Letters to the Editor

Prediction of Serum Cholesterol Changes Produced by Dietary Fat

Dear Sir:

I have read with great interest the editorial "Some Thoughts Regarding the P:S Ratio Concept" by Dr. L. W. Kinsell, published in the March issue of your Journal. Dr. Kinsell should be commended for his effort to discourage the use of the P:S ratio concept. Our group in Minnesota shares Dr. Kinsell's views in this respect and we consider the P:S ratio to be a misleading way of expressing the potential effect of a dietary fat on the serum cholesterol concentration of man. Personally, I have maintained this opinion publicly in several meetings in recent years. There are some points in Dr. Kinsell's editorial, however, which demand further clarification.

In referring to the equation introduced by Keys, Anderson and Grande in 1957 (*Lancet*, 2:959), Dr. Kinsell writes: "This formula is based on the hypothesis that a critical relationship exists between the relative amounts of polyunsaturated and saturated fatty acids. Monounsaturated fatty acids (regardless of amount) were assumed to be neutral or nearly so." This is incorrect. The basic hypothesis in the analysis of a large series of experimental data from which our equation was derived was that the effect of a given fat on serum cholesterol concentration is the resultant of the effects of the various kinds of fatty acids and that each of the main groups of fatty acids has a specific effect independent of the effect of the others. We considered three main classes of fatty acids —saturated, monoene and polyene. By multiple correlation analysis we computed the coefficients relating the changes in the amounts of each group of dietary fatty acids (expressed as per cent of the total calorie intake) to the serum cholesterol changes. This analysis showed the coefficient for the saturated fatty acids to be positive, the coefficient for the polyunsaturated fatty acids to be negative and the coefficient for the monounsaturated fatty acids to be, statistically, not significantly different from zero. This last result indicated that changes in the proportion of monoene fatty acids in the diet were not associated with serum cholesterol changes. Accordingly the term for the monounsaturated fatty acids was omitted and the equation expressing the relationship between serum cholesterol changes (Δ Chol.) and the changes in dietary saturated and polyunsaturated fatty acids was written:

$$\Delta \text{ Chol.} = 2.68\ S - 1.23\ P$$

In this equation Δ Chol. represents the mean change of serum cholesterol concentration (mg. per 100 ml.) and S and P the change in saturated and polyunsaturated glycerides of the diet expressed as per cent of the total calorie intake. This simply means that, other factors being constant, in our experiments the mean serum cholesterol concentration increased by 2.68 mg. per 100 ml. when the intake of saturated fatty acids increased by 1 per cent of the total calories and that it decreased by 1.23 mg. per 100 ml. when the dietary intake of polyene fatty acids increased by 1 per cent of the total calories. The lack of effect of the monoene (oleic acid) was confirmed in independent critical experiments (KEYS, A., ANDERSON, J. T. and GRANDE, F. *Proc. Soc. Exper. Biol. & Med.*, 98:387, 1958).

The formula indicates that the serum cholesterol change is approximately a function of the expression 2S–P, but of course 2S–P is not equivalent to P:S. The expression P:S, being a ratio, is independent of the total amount of fat and of the units in which the fatty acids are expressed. The term 2S–P on the other hand, changes not only with the relative amounts of S and P but also with the

absolute amount of fat and its value depends on the units used.

In his editorial Dr. Kinsell fails to emphasize this basic difference between our equation and the P:S ratio. This difference is apparent in Figure 1, which shows the relationship between the values of 2.68 S–1.23 P and the corresponding values of P:S, for various levels of fat intake. It is easy to see that the same P:S ratios correspond to different values of 2.68 S–1.23 P. Therefore, fats of equal P:S ratio will produce different effects on serum cholesterol levels, as predicted from our equation, depending on the level of intake. Conversely, it is possible to produce similar serum cholesterol changes using fats of different P:S value by changing the level of fat intake. The curves represented in Figure 1 have only one point in common, the point when P is equal to 2.18 S. At this point obviously 2.68 S–1.23 P becomes 0, since 1.23 times 2.18 is equal to 2.68. The corresponding P:S value will be 2.18 (2.18 S/S).

