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LETTERS TO THE EDITOR

Alcoholic Ketoacidosis as a Cause of Death, Who Came First?

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I read with interest the article 'The Postmortem Diagnosis of Alcoholic Ketoacidosis' by Palmiere and Augsburger (2014).

However for the sake of truth I must protest against the statement on page 272: 'The first report in the forensic field suggesting that ketoacidosis could be partially responsible for unexplained deaths in alcoholics dates back to 1993 and concerns a study performed by L.N. Denmark on 49 autopsy cases that included chronic alcohol-abuse related deaths'.

Together with my co-authors I submitted an article that was acknowledged by Forensic Science International on 19 January 1993 and published in vol. 60 (Thomsen *et al.*, 1993). In that article we described our results as 'strongly indicative of ketoacidosis as the sole or contributing cause of death…'. We were convinced that we solved the riddle of 'Fatty liver deaths'.

L.N. Denmarks excellent work on beta-hydroxybutyrate was received at *Forensic Science International*, 4 April 1993 and published in vol. 62.

It had been known for many years that alcoholics, who stop drinking after a binge, may be found dead shortly after. The only abnormality to be found is a fatty liver. There are no drugs to be detected and only insignificant levels of alcohol or none at all.

There have been numerous speculations as to the cause and mechanism of death. Severe metabolic disturbances including high levels of free fatty acids do probably play a major role due to the effect on the Krebs Cycle.

It has since our publications been confirmed that alcoholic ketoacidosis is the cause of death in a substantial number of alcohol abusers.

A quantitative measurement of ketone bodies is now a routine analysis at the institutes of forensic medicine in Denmark.

Denmark (1993) measured the levels of beta-hydroxybutyrate in vitreous and urine in 49 forensic cases and found high concentrations in six chronic alcohol abusers with no specific immediate cause of death.

He rightly mentioned diabetes, hypothermia and starvation as possible differential diagnoses.

In my opinion alcoholic ketoacidosis may well be signed out as the cause of death, but we must be aware of the fact that the mechanism of death is not yet fully understood. The pH levels are usually not very low, and as described by Palmiere and Augsburger (2014), a multitude of biochemical indicators are affected in these cases.

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Alcoholic Ketoacidosis as the Cause of Death: Thomsen and Co-workers Came First

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Thomsen *et al.* (1993) published an extremely interesting and innovative preliminary communication in Forensic Science International, vol. 60 (1993), in which they presented the results of a forensic study performed on 27 alcoholics with known causes of death, 16 alcoholics with unknown causes of death and 79 control subjects. The determination of blood acetone + acetoacetate revealed significantly increased levels in alcoholics with unknown causes of death compared with the other studied groups. Based on these findings, the authors concluded that their results strongly indicated ketoacidosis as the sole or contributing cause of death in chronic alcoholics with negative postmortem investigation results.

In Forensic Science International, vol. 62 (1993), Denmark (1993) reported the results of a study focusing on beta-hydroxybutyrate as a marker for sudden death in chronic alcoholics. Denmark measured beta-hydroxybutyrate concentrations in vitreous humor and urine. In 6 out of 49 studied subjects, the author found vitreous beta-hydroxybutyrate levels ranging from 19 to 26.9 mg/dl and urine beta-hydroxybutyrate values ranging from 26.7 to 493 mg/dl. In all these six cases, death was initially thought to be related to chronic alcohol abuse and no specific causes of death were obtained based on postmortem investigation findings. Demark concluded that increased beta-hydroxybutyrate concentration might suggest alcoholic ketosis in subjects with a history of chronic alcoholism, even in those in which previous withdrawal seizures were documented, and therefore be useful in explaining the death. Nevertheless, Denmark emphasized that other situations such as diabetic ketoacidosis and starvation could be responsible for metabolic changes potentially leading to marked ketosis.

Professor Thomsen and his research team provided an extraordinary contribution to the identification of alcoholic ketoacidosis as the main or contributing cause of death in chronic alcoholics with negative postmortem investigation results (Thomsen *et al.*, 1993, 1995, 1997; Thomsen and Frohlich, 1995; Thomsen, 1996). In addition, it cannot be denied that the preliminary communication published in Forensic Science International, vol. 60 (1993), preceded Denmark's article in Forensic Science International, vol. 62. We sincerely apologize to Professor Thomsen, who can be rightly considered the first published author in the medicolegal setting to have seen the connection between alcoholic ketoacidosis and the cause of death in autopsy cases with inconclusive findings.

Quantitative analysis of acetone