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Stability of Plasma Total Cholesterol, Triglycerides, and Apolipoproteins B and A-I During the Early Postmortem Period

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ABSTRACT: The stability of plasma lipids and apolipoproteins during the early postmortem period was studied by taking four duplicate blood samples from eight cadavers 2, 6, 12, and 24 h after death. The bodies were kept at +4°C. The plasma samples were analyzed for total cholesterol (TC), triglycerides (TG), apolipoprotein B (apo B), and apolipoprotein A-I (apo A-I).

In TC, values rose by 6 and 11% in two cases, and in six cases diminished 3 to 15% during the first 6 h compared to values obtained 2 h postmortem. The greatest changes were a continuing rise in one case by 33% and a fall by 21% in another case during 24 h. In TG values marked changes took place including one case with a rise of 67% within 24 h. The concentrations of apo B rose by 9 to 11% in three cases and fell by 3 and 4% in two cases during 6 h, but during the whole study period a rise up to 78% occurred. In the concentrations of apo A-I, cases fell by as much as 42% in 6 h, and in one case rose by 20% during 6 h. The results indicate that unpredictable fluctuations occur in plasma lipid and apolipoprotein values within 24 h after death, and they should be interpreted cautiously if the samples have been taken after a prolonged postmortem period.

KEYWORDS: pathology and biology, blood, lipids, apolipoproteins, human plasma, postmortem changes, cholesterol, triglycerides, apolipoprotein B, apolipoprotein A-I

There is overwhelming evidence linking hypercholesterolemia to advanced atherosclerosis [*1–3*], but difficulties have been encountered in correlating blood cholesterol levels with atherosclerotic lesions, especially in the early stages of the disease. It is possible that in young victims (below 50 years of age) of sudden coronary death a familial hyperlipidemia is present, but no antemortem data on blood lipids are available.

For diagnostic and epidemiological reasons, a postmortem assay of blood lipids would be of importance. Such studies have been made and high concentrations of blood lipids have been found in sudden coronary deaths [*4–6*], but the application of postmortem lipid results

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on individual cases is still uncertain. Postmortem changes restrict the use of blood chemistry after death since the function of organs in the period between clinical and cellular death, the postmortem action of enzymes, and changes in the permeability of dying cells all contribute to variations in the blood concentrations of many compounds. Blood is also very sensitive to autolytic and bacterial action during decomposition. Hydrolytic splitting of proteins, nucleic acids, carbohydrates, and fats has been observed during the autolytic process [*7–9*]. A rise in serum potassium during the first hours postmortem, together with a decrease in corpuscular potassium, seems to reflect the destruction of cell membranes [*10–12*].

It is therefore likely that postmortem changes also take place in plasma and serum lipids because of disintegration of the cell membrane and changes of water content in blood. In earlier studies, in which the means of blood lipids were correlated to postmortem time, the lipid values stayed relatively stable after death [*4–6, 13, 14*].

In some cases of sudden death it would be beneficial to relate the degree of atheromatous lesions to blood lipid values at autopsy by using one postmortem blood sample. This is usually the case in forensic science work, where only one blood sample is available taken during autopsy. Perhaps the assay could also be used as a support for the cause of death in cases of sudden coronary disease death in young persons in which the disease is probably caused by hyperlipemia. We are unaware of previous studies having been performed. Therefore, the stability of the blood was studied and results on plasma total cholesterol (TC), triglycerides (TG), apolipoproteins B and A-I (apo B) and (Apo A-I) lipoproteins during the early postmortem period are reported.

Materials and Methods

The corpses of eight men (age range 31 to 74 years, mean age 50.7 years) who had died suddenly of coronary heart disease ($n = 6$), shotgun trauma ($n = 1$), and choking from a laryngeal foreign body ($n = 1$) were used. The bodies were stored at +4°C from 30 to 60 min after death, the femoral or brachial veins were cut, and four duplicate blood samples under direct vision were collected in tubes containing sodium citrate at 2, 6, 12 and 24 h after death. After centrifugation, an aliquot of each plasma sample was placed in an ice bath and the rest was stored at −70°C until analyzed. In eight cases, plasma TC was determined by gas chromatography using coprosterol as an internal standard [*15*]. TG was quantified colorimetrically according to the method of Carlson et al. in eight cases [*16*]. In five cases, the concentrations of apo B and apo A-I were determined from unfrozen samples using radial immunodiffusion [*16*]. The coefficient of variation for each analysis has been reported [*15, 16*]. It was below 2% for TC, below 5% for apo B and Apo A-I, and below 6% for TG.

Results

Plasma Total Cholesterol

As illustrated in Fig. 1, plasma TC varied in the range 2.8 to 8.9 mmol/L (mean 6.0 ± SD 1.8) after 2 h postmortem. In two cases, the values had risen by 6 and 11%, respectively, during the first 6 h, and in six cases they had diminished by 3 to 15%. Thereafter, the concentrations either diminished or rose. The greatest changes were a continuing rise in one case by 33% during 24 h and in another case a fall by 21% during the same interval.

