

galaxy and of the dynamics and statistics of encounters between stars Dr. Chandrasekhar has become one of the leading authorities in the field of galactic dynamics. In the new volume he has blended his own researches and those of others in a well-rounded book, which should for many years to come be "must" reading for every prospective student of galactic structure and dynamics.

The book opens with a chapter on "Kinematics." Beginning with a brief analysis and descriptions of the properties of stellar motions for the regions in the immediate vicinity of the sun, the author describes the phenomena of galactic rotation and of the asymmetry in stellar motions for high velocity stars. The chapter closes with a survey of the properties of external galaxies and a brief mention of some characteristics of star clusters.

In the second chapter, "The Time of Relaxation of a Stellar System," we find a clear discussion of the effects of stellar encounters. The presentation follows closely that of a series of papers by Chandrasekhar and Williamson. Even in the two-body approximation the problem is quite complex. No attempt has been made to extend the analysis so as to include the effects of multiple encounters by adapting the theory of fluctuations to the stellar case. A first trial in this direction has recently been made by Chandrasekhar and von Neumann, but the two-body approximation will probably remain important for rough estimates for many years to come.

The dynamics of a stellar system with differential motions, such as our own galaxy, is presented in the third chapter. The treatment follows closely that of the author and many astronomers will be delighted to have here an authoritative summary of Chandrasekhar's earlier papers.

The discussion of the dynamics of stellar systems is contained in the fourth chapter, in which special attention is given to the dynamical interpretation of spiral structure. The sections on Lindblad's theory of spiral structure, which present a fair and critical

evaluation of current achievements and remaining difficulties, will probably be more widely read than any other part of Chandrasekhar's volume.

The book closes with a chapter on the dynamics of star clusters. The problem of globular clusters receives only scant attention, but the treatment of galactic clusters is quite complete and excellently written. In this chapter Chandrasekhar indicates in which way the theories for the dissolution of galactic clusters under the influence of the shearing forces of galactic rotation must be adapted in order to include the effects of encounters between cluster members.

At the conclusion of every chapter there appear bibliographical notes that contribute much to the general value of the volume. A detailed subject index and some appendices will undoubtedly prove very useful.

Chandrasekhar's volume comes at a time when there exists a real need for a book on stellar dynamics. Research in this field has recently developed along rather divergent lines and none of the books published during the past ten years has succeeded in providing a unified treatment. Chandrasekhar's book does this for the first time. Some of us who have worked in the field of galactic dynamics might here and there have preferred a somewhat different approach, but when it comes to judging the book as a whole we all pay our respects to the skill and insight of the author.

This book should exert a profound influence on the future developments in the field of galactic dynamics. I can recommend its study unreservedly to newcomers in the field and to those who already have a passing acquaintance with its problems. The experts can profit from reading it. If I were stranded in a far-off prison camp where I would be allowed one book I would ask for Chandrasekhar's volume. I am sure that per ounce of paper it would provide the most stimulation for continued research in theoretical astronomy.

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## SPECIAL ARTICLES

### TREATMENT OF EXPERIMENTAL RENAL HYPERTENSION WITH VITAMIN A

RECENTLY Pena and Villaverde reported favorable results in the treatment of essential hypertension in man with large doses of vitamin A orally.<sup>1</sup> Several case histories confirmatory of this finding have been reported to the senior author by medical colleagues. In view of these reports and the many similarities between experimental renal hypertension in the dog and essential hypertension in man, inclusive of a probable partial common pathogenesis, we have studied the

<sup>1</sup> J. Govea Pena and M. Villaverde, *Rev. Cubana Cardiol.*, 2: 322, 1940.

effect of vitamin A by mouth in experimental renal hypertension in dogs. This report summarizes our preliminary results.

Five dogs were rendered hypertensive by the Goldblatt technique<sup>2</sup> and the resulting hypertension was permitted to stabilize over a period of five to eight months. Mean blood pressure readings were obtained by puncture of a femoral artery two to three times a week. Studies on the blood urea nitrogen, urinalyses and determinations of body weight were made at monthly or bimonthly intervals. Three of the dogs

<sup>2</sup> H. Goldblatt, J. Lynch, R. F. Hanzal and W. W. Summerville, *Jour. Exper. Med.*, 59: 347, 1934.

were treated daily with 200,000 units of vitamin A dissolved in 1 cc of sesame oil<sup>3</sup> by mouth for three months, followed by 400,000 units of vitamin A in 2 cc of sesame oil for an additional three months. The other two dogs served as controls and were given oral daily doses of 1 cc of sesame oil for three months, to be followed by 2 cc of sesame oil for another three months. A limited number of blood serum vitamin A determinations (method of McCoord and Luce-Clausen<sup>4</sup>) were made on these five animals and on two untreated normotensive and two untreated hypertensive dogs.<sup>5</sup>

