

rocytic life span as was previously considered (1).

**Summary.** 1. Glucose utilization, phosphate uptake and reduced glutathione content of erythrocytes are significantly lowered following uretero-caval anastomosis and contralateral nephrectomy of the dog. 2. Above biochemical changes are of the same magnitude as following bilateral nephrectomy. Thus presence of hypertrophying renal tissue without an excretory outlet is not protective toward these alterations.

1. Muirhead, E. E., Jones, F., *J. Lab. and Clin. Med.*, 1958, v51, 49.

2. Muirhead, E. E., Jones, F., Groves, M., *Am. J. Med.*, 1957, v22, 971.

3. Muirhead, E. E., Stirman, J. A., *J. Clin. Invest.*, 1958,

4. ———, *Am. J. Path.*, 1958, v34, 561.

5. Somogyi, M., *J. Biol. Chem.*, 1945, v160, 69.

6. Hollingsworth, J. W., *J. Lab. and Clin. Med.*, 1955, v45, 920.

7. Pranker, T. A. J., *Nature*, 1954, v173, 871.

8. Grunert, R. R., Phillips, P. H., *Arch. Biochem.*, 1951, v30, 217.

9. Patterson, J. W., Lazarow, A., Levey, S., *J. Biol. Chem.*, 1949, v177, 197.

10. Taylor, W. F., Blair, W. M., *J. Lab. and Clin. Med.*, 1932, v17, 1256.

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## Influence of Vitamin A on Cholesterol Blood Levels. (25245)

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There is evidence that a relationship exists between elevated serum cholesterol levels and atherosclerosis(1,2). It therefore seemed worthwhile to investigate further substances which might be capable of reducing serum cholesterol levels. Vitamin A\* was chosen because of favorable reports of its antihypercholesteremic properties in animals. Weitzel, Schon, and Gey(3) reported that Vit. A had a definite protective effect on experimental atherosclerosis in rats. Later, the same workers(4) gave large oral doses of the fat-soluble Vit. A, E, and K to old atherosclerotic hens, over a period of 75 to 100 days. With Vit. E, a slight antiatherosclerotic effect was observed in a few cases. With Vit. A, however, macroscopic examination showed marked regression of the atheromatosis in all the test groups and a decrease in total fat content of the aorta. However, Oppenheim and Bruger,(5) reported that oral doses of Vit. A did not alter the pattern of development of experimental atherosclerosis in rabbits. Wendt(6) reported that massive doses of Vit. A caused an increase in cholesterol content of human serum. Lasch(7) reported that Vit. A, given as "Vorgan"

3 times a day to human beings, in doses of 40,000 to 80,000 I.U. caused an increase in serum cholesterol within 5 to 10 days. This increase was due to an increase in serum cholesterol esters.

**Method.** Two types of patients were used in this investigation: first, normal individuals, aged 30 to 50; and second, individuals having experienced a myocardial infarction within the year, aged 40 to 55. The above groups were subdivided; those receiving Vit. A and those receiving no medication. Thus there were 4 different experimental groups. **Group A.** Each of these patients experienced at least one myocardial infarction within the year. All individuals showed elevated serum cholesterols, total, free, and ester levels. 100,000 I. U. of Vit. A acetate per day was administered orally to each patient. **Group B.** Each of these patients had suffered at least one myocardial infarction within the year. All had elevated cholesterol levels, total, free, and esters. No medication was administered to this group. **Group C.** All patients had normal cholesterol levels, total, free, and esters. No clinical history of coronary artery disease. 100,000 I. U. of Vit. A acetate per day was administered orally to

\* Vit. A was furnished by Hoffman-La Roche, Nutley, N. J.

TABLE I. Average Blood Levels of Groups A, B, C, and D.

| Groups | No. of patients | Total cholesterol, mg % |               | Vit. A, $\mu$ g % |               |
|--------|-----------------|-------------------------|---------------|-------------------|---------------|
|        |                 | Before therapy          | After therapy | Before therapy    | After therapy |
| A      | 8               | 355 $\pm$ 51*           | 275 $\pm$ 24  | 56 $\pm$ 8        | 107 $\pm$ 29  |
| B      | 5               | 318 $\pm$ 59            |               | 59 $\pm$ 22       |               |
| C      | 5               | 240 $\pm$ 24            | 236 $\pm$ 15  | 51 $\pm$ 38       | 101 $\pm$ 15  |
| D      | 5               | 230 $\pm$ 28            |               | 69 $\pm$ 22       |               |

\* Stand. dev.

each patient. *Group D.* As in Group C, all patients had normal cholesterol levels, total, free, and ester. No clinical history of coronary artery disease. No medication was given to this group. In Groups A and B, serum was obtained every 2 weeks for 6 months, and in Groups C and D, for 3 to 4 months. All patients were requested to restrict their fat intake. Average dietary intakes are given in Table II. Weekly diet charts were recorded at intervals during the investigative period. Cholesterol determinations, total, free, and esters, were carried out on all patients in triplicate, biweekly, by the method of Schoenheimer and Sperry(9). With these patients in Groups A and C, several determinations were made to establish a mean cholesterol level before initial Vit. A therapy. Vit. A determinations were carried out monthly on all patients using the Carr-Price antimony trichloride method(8).

*Results.* Following administration of Vit. A, all of the atherosclerotic patients (Group A), showed a decrease in total cholesterol, (Table I) ranging from 20 mg % to 175 mg %, which was attributed to a decrease in the ester fraction. The greatest reductions were seen in patients with the highest initial levels. Free cholesterol remained constant in all cases.

