Though the data in the first three weeks of oestrogen therapy would be consistent with an effect of oestrogen on testicular function mediated through the pituitary, the later observations showing discrepancies between luteinizing hormone and testosterone levels would suggest that the effects are complex and that oestrogens may have a direct effect on the testes independently of the pituitary. Such effects have been demonstrated in experimental animals—for example, by Samuels *et al.* (1964). It is also conceivable that failure of complete suppression could be accounted for by protein-binding phenomena, though these have not been shown to be significant for luteinizing hormone or for testosterone.

The investigation also demonstrates that oestrogen therapy does not suppress pituitary production of growth hormone or of A.C.T.H.; it thus gives further support to the belief that the place of early hypophysectomy in the treatment of metastatic cancer of the prostate warrants further study.

Summary

Nine patients with carcinoma of the prostate have been treated with large doses of oestrogens, and their plasma concentrations of luteinizing hormone and testosterone have been measured during treatment. There was an acute decrease in the levels of both hormones, so that after two to three weeks of treatment luteinizing hormone concentration had fallen by 53.5% and testosterone by 67.2%. This suppression was not sustained in all cases. It is concluded that though the acute effects of oestrogens on the suppression of androgen production may be mediated through the pituitary the effects are in general more complex, and escape from suppression may occur.

This work was supported by grants from the Australian Research Grants Committee and the National Health and Medical Research Council. We are grateful to Dr. K. J. Catt for helpful discussion, to Miss J. Spinks for assistance with the growth hormone assays, and to Dr. J. McKenzie for the measurement of plasma cortisol.

Requests for reprints should be addressed to Dr. Henry Burger.

References

Birke, G., Franksson, C., and Plantin, L.-O. (1955). *Acta chir. scand.*, **109**, 1, 129.
Burger, H. G., Oliver, J. R., Davis, J., and Catt, K. J. (1967). Submitted for publication.
Catt, K. J., Niall, H. D., and Tregear, G. W. (1967). *J. Lab. clin. Med.* In press.
Coppage, W. S., jun., and Cooner, A. E. (1965). *New Engl. J. Med.*, **273**, 902.
Forchielli, E. *et al.* (1965). *Acta endocr. (Kbh.)*, **50**, 51.
Glick, S. M., Roth, J., Yalow, R. S., and Berson, S. A. (1963). *Nature (Lond.)*, **199**, 784.
Hudson, B., Coghlan, J. P., and Dulmanis, A. (1967). *Ciba Foundation Colloquia on Endocrinology*, vol. 16, p. 140. London.
—— —— —— Wintour, M., and Ekkel, I. (1963). *Aust. J. exp. Biol. med. Sci.*, **41**, 235.
Huggins, C., and Clark, P. J. (1940). *J. exp. Med.*, **72**, 747.
—— and Hodges, C. V. (1941). *Cancer Res.*, **1**, 293.
—— Masina, M. H., Eichelberger, L., and Wharton, J. D. (1939). *J. exp. Med.*, **70**, 543.
Mattingly, D. (1962). *J. clin. Path.*, **15**, 374.
Odell, W. D., Ross, G. T., and Rayford, P. L. (1966). *Metabolism*, **15**, 287.
—— —— —— (1967). *J. clin. Invest.*, **46**, 248.
Samuels, L. T., Short, J. G., and Huseby, R. A. (1964). *Acta endocr. (Kbh.)*, **45**, 487.
Whitmore, W. F., jun. (1956). *Amer. J. Med.*, **21**, 697.

Hypocholesterolaemic Effect of Bengal Gram: a Long-term Study in Man*

K. S. MATHUR,† M.D., F.R.C.P., F.A.M.S., F.N.I.; M. A. KHAN,‡ M.D.; R. D. SHARMA,§ PH.D.

Brit. med. J., 1968, **1**, 30–31

The frequent association of hypercholesterolaemia with ischaemic heart disease has stimulated search for agents which reduce the cholesterol level in the blood. Our earlier studies have shown that Bengal gram, or "chana" (*Cicer arietinum*), significantly lowers experimentally induced high levels of cholesterol in both serum and tissues of albino rats (Mathur *et al.*, 1963, 1964) and rabbits (Mathur *et al.*, 1965). A long-term study extending to 67 weeks in man has now been undertaken to assess the hypocholesterolaemic effect of Bengal gram.

Material and Methods

Thirty male subjects who were free from any systemic disease were studied. Their ages ranged from 15 to 50 years (mean 33.5 years). Their mean weight was 117.2±24.6 lb. (54±11.2 kg.). They were divided into two groups.