Plasma Triglycerides

The initial plasma TG values varied in the range 0.85 to 3.6 mmol/L (mean 1.63 ± SD 0.05) (Fig. 2). In three cases they diminished by 5 to 36% during the first 6 h, in one case there was no change, and in four cases there were rises of 5 to 25%. Subsequent changes were still marked, the greatest rise being 67% and the greatest fall 42% in 12 h.

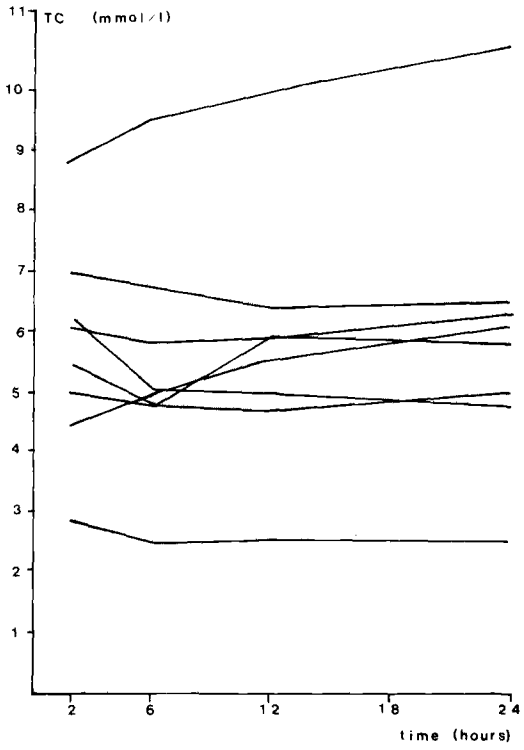

FIG. 1—*Plasma total cholesterol concentration as a function of time postmortem. Each curve represents one case.* TC = *total cholesterol.*

Plasma Apolipoprotein B

The initial postmortem values for apo B varied between 80.0 and 267.5 mg/100 mL (mean 165.5 ± SD 67.9). In three cases they rose by 9 to 11% during the first 6 h, and in two cases they fell by 3 and 4%. In three cases changes remained under 10% during the whole study period, but in two cases marked changes occurred, for example, a rise of 62.5 mg/100 mL during the 24 h (Fig. 3).

Plasma Apolipoprotein A-I

Initial apo A-I values varied between 80.0 and 165 mg/100 mL (mean 118.0 ± SD 34.4) (Fig. 4). In three cases, the concentration decreased by 2 to 33% during the first 6 h postmortem, but in two cases there was a rise of 4 and 20%, respectively. Subsequent changes continued in both directions. During the whole study period, apo A-I concentration remained quite stable in two cases, where only 3- to 7-mg/100-mL fluctuations occurred. On the other hand, in one case apo A-I concentration decreased from 165.0 to 95.0 mg/100 mL during 12 h.

Discussion

In spite of the standardized conditions and blood sampling, both rises and falls in plasma TC were observed during the first 6 h postmortem. Glanville [*11*] in comparing premortem and postmortem serum cholesterol concentrations, failed to find any major fluctuations, and

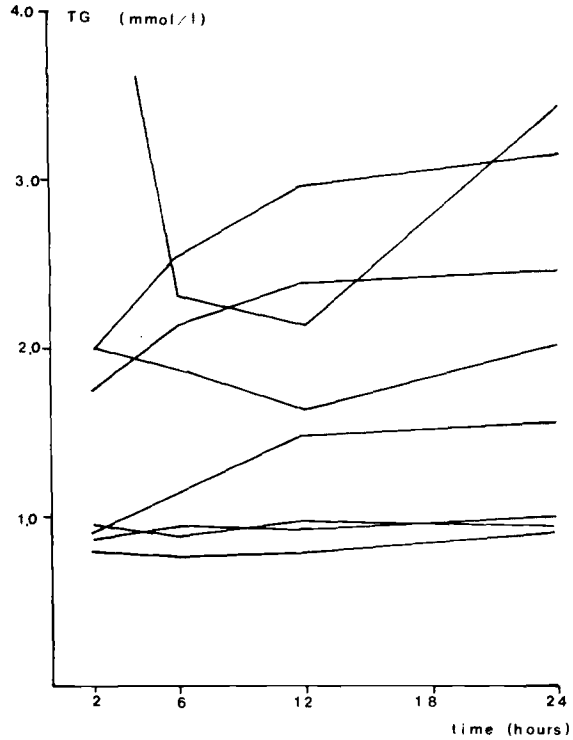

FIG. 2—*Plasma triglyceride concentration as a function of time postmortem. Each curve represents one case.* TG = *triglyceride.*

noted that in two cases the cholesterol level at 90 h after death was quite close to that found before death. According to Enticknap [*10,12*], only relatively minor changes in postmortem plasma lipid values occur at increasing intervals from 0 to 12 h up to more than 60 h after death. His results were based on a mean value of analyses made from one sample only of each cadaver at different postmortem times, but the possible individual changes were not reported.

