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# Effect of Gold Administration on Liver Function in Dogs.

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It is a well-established fact that patients with rheumatoid arthritis experience much relief following the development of jaundice.[1] The jaundice apparently must be of the immediate direct reacting type (*i.e.* nonhemolytic), in order to be benficial. Hench[2] has suggested that the ameliorating effect of gold in rheumatoid arthritis is perhaps analogous to, if not basically identical with, that induced by intercurrent jaundice or pregnancy.

Hartung[3] found jaundice to be an uncommon sequela of gold salt therapy (2 in 800 cases). Altogether Hartung reports 4 patients who developed jaundice following a course of gold therapy. The onset of jaundice was accompanied by an improvement in the patients' subjective and objective symptoms, with relapses occurring almost immediately after the jaundice subsided. Hartung feels it to be highly questionable whether or not the jaundice was actually due to the gold salt therapy.

In this laboratory we have been concerned with the relationship of liver function to rheumatoid arthritis, and some of us[4] have described a method by means of which artificial jaundice of the direct reacting type may be produced. The present study was undertaken in order to ascertain the effect of gold administration on liver function.

*Experimental.* The following tests were carried out:

1. Rose Bengal Clearance[5]
2. Alkaline phosphatase[6]
3. Direct and indirect quantitative van den Bergh reaction for Bilirubin[7]

Two dogs, which were in good health and which weighed 13.2 and 14.1 kg were used.

Following the determination of control values for the above tests, 25 mg of gold in the form of sodium gold thiomalate (myochrysine) were administered to each dog intramuscularly each day for one week. Again their liver functions were tested. Next the gold administration was repeated, using 75 mg per day instead of 25. After one week liver function tests were repeated. Then, following a period of 2 weeks, the tests were again repeated.

Following this we administered 100 mg per day of gold thioglucose (solganal-B) in a 10% aqueous solution. Four days following the last administration, all the tests were repeated. The results are shown in Table I. It is apparent from the results that in no case did any of the liver functions tested, vary beyond the values accepted as normal.

*Discussion.* Rawls *et el.*[8] showed that patients with rheumatoid arthritis in many instances exhibit abnormal values for tests of liver function. Apparently considerable disturbance of liver function is needed before an amelioration of rheumatic symptoms is noted. Hence it appears unlikely that gold acts by producing sufficient effect on the liver to produce the relief from arthritic symptoms in this manner. On the other hand the poorly functioning liver of rheumatoid arthritis patients may be more easily open to the effect of gold therapy. In order to decide that, more quantitative studies on patients receiving gold therapy are needed.

[1] Hench, P. S., *Med. Clin. No. Am.*, 1940, **24**, 1209.

[2] Hench, P. S., *Ann. Int. Med.*, p. 618, April, 1947.

[3] Hartung, E. F., *Med. Clin. No. Am.*, p. 553, May 1946.

[4] Snapp, F. E., Gutman, M., Li, T. W., and Ivy, A. C., *J. Lab. Clin. Med.*, 1947, **32**, 321.

[5] Stowe, W. P., Delprat, G. D., and Weeks, A., *Am. J. Clin. Path.*, 1933, **3**, 55.

[6] Shinowara, Jones and Reinhart, *J. Biol. Chem.*, 1942, **142**, 921.

[7] Hoffman, W. S., *Photelometric Clinical Chemistry*, New York, 1941, p. 231.

[8] Rawls, W. B., Weiss, S., and Collins, V. L., *Ann. Int. Med.*, 1939, **12**, 1455.

TABLE I.
Effect of Gold Therapy on Liver Function.

| Dog | Alkaline phosphatase, units % | Rose Bengal clearance, % | van den Bergh reaction | |
|---|---|---|---|---|
| | | | Direct, mg % | Indirect, mg % |
| Control Values. | | | | |
| 1 | 6.2 | 119 | 0.0 | 0.2 |
| 2 | 4.4 | 109 | 0.0 | 0.1 |
| Following 1 wk of daily administration of 25 mg of gold (sodium auro thiomalate). | | | | |
| 1 | 6.4 | 94 | 0.1 | 0.0 |
| 2 | 5.8 | 96 | 0.0 | 0.0 |
| Following 1 wk of daily administration of 75 mg of gold (sodium auro thiomalate). | | | | |
| 1 | 7.2 | 111 | 0.1 | 0.0 |
| 2 | 8.2 | 111 | 0.1 | 0.0 |
| Two wks later. No gold given during this interval. | | | | |
| 1 | 6.3 | 96 | 0.0 | 0.1 |
| 2 | 6.4 | — | 0.0 | 0.0 |
| Following 1 wk of daily administration of 100 mg of gold thio glucose. | | | | |
| 1 | 7.0 | 115 | 0.0 | 0.0 |
| 2 | 6.4 | 95 | 0.0 | 0.0 |

In this study on dogs, the doses used, in terms of human therapy, were large, and a course of treatment which would require weeks in man is compressed into one week.

*Summary.* 1. Two dogs received gold in the form of sodium auro thiomalate and of thioglucose daily for a total of 3 weeks.

2. Determinations of Rose Bengal Clearance, alkaline phosphatase, and direct and indirect quantitative van den Bergh revealed no pathological changes in liver function.

3. These observations do not support the view that the ameliorating effect of gold therapy in rheumatoid arthritis is due to the effect of the gold on the liver.

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## Failure of Thyroidectomy and Thiouracil to Protect Rat Liver from Acute Carbon Tetrachloride Injury.

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(Introduced by K. M. Endicott.)

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Leach and Forbes[1] have reported that sulfanilamide administered to rats protected the liver from inhaled carbon tetrachloride. In a subsequent experiment Forbes, Leach and Williams[2] found that sulfanilamide also retarded the development of hepatic cirrhosis induced by $CCl_4$. They suggested that the protective action might be related to the inhibition of thyroid activity known to be induced by sulfanilamide. György and Goldblatt[3] and György, Rose and Goldblatt[4] have shown that thiouracil and propylthiouracil exert a marked preventive effect on the incidence and degree of dietary cirrhosis in rats. These authors also suggested that the pre-

[1] Leach, B. E., and Forbes, J. C., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 361.

[2] Forbes, J. C., Leach, B. E., and Williams, G. Z., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 47.

[3] György, P., and Goldblatt, H., *Science*, 1945, **102**, 451.

[4] György, P., Rose, C. S., and Goldblatt, H., PROC. SOC. EXP. BIOL. AND MED., 1948, **67**, 67.