Group 1.—Twenty subjects were given "low-fat diet" containing 10 g. of fat for two weeks. Lipid studies were then made to determine the basal values. They were then fed on "high-fat diet" containing 156 g. of butter-fat and supplying 2,812 calories daily. After 10 weeks of high-fat diet, when the serum-lipid levels had become stabilized, they were put on "high-fat + Bengal gram diet" by substituting Bengal gram for wheat-flour and other cereals while maintaining the quantity of butter-fat and total calories at the same level. They were observed on this diet for the next 55 weeks.

Group 2.—Ten subjects were put on low-fat diet for the first two weeks. They were then given the routine hospital diet consisting of 35 g. of fat and supplying 2,756 calories, and were observed for the same period as in group 1.

The composition of the various diets is given in Table I.

TABLE I.—*Composition of Diet*

Diet	Total Calories	Carbohydrate		Proteins		Fat	
		G.	Cal. %	G.	Cal. %	G.	Cal. %
Low-fat ..	2,730	550	80·7	110	16·0	10	3·3
High-fat ..	2,812	290	42·0	57	8·1	156	49·9
Bengal gram	2,831	247	35·1	85	12·0	167	52·9
Hospital ..	2,756	500	72·6	110	16·1	35	11·3

Blood samples were collected in the morning at weekly intervals throughout the experiment. They were analysed for serum total cholesterol and free and ester cholesterol by the techniques of Zak *et al.* (1954), for serum lipid phosphorus by

* From the Department of Medicine, S. N. Medical College, Agra, India. Financial assistance for this work was provided by the Indian Council of Medical Research.
† Professor and Head of the Department of Medicine.
‡ Research Fellow.
§ Research Officer.

the method of Fiske and Subbarow (1925), and for cholesterol contents of alpha- and beta-lipoproteins by the technique of Langan *et al.* (1955). The 24-hour excretion of faecal bile acids and Liebermann–Burchardt reacting sterols were estimated by the method of Mosbach *et al.* (1954) and Kenny (1952) respectively. The average of the three days' faecal matter was taken as the amount excreted in 24 hours.

Results

Table II shows the mean values of serum total cholesterol, free and ester cholesterol, lipid phosphorus, and cholesterol contents of alpha- and beta-lipoproteins on the low-fat diet, on the high-fat diet, and at the end of 55 weeks of the Bengal gram diet.

TABLE II.—*Mean Serum Lipid Levels in mg./100 ml. on Different Diets*

Serum Lipid fractions	Low-fat Diet	High-fat Diet	High-fat + Bengal Gram Diet
Serum total cholesterol	122·6 ± 23·1	206·4 ± 20·0	160·0 ± 24·1
Serum free cholesterol	40·0 ± 11·1	51·9 ± 8·7	43·4 ± 6·5
Serum ester cholesterol	82·6 ± 24·5	154·5 ± 15·7	116·6 ± 22·0
Serum lipid phosphorus	7·9 ± 0·26	8·6 ± 1·20	8·3 ± 1·15
C:P ratio	15·5 ± 5·0	23·5 ± 5·5	18·7 ± 5·3
Cholesterol contents of:			
Alpha-lipoproteins	30·8 ± 5·6	55·3 ± 7·8	49·1 ± 6·3
Beta-lipoproteins	94·0 ± 18·4	150·7 ± 29·4	113·8 ± 13·2

The difference in serum total cholesterol level between the high- and low-fat diets was statistically highly significant ($P<0.001$). Isocaloric substitution of Bengal gram with high-fat diet resulted in a highly significant ($P<0.001$) reduction of the mean serum total cholesterol level from 206.4 ± 20.0 mg./100 ml. to 160.0 ± 24.1 mg./100 ml. respectively. The levels of serum total cholesterol were found to fall at the end of the fourth week of treatment, and this was followed by a progressive fall up to the twentieth week.

The fall in the mean values of ester cholesterol and of beta-lipoprotein were also statistically highly significant ($P<0.001$). On the other hand, the reduction in free cholesterol, lipid phosphorus, and alpha-lipoproteins was not so definite.