Striking reductions in the blood pressures were observed in each of the three dogs treated with vitamin A. The results for the first dog, which are typical for the other two animals, are illustrated in Fig. 1. The normotensive blood pressure range for this dog, which weighed 16 Kg., was 100–120 mm Hg. Following bilateral constriction of the renal arteries, the dog developed a hypertension which ranged from 150–180 mm Hg. during the succeeding eight months. During the second week of vitamin A therapy, the blood pressures of the animal decreased approximately 20 mm Hg. and then ranged from approximately 120–140 mm Hg. for the remainder of the first three months of treatment. Three additional months of therapy just completed at the increased dosage of 400,000 units of vitamin A daily resulted in a further gradual reduction in blood pressure to the normotensive level of 100–120 mm Hg. The blood pressures of the second dog, which weighed 12 Kg., were similarly reduced from a hypertensive range of 190–210 mm Hg. to the pre-constriction normotensive level of 130–140 mm Hg. The blood pressures of the third dog weighing 15 Kg. were decreased from a hypertensive range of 150–170 mm Hg. to a level of 130–150 mm Hg. during the second week of vitamin A therapy and have remained in this range to date (third month of treatment).

The two control dogs treated with sesame oil have thus far shown no significant changes in their hypertensive levels of 150–170 mm Hg. and 160–180 mm Hg., respectively. Moreover, we have never seen spontaneous blood pressure decreases similar to the reductions observed in the three dogs treated with vitamin A in 75 renal hypertensive dogs during the past three years.

Serum vitamin A determinations on the untreated normotensive and hypertensive dogs showed values of 40–70 units per 100 cc. During vitamin A therapy the serum vitamin A values of the three dogs varied

<sup>3</sup> Generously supplied by Dr. J. B. Rice, Department of Medical Research of the Winthrop Chemical Company.

<sup>4</sup> A. B. McCoord and E. M. Luce-Clausen, *Jour. Nutrition*, 7: 557, 1934.

<sup>5</sup> We are grateful to Dr. H. P. Popper, of the Department of Pathology, for these determinations.

from approximately 500–3,000 units per 100 cc, whereas the two dogs given sesame oil ranged from 40–70 units per 100 cc.

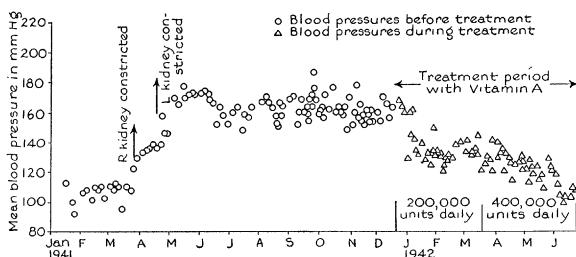


Fig. 1

No toxic effects from the vitamin A therapy were detected in any of the animals, although our present observations do not rule out this possibility. The appetites of the dogs remained excellent, their weights constant, and their blood urea nitrogens and urines normal throughout. The two dosage levels of vitamin A used were somewhat less than 1/20 and 1/10 of the amounts reported toxic for rats by some workers<sup>6, 7, 8</sup> but less than 1/100 and 1/50 of the toxic levels reported by others<sup>9, 10</sup> who contend that the lower values of the former investigators are due to impurities.

The mechanism of the striking reductions in the blood pressures of these three renal hypertensive dogs by high dosage vitamin A therapy is obscure. We have seen no evidence of hypovitaminosis A in experimental renal hypertension in dogs, and the few serum vitamin A determinations reported above are confirmatory in this respect. The fact that vitamin A in high dosage has been shown to raise the urea clearance of dogs 40 per cent. above normal<sup>11</sup> suggests that vitamin A in large doses may disturb the pathophysiologic pressor mechanisms produced by renal artery constriction. The antihypertensive action of vitamin A in experimental renal hypertension may, of course, be totally unrelated to its specific vitamin effects. Indeed, one or more chemically related compounds with little or no vitamin A action may prove to be more effective than vitamin A as hypotensive agents. The vitamin A preparation used contained traces of impurities. The unlikely possibility that one or more of these impurities is responsible for the reductions in blood pressure must be investigated.

In any event, we purpose to enlarge considerably this preliminary study of vitamin A in experimental

<sup>6</sup> G. Domagk and P. von Bobeneck, *Virch. Arch. of Path. Anat.*, 290: 385, 1933.

<sup>7</sup> W. von Drigalski, *Klin. Woch.*, 12: 308, 1933.

<sup>8</sup> H. Popper and S. Brenner, *Jour. Nutrition*, 23: 431, 1942.

<sup>9</sup> E. B. Vedder and C. Rosenberg, *Jour. Nutrition*, 16: 57, 1938.

<sup>10</sup> I. Ikegaki, *Ztschr. f. Vitaminforsch.*, 7: 113, 1938.

<sup>11</sup> R. C. Herrin and H. J. Nicholes, *Am. Jour. Physiol.*, 125: 786, 1939.

renal hypertension and also to determine the possible antihypertensive effects of other compounds chemically related to vitamin A.

