation of soybean fatty acids and their urea complexes was followed for several weeks by means of their peroxide contents (Table 1). From these experiments, performed in October, 1949, it is apparent that the unsaturated fatty acids are inaccessible to oxygen in the form of complexes. This is understandable from the crystal structure of urea addition complexes (*2*).

[1] German patent application O.Z. 12438 (March 18, 1940); Technical Oil Mission Reel 6 frames 263–270 in German, Reel 143 pages 135–139 in English.

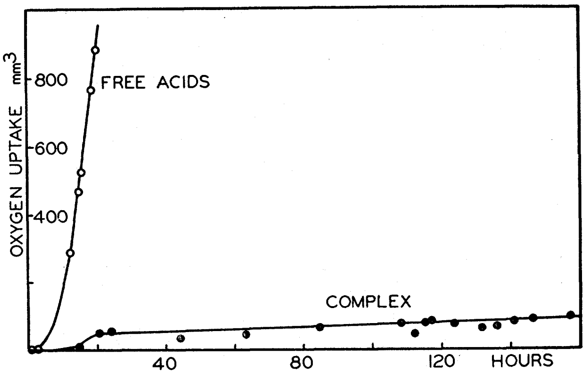

Fig. 1. Oxygen absorption of soybean fatty acid complexes and their freed acids in the Warburg respirometer at 37° under air. Samples: 400 mg complex, 90 mg freed acids.

TABLE 1

Peroxide Values of Soybean Fatty Acids and Their Complexes Exposed to Air at Room Temperature

	Weeks			
	0	1	2	3
Free acids	1	82	193	260
Complex acids	1	..	6	3

TABLE 2

Enrichment of the Saturated and Unsaturated Components of Fatty Acid Mixtures

Fatty acids		Urea	Complex acids		Non-complex acids	
Source	g	g	Yield, g	I.V.*	Yield, g	I.V.
Soybean, I.V. = 141	100	30	9	56	81	162
Soybean, I.V. = 141	100	100	37	88	56	180
Soybean, I.V. = 141	100	200	67	119	27	191
Chinese tallow, I.V. = 19	51	100	27	6.5	18.5	38
Olive, I.V. = 80	50	15	5.5	54	36	93

* I.V. = Iodine value.

Although all normal saturated and unsaturated fatty acids thus far investigated form urea addition complexes, the yields under identical conditions vary widely. This can be caused by differences in the relationships:

$$x \text{ Acid} + y \text{ Urea} \rightleftharpoons \text{Acid}_x \cdot \text{Urea}_y$$

and can be used as a basis of separation of various types