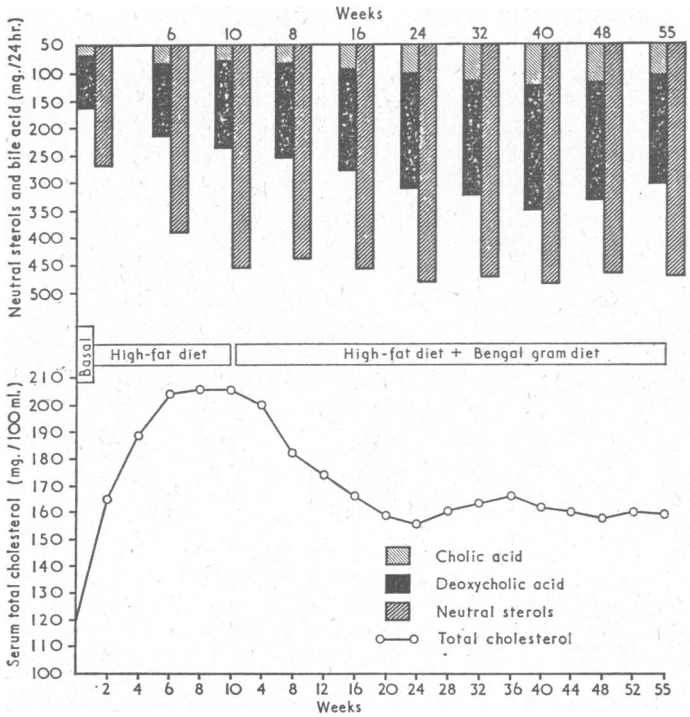
Table III shows the mean values of faecal cholesterol end-products on the various diets. Their relation to serum cholesterol during the entire period of study is shown in the Chart.

There were significant increases in both total bile acid excretion and Liebermann–Burchardt reacting sterols excretion when the diet was exchanged from the low-fat diet to high-fat diet. Substitution of Bengal gram with high-fat diet resulted in a further highly significant ($P<0.001$) increase in the 24-hour excretion of total bile acids, but the excretion of Liebermann–Burchardt reacting sterols was not affected.

The mean serum total cholesterol in group 2 subjects rose from 116.8 ± 20.1 mg./100 ml. on the low-fat diet to 130.5 ± 13.1 mg. on the hospital diet during the 67 weeks' study.

TABLE III.—*Mean Values of Faecal Cholesterol End-products in mg./24 Hours on Different Diets*

Faecal Cholesterol End-products	Low-fat Diet	High-fat Diet	High-fat + Bengal Gram Diet
Total bile acids	163·9 ± 64·0	236·6 ± 73·5	305·9 ± 57·5
Cholic acid	59·3 ± 18·8	73·9 ± 16·0	105·9 ± 30·5
Deoxycholic acid ..	104·6 ± 47·0	162·7 ± 65·5	200·0 ± 46·2
L.B. reacting sterols ..	272·1 ± 65·1	454·8 ± 62·5	470·1 ± 59·6



Effect of Bengal gram on serum total cholesterol and faecal cholesterol end-products.

Discussion

Bengal gram, popularly known as chana in North India, has formed a staple diet of the poor for generations, and may account in part for the lower levels of serum cholesterol in that section of the population (Mathur *et al.*, 1959). The present study has shown that Bengal gram significantly lowers serum lipids in man. A reduction of more than 15% in 16 of the 20 subjects, and its sustained action during long-term administration, not only indicate a definite effect but show that it is superior to many known hypocholesterolaemic substances. Similar observations have been reported in rats and rabbits (Mathur *et al.*, 1963, 1964, 1965).

The mechanism of hypocholesterolaemic action of Bengal gram is uncertain. A significantly increased excretion of faecal bile acids and a corresponding decrease in serum cholesterol suggests that an increased catabolism of cholesterol into bile acids in the liver may be a possible explanation.

Summary

Bengal gram (*Cicer arietinum*) was capable of lowering induced hypercholesterolaemia in 16 out of 20 subjects during a period of study extending over 67 weeks. This effect was greatest at the twentieth week of administration of the diet, and was maintained throughout the period of study. The hypocholesterolaemic effect was associated with a statistically highly significant increase in 24-hour faecal excretion of total bile acids without any significant increase in neutral or Liebermann–Burchardt reacting steroids.

REFERENCES

Fiske, C. H., and Subbarow, Y. (1925). *J. biol. Chem.*, **66**, 375.
Kenny, A. P. (1952). *Biochem. J.*, **52**, 611.
Langan, T. A., Durrum, E. L., and Jencks, W. P. (1955). *J. clin. Invest.*, **34**, 1427.
Mathur, K. S., Gupta, D. N., and Sharma, R. D. (1965). *J. Ass. Phycns. India*, **13**, 923.
—— Singhal, S. S., and Sharma, R. D. (1964). *J. Nutr.*, **84**, 201.
—— Wahi, P. N., Malhotra, K. K., Sharma, R. D., and Srivastava, S. K. (1959). *J. Indian med. Ass.*, **33**, 303.
—— —— and Sharma, R. D. (1963). Ibid., **41**, 379.
Mosbach, E. H., Kalinsky, H. J., Halpern, E., and Kendall, F. E. (1954). *Arch. Biochem. Biophys.*, **51**, 402.
Zak, B., Dickenman, R. C., White, E. G., Burnett, H., and Cherney, P. J. (1954). *Amer. J. clin. Path.*, **24**, 1307.