

osmotic pressure was restored to normal by the addition of NaCl. As controls, unmixed horse serum and swine serum were similarly diluted, heated and restored to normal osmotic pressure.

Rabbits were immunized against the artificial horse-swine hybrid serum. A typical set of serological tests with the resulting anti-hybrid precipitin is recorded in Table I.

From the table it is seen that the artificial horse-swine hybrid serum contains one or more specific factors not present in horse serum or swine serum.

If an analogous fusion of paternal and maternal protein specificities takes place during sexual reproduction, the apparent emergent evolution of one or more new protein characters in certain hybrids would be in accord with Mendelian laws.

The above data are consistent with the current theory that the specific antigenicity of a given biological product is not determined solely by its specific hapten content, but is largely dependent on the topographical distribution of these haptens on or within colloidal molecules.

8140 C

Iodine Values and Total Lipids of Leprous Human Blood Sera.*

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Recent renewed interest in serum lipid changes relative to the therapeutic effects of various unsaturated oils in skin diseases¹ prompted us to determine the iodine values and serum lipids of leprosy patients receiving chaulmoogra therapy. Unsaturated oils, in addition to those of the chaulmoogra group, have been used with some success in leprosy, notably olive, cod liver, dilo, soy bean, margosa, and coconut, according to Cole.² De Vera has shown

* In cooperation with the Health Department of the Panama Canal and the Gorgas Memorial Laboratory, Panama; through the courtesy of Dr. H. C. Clark, Col. J. F. Siler, Dr. D. P. Curry, Dr. Ezra Hurwitz, and Mr. Everett Jacob. Supported in part by Eli Lilly and Co., Indianapolis, Indiana.

¹ Hansen, A. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 1198; *ibid.*, 1933, **31**, 160, 161.

² Cole, H. I., *Intern. J. Leprosy*, 1933, **1**, 159.

that in a series of oils of diminishing saturation, the greater the unsaturation, the greater is the therapeutic action.³ Walker and Sweeny⁴ demonstrated that unsaturation is but partly responsible for the *in vitro* activity of non-chaulmoogra oils. The mechanism of action of non-chaulmoogra unsaturated oils has been studied in other skin diseases recently. Hansen found the iodine values of the blood in infantile eczema to be abnormally low. By administering linseed oil in large amounts an increase of the degree of unsaturation was noted which paralleled clinical improvement.

The blood plasma lipids in leprosy have been studied by Paras⁵ working at Culion in the Philippine Islands. Quoting Rogers, who suggested an increased lipolytic activity of the blood as a result of treatment, Paras postulates that the blood lipoids would tend to increase in rapidly improving cases of leprosy, in which the mycobacteria are presumably destroyed in large numbers. In untreated and treated groups showing little or no improvement, and in which the mycobacteria continue to multiply, the blood lipoids would tend to remain low. While Paras' findings did not support his hypothesis he felt that the possibility was of sufficient importance to warrant further study. He found, incidentally, in untreated cases low values for total blood lipoids, and in treated ("positive") cases, values but slightly lower than normal were noted, while in treated ("negative") patients the lipoids were within normal limits. One of the possibilities suggested by these findings was, according to Paras, "that the leprosy bacilli attempt to protect themselves from the destructive action of the defense mechanism of the body by utilizing part of the plasma lipoids".

We have had an opportunity to examine the blood sera of patients with "cutaneural" (*i. e.*, mixed) leprosy at the Palo Seco Leper Colony at Panama. Determinations of fatty acid unsaturation in terms of iodine values were made following the method of Page, Pasternak, and Burt⁶ and are shown in Table I together with the total lipids in various groups of patients. Since anemia, malnutrition, and nephritis are thought to cause lipemia,⁷ average hemoglobin findings and weights are recorded. All patients were examined for evidence of kidney damage and those reported had

³ de Vera, B., *J. Phil. Isl. Med. Assn.*, 1925, **5**, 374.

⁴ Walker, E. L., and Sweeney, M. A., *J. Infect. Dis.*, 1920, **26**, 238.