In comparison to the earlier studies, the time intervals used in the present study between the blood samples were relatively short, that is, 4 to 12 h, while Glanville and Enticknap used intervals from 12 to more than 60 h. In the present study, four consecutive blood samples were taken from each cadaver allowing a followup to the individual postmortem changes. Thus, we could find fluctuations in plasma lipid values shortly after death, while the changes later returned to the initial levels in some cases. The fluctuations were large enough to exceed the cholesterol quintile limits used in many epidemiological studies on the risk of atherosclerotic disease associated with different blood cholesterol concentrations [*17-19*]. It may be for this reason that early attempts to relate the degree of atherosclerosis to postmortem blood cholesterol levels were largely unsuccessful [*20-23*].

Postmortem plasma TG, which showed the greatest fluctuations, are likely to be of limited value as an indicator of premortem levels, especially as they are known to be influenced by the length of agony [*24*].

We have not found any previous reports on the stability of blood apolipoproteins after death. In the concentrations of apo B and A-I, clear unpredictable fluctuations took place during the early postmortem period, while in some cases concentrations remained quite stable during the whole study period. The greatest change in apo B concentration was a rise of

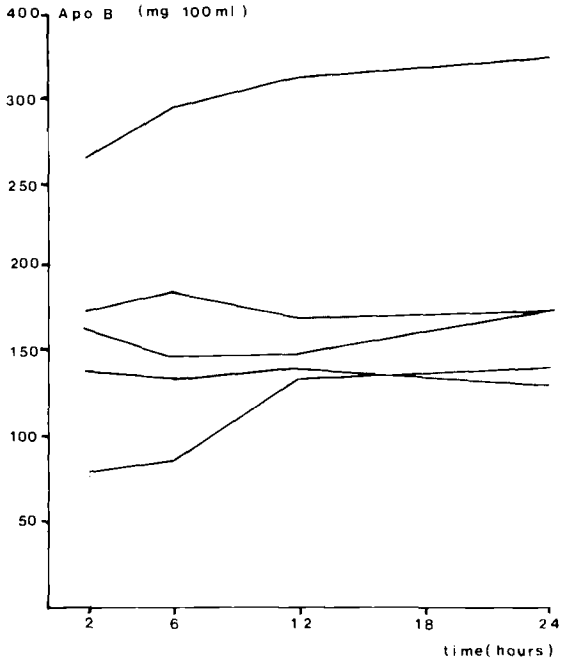

FIG. 3—*Plasma apolipoprotein B concentration as a function of time postmortem. Each curve represents one case.* Apo B = *apolipoprotein B.*

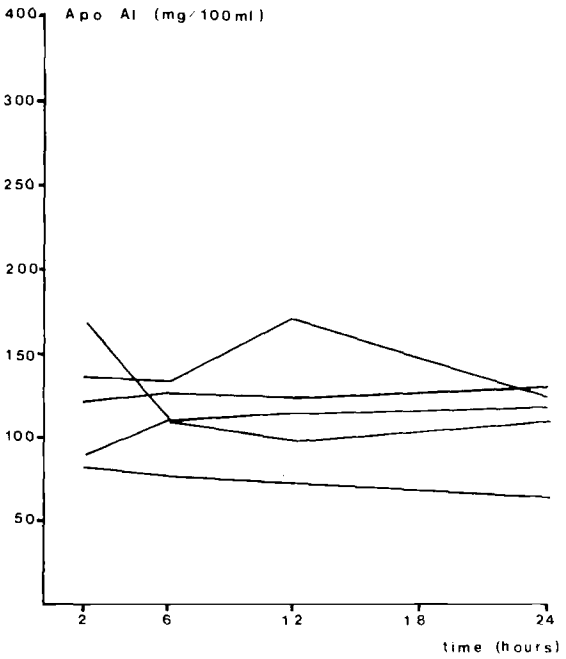

FIG. 4—*Plasma apolipoprotein A-I concentration as a function of time postmortem. Each curve represents one case.* Apo A-I = *apolipoprotein A-I.*

62.5 mg/100 mL during 24 h postmortem. In one study of atherosclerosis, mean apo B levels were found to be only 20 mg/100 mL higher in coronary artery disease than in the noncoronary artery disease group [25], which is one third of the postmortem change observed in one of our cases.

The fluctuations in concentrations of plasma lipids and apolipoproteins did not follow any predictable pattern and occurred during the whole study period. The cause of the fluctuations remains speculative, but it may lie in early autolytic changes and the change of water content in the blood after death [6, 7]. Most plasma samples were hemolytic in appearance after 6 h, and four blood samples for cholesterol analysis had to be rejected for this reason. The variation in TC values between 10 and 40 mmol/L noted in these cases must be considered as an artifact. Some of the plasma samples for the apo A-I and B analyses also had to be discarded because of their uneven flocculent quality. In postmortem samples, one cannot exclude the effect of postprandial hyperlipemia on the results.

After death, mean plasma lipid values have been observed which correspond to values measured in living persons [26–29], but already during the first 24 h postmortem unpredictable fluctuations can take place in plasma lipid and lipoprotein values. For this reason, it is difficult to estimate the premortem lipid level from one postmortem sample and to establish exact correlations between postmortem lipid levels and morphological autopsy findings based on atherosclerotic lesions.

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