We have discussed the limitations of our equation when used for the prediction of serum cholesterol changes from changes in the intake of saturated and polyunsaturated fatty acids (*Circulation*, 19:201, 1959). The equation was derived from data obtained in groups of middle-aged men who had average serum cholesterol levels between 200 and 250 mg. per 100 ml., when they were eating diets of the usual U. S. type of about 3,000 calories per day with

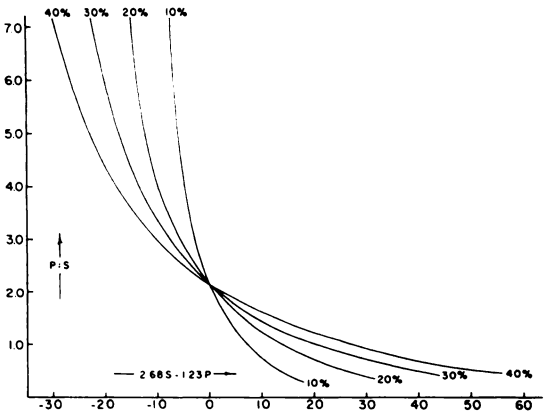

FIG. 1. The relation between P:S and 2.68 S–1.23 P, for various levels of fat intake. Fat intake (as per cent of the total calories) indicated by the figures on the lines.

TABLE I

Serum Cholesterol Differences Observed by Dr. Kinsell and Predicted from His Data by the Keys, Anderson and Grande Equation

Oil	Cholesterol Difference* (mg./100 ml.)	
	Observed	Predicted
Safflower oil	115	137
Cottonseed oil	115	106
Soy bean oil	130	123
Corn oil	135	121
Avocado oil	165	101

* Cholesterol difference = serum cholesterol on coconut oil diet, minus serum cholesterol on the different oils.

total fat providing 40 to 45 per cent of the total calories. No satisfactory prediction is expected when the equation is applied to data obtained from men who differ from these specifications under other conditions. However, the equation has predicted with reasonable accuracy the serum cholesterol changes reported by other workers, when applied to their data (AHRENS, E. H. et al. *Lancet*, 1:943, 1957; MALMROS, H. and WIGAND, G. *Lancet*, 2:1, 1957; TURPEINEN, O. et al. *Lancet*, 1:196, 1960; HASHIM, S. A. et al. *Lancet*, 1:1105, 1960).

It will be perhaps surprising for Dr. Kinsell to know that the serum cholesterol changes observed in one patient and described in his editorial are in good agreement with our prediction. Using the data given by Dr. Kinsell we have computed the differences in serum cholesterol between the coconut oil diet and each of the other diets. The predicted differences are compared with the differences observed by Dr. Kinsell in Table I. In the case of corn oil the agreement would be better if the figure were corrected for the effect of the unsaponifiable material (GRANDE, F., ANDERSON, J. T. and KEYS, A. *Proc. Soc. Exper. Biol. & Med.*, 98:436, 1958).

The only serious disagreement was found in the comparison between coconut oil and avocado oil. It must be noted that avocado oil was never used in our own experiments, and that the composition of this oil, computed

from Dr. Kinsell's data, is approximately 3 per cent saturated, 2 per cent polyene and 95 per cent monoene. This is an unusual composition and I found no example in the literature with such a low content of saturated fatty acids. Moreover the iodine value given by Dr. Kinsell is lower than the theoretic value corresponding to that composition.

Dr. Kinsell seems to favor the use of the iodine value as a predictor of the effect of a given fat on serum cholesterol concentration. We have discussed the reasons why iodine value (even if the amount of fat is taken into account) cannot be a good predictor (KEYS, A., ANDERSON, J. T. and GRANDE, F. *Lancet*, 2:959, 1957). Recently we have compared again the effect of a mixture of vegetable oils with that of a fish oil. The vegetable oil mixture had the same proportion of saturated, monoene and polyene fatty acids as the fish oil, but the main polyene of the vegetable mixture was linoleic acid, whereas the fish oil contained a high proportion of polyene fatty acids with more than two double bonds. Both oils fed at the level of 100 gm. per day produced similar serum cholesterol levels in a group of men, despite the fact that the iodine value of the vegetable oil mixture was 90 and that of the fish oil 177.

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