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### RENAL HYPERLIPEMIA IN DOGS

OBSERVATIONS made in studies on children suffering from nephrosis gave rise to the question whether or not the kidney itself may exert a regulatory influence on the blood lipids, disturbance of which could lead to the hyperlipemia manifested in nephrosis. This problem was studied by determining the content of total fat and of total and free cholesterol in the blood serum of 18 dogs which had been subjected to nephrectomies<sup>1</sup> or to subcutaneous injections of bichloride of mercury, uranium nitrate or potassium bichromate.

Bilateral nephrectomy, performed on three dogs, was followed by a continuous rise in the level of serum cholesterol. The effect observed in one of these dogs after the second kidney had been removed is shown in

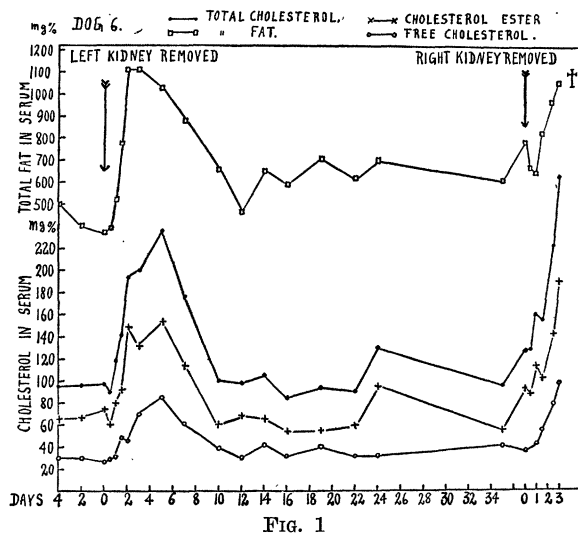


FIG. 1

Fig. 1. It can be seen that the total fat content increases beyond the extent that could be accounted for by the increase in cholesterol, thus indicating that lecithin and probably also fatty acids and neutral fat participate in this increase.

The effect of unilateral nephrectomy was studied in two dogs. In both animals the level of blood lipids rose for from 4 to 7 days and then returned to normal in 12 or 14 days after the operation (Fig. 1). The increase is obviously connected with the sudden removal of one kidney, while the return to normal level

<sup>1</sup> I am indebted to Dr. Harry Goldblatt and Dr. Joseph R. Kahn, of the Institute of Pathology, School of Medicine, Western Reserve University, for performing the operations on the dogs.

may well be due to the subsequent hypertrophy of the remaining kidney. A sham operation performed as control did not influence the blood lipid level.

In 10 dogs a single dose of bichloride of mercury administered subcutaneously was followed in every instance by an increase in the content of total fat as well as of free cholesterol and cholesterol ester. One lethal dose of 16 mg per kilogram of body weight led to a continuous increase until death. When a smaller dose was injected, however, the resulting hyperlipemia subsided and the values returned to normal. The results of one of the eight experiments carried out with a single injection of 5 mg of bichloride of mercury per kilogram of body weight are shown in Fig. 2. The resulting hyperlipemia is not

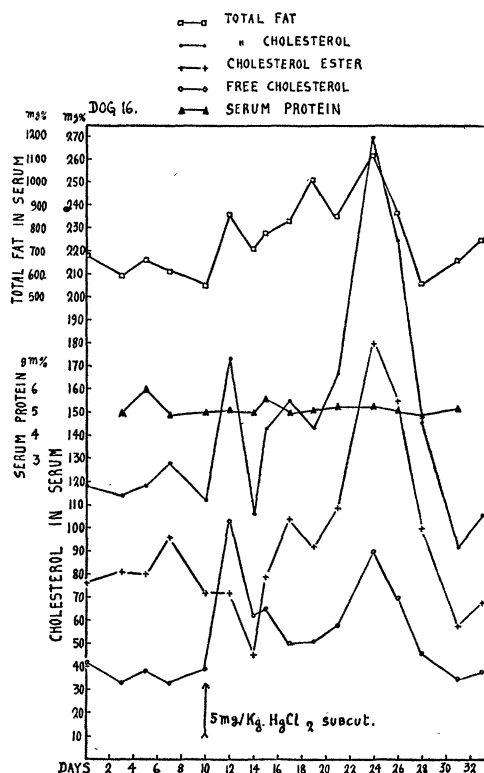


FIG. 2

accompanied by a decrease in the content of serum protein. This observation is of importance in connection with the theory which explains the hyperlipemia in nephrosis on the basis of hypoproteinemia. A smaller dose of bichloride (2 mg per kilogram of body weight) was injected intramuscularly in two other dogs twice a week for between three and four weeks. In these dogs hyperlipemia developed slowly and the level of total fat and of cholesterol continued to rise as long as the injections were given.

Subcutaneous injection of potassium bichromate (7 mg per kilogram of body weight) in one dog and of uranium nitrate (6 mg per kilogram of body weight)