No significant change was seen in the cholesterol levels, total (Table I), free and ester in any of the other experimental groups.

Vit. A levels determined on all patients were either within normal limits or slightly

elevated, before initiation of Vit. A therapy. Patients in Groups A and C who received supplementary Vit. A exhibited an average Vit. A blood level of 107  $\pm$  28.6 and 101  $\pm$  15.2  $\mu$ g % respectively 4 to 6 months after vitamin therapy was initiated (Table I). All patients tolerated 100,000 I.U. of Vit. A acetate without untoward symptoms.

As shown in Table II, about 20% of dietary intake in all patients was fat, and daily caloric intake was approximately 2,300 calories.

*Discussion.* The effect of Vit. A therapy on cholesterol levels in patients suffering from atherosclerosis of varying degrees, (Group A) was encouraging. Average total cholesterol blood level in this group before therapy was 355  $\pm$  50.9 mg % and 275  $\pm$  24.4 mg % after therapy (Table I). This difference was shown to be statistically significant. Statistically no significant change was seen in the other experimental groups.

Since the accuracy for the Schoenheimer-Sperry procedure for cholesterol determination ranges between 10-15 mg %, part of the deviation seen in each group may be attributed to limitations of the method.

A small percentage of the deviation in all groups might be attributed to diet but this cannot be considered too significant since all patients ingested a similar diet.

Although little is known about mode of action or site of action of this vitamin in the body, it would seem that one of its actions is to affect elevated serum cholesterol levels. No significant effect was noted in Group C in

TABLE II. Average Daily Dietary Intakes.

| Group | CHO, g        | Fat, g      | Fat, %*     | Protein, g   | Table calories |
|-------|---------------|-------------|-------------|--------------|----------------|
| A     | 253 $\pm$ 98† | 69 $\pm$ 70 | 19 $\pm$ 11 | 83 $\pm$ 86  | 2298 $\pm$ 624 |
| B     | 276 $\pm$ 52  | 80 $\pm$ 69 | 20 $\pm$ 8  | 91 $\pm$ 33  | 2412 $\pm$ 219 |
| C     | 237 $\pm$ 43  | 75 $\pm$ 52 | 18 $\pm$ 7  | 101 $\pm$ 71 | 2300 $\pm$ 416 |
| D     | 266 $\pm$ 49  | 98 $\pm$ 75 | 21 $\pm$ 11 | 91 $\pm$ 75  | 2410 $\pm$ 612 |

\* % fat calculated on basis of percentage of total 6 ms. carbohydrate, protein, and fat.

† Stand. dev.

which the patients had normal cholesterol levels. It might be postulated that Vit. A either inhibits synthesis of cholesterol in cases of over-synthesis, or causes mobilization and excretion of cholesterol when blood levels become excessively high.

These results are in direct disagreement with work done by Wendt(6) and Lasch(7). Their reported increase in serum cholesterol after Vit. A administration may be explained on the basis of the interference of Vit. A with cholesterol determination as pointed out by Kinley and Krause(10). Since Lasch and Wendt were using a reagent containing ferric chloride which was used both for cholesterol determinations and Vit. A determinations, their apparent elevations were possibly due to a color produced by both cholesterol and Vit. A. The same type of elevation was seen in this laboratory until the Schoenheimer-Sperry method was adopted for separation of Vit. A from the serum before carrying out cholesterol determinations.

*Summary.* Oral administration of 100,000

I. U. of Vit. A acetate for 4 to 6 months significantly reduced the elevated serum cholesterol levels in atherosclerotic patients but had no effect on individuals with normal cholesterol levels.

1. Virchow, R., *Arteriosclerosis*, Ed. F. Chance, N. Y. Dewitt Co.
2. Schoenheimer, R., *Z. physiol. Chem.*, 1928, v177, 143.
3. Weitzel, G., Schon, H., Gey, F., *Klin. Wochschr.*, 1955, v33, 772.
4. ———, *Z. physiol. Chem.*, 1956, v304, 247.
5. Oppenheim, E., Bruger, M., *Arch. Path.*, 1952, v53, 520.
6. Wendt, H., *Dent. med. Wochschr.*, 1936, v62, 1213.
7. Lasch, F., *Klin. Wochschr.*, 1934, v13, 1534.
8. Carr, R. H., Price, E. A., *J. Biol. Chem.*, 1926, v20, 497.
9. Schoenheimer, R., Sperry, W. M., *ibid.*, 1934, v106, 745.
10. Kinley, L. J., Krause, R. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1958, v99, 244.

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### Further Studies of Gaseous Ion Action on Trachea.\*† (25246)

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During the past 3 years, it has been demonstrated that light air ions markedly affect the functional efficiency of the mammalian trachea(1,2). In general, (+)ions depress ciliary activity, contract the tracheal wall and induce a state of vasoconstriction and hyper-reactivity to mechanical trauma. (-)ions accelerate the rate of ciliary beat, reverse the (+)ion-induced contraction of the wall, and do not alter normal vascularity or the response to trauma. Experiments performed to determine which atmospheric components in

ionized form account for the observed functional changes implicated negatively charged oxygen and positively charged carbon dioxide respectively as the specific mediators for acceleration and inhibition of ciliary activity (3). However, these observations apply to only one physiological effect, ciliary activity. Because experiments on other effects, such as enhanced vulnerability to trauma, require exposure of the trachea *in situ* to nitrogen and carbon dioxide for long periods of time, a procedure not compatible with life, a method was devised which permitted the animal to respire through a separate airway while response of the trachea to treatment with various gases was observed.

*Methods.* 1) Operative technic: Albino rabbits weighing 10-12 lb were anesthetized

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