⁵ Paras, E. M., *J. Phil. Isl. Med. Assn.*, 1931, **11**, 1.

⁶ Page, I. H., Pasternak, L., and Burt, M. L., *Biochem. Z.*, 1930, **223**, 445.

⁷ Peters, J. P., and Van Slyke, D. D., *Qualitative Clinical Chemistry*, Vol. 1, Interpretations, Williams and Wilkins Co., Baltimore, 1931.

TABLE I.
Average Iodine Values and Total Lipids of Blood Sera of 53 Patients under Treatment for "Cutaneous" (Mixed) Leprosy at Palo Seco Leper Colony, Panama.[†]

Stage and course of disease	No. of patients	Av. age in years	Av. wt. in kilos	Av. Hgb. Gm./100 cc.	Probable av. amount of		Iodine value	Total lipids Gm./100 cc.
					Chaulmoogra av. duration of disease in years	esters given in kilos		
Early predominantly cutaneous leprosy [‡]	18	30.1	57.2	12.15	4.1	1.44	50.1 ±13.6	0.995 ±0.129
All stages—improving [§]	13	30.4	59.9	11.85	5.3	1.57	54.5 ±18.1	0.813 ±0.194
Advanced—stationary	11	31.9	56.2	11.02	9.4	2.25	66.9 ±14.1	0.720 ±0.200
All stages—advancing	11	33.1	58.7	12.67	9.8	2.74	77.8 ±19.8	0.572 ±0.148

[†] Normal values: Total lipids, 0.589 Gm./100 cc.; Iodine value of total fatty acids, 88. (Boyd, E. M., *J. Biol. Chem.*, 1933, **101**, 323.)

Average values for 53 leprosy patients: Total lipids, 0.805 ±0.161 Gm./100 cc. Iodine value, 58.5 ±15.9.

[‡] Three patients untreated.

[§] One patient with lepra fever. Iodine value, 31.2; total lipids, 1.016 Gm./100 cc.

normal phenolsulphonphthalein excretion. The level of total lipids supposedly increases with age, but our data do not show this trend in leprosy. All patients exhibited acid-fast organisms in the nasal mucosa or in skin biopsy material.

Analyzing the findings presented, we note abnormally low iodine values in early "cuta-neural" leprosy, 3 untreated cases exhibiting numbers of 40.0, 41.6, and 44.4 respectively. The total lipids are above the normal range. Clinically improving cases have slightly higher iodine values and lower total lipids, which might be explained by the higher average dosage of chaulmoogra esters given. Advanced treated cases of leprosy show greater unsaturation of the blood fatty-acids and lower total lipids, but again the findings are masked by the large amounts of chaulmoogra administered.

A possible explanation of the decrease in unsaturated blood fatty acids in the early leprosy is that since the *Mycobacterium leprae* requires such substances in its metabolism there may occur a gradual depletion in the tissues of these unsaturated acids, and a resultant lowering of the blood levels as equilibrium is reached. There does not seem to be a marked increase in iodine values in cases improving under extensive treatment with chaulmoogra esters as has been noted in infantile eczema treated with linseed oil. In fact, the 3 highest numbers—108.0, 120.4, and 129.3—occurred in treated patients rapidly becoming worse. This might indicate that the unsaturated chaulmoogric acids (iodine value of U.S.P. chaulmoogra oil 98-104) are utilized by the *Mycobacterium leprae* or are converted into a substance suitable for its growth and development. Such a circumstance would prevent the concentration of unsaturated fatty acids in the blood of patients receiving relatively large amounts of chaulmoogra.

Summary. The blood of 53 "cuta-neural" (*i. e.*, mixed) cases of leprosy were examined. The average iodine value for the group was 58.5 ± 15.9 , the total lipids being 0.805 ± 0.161 Gm./100 cc. Early "cuta-neural" leprosy and cases improving under chaulmoogra therapy exhibited higher unsaturation of the fatty acids but lower lipids than did the blood of more extensively treated advanced cases which were stationary or progressing.