Editorial

Fumbling with the Friedewald Formula

The September 1991 issue of the American Journal of Clinical Nutrition (AJCN) carried an interesting letter (1). The letter questioned some of the conclusions drawn by the authors of a paper published in the December 1990 issue of the same journal (2). The bone of contention was the manner in which the authors had used the Friedewald formula (3) for estimating the low-density lipoprotein (LDL) cholesterol of their subjects. The total cholesterol (C) is distributed between the LDL, high-density lipoprotein (HDL) and very low-densiity lipoprotein (VLDL) fractions. Knowing the distribution of cholesterol between these three fractions is important not only for classification of hyperlipidaemias (3) but also for prediction of the risk for atherosclerosis (4). While C and HDL can be determined rather rapidly, total fractionation is time consuming and expensive. Friedewald et al (3) observed that barring a few specific situations, if all concentrations are expressed in mg/dL, the VLDL fraction has a concentration about one-fifth that of plasma triglycerides (TG). Plasms TG are also relatively simple to determine. Hence they suggested a formula for the calculation of LDL cholesterol, viz.

$$LDL = C - HDL - TG/5$$

While presenting data on the validity and limitations of their formula, Friedewald et al (3) also pointed out the errors inherent in using the formula if plasma has chylomicrons (i.e. the patient is not fasting), or if the patient has type III hyperlipoproteinaemia, or if the plasma triglyceride concetration exceeds 400 mg/dL. Provided these three rather infrequent exceptions are kept in mind, the formula has served a very useful purpose for two decades. Two objections were raised by Masse (1) to the use of the Friedewald formula by Green et al (2). First, that the original formula was valid only for concentrations expressed in mg/dL. For use with concentrations expressed in SI units (mmol/L), the formula must be adapted :

$$LDL = C - HDL - TG/2.18$$

Green et al had used the formula in the original form while working with concentrations expressed in mmol/L. Second, that Green et al had used the formula also for patients having triglyceride concentrations above 400 mg/dL. Both these objections were considered valid and accepted gracefully by Green (5).

At least three lessons may be learnt from the episode outlined above. *First,* one cannot be too careful in the use of formulae. Formulae are convenient, they save time, and their apparent precision has a strong mathematical appeal. But the use of a formula should be critical, and accompained by a thorough understanding of the basis of the formula. These comments apply not only to mathematical formulae, but also to other short-cuts and conveniences such as computer software, and elegant instruments which give a digital or graphic output after considerable processing of the data in a black box which the investigator may know little about. *Second,* our

system of screening papers prior to publication is not perfect. Not only the authors made a slip, the referees and editors of a prestigious journal like AJCN also missed the slip. *Finally*, an open system of healthy criticism, to which all scientists are committed, is our best guarantee against errors. Scientific journals run a correspondence column primarily as an expression of their commitment to constructive debate. We invite and request our readers to uphold the finest traditions of science by writing to us, specially when we have slipped somewhere.

REFERENCES

1. Masse J. Effects of fish-oil ingestion on cardiovascular risk factors (letter). *Am J Clin Nutr* 1991; 54 : 610-611.

2. Green P, Fuchs J, Schoenfeld N, Leibovici L, Luri Y, Beigel Y, Rotenberg Z, Mamet R, Budowaski P. Effects of fish-oil ingestion on cardiovascular risk factors in hyperlipidemic subjects in Israel : a randomized, double-blind crossover study. *Am J Clin Nutr* 1990; 52 : 1118-1124.

3. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18 : 499–502.

4. Rifkind BM. Policies for the prevention of coronary heart disease through cholesterol lowering. *Br Med Bull* 1990; 46 : 1059-1074.

5. Green P. Reply to J Masse. *Am J Clin Nutr* 1991; 54: 611.

Announcement

Prof. Georgy N. Kryghanovsky, President of the *International Society for Pathophysiology (ISP)*, would like our readers to know about the establishment of this new society. The 2nd Congress of ISP will be held from 19-24 November 1994 at Kyoto, Japan. The ISP will also publish the *International Journal of Pathophysiology*. For further information, please contact Dr. Vladimir Shinkarenko, ISP Secretary General, Beltiyskaya ul. 8, Moscow 125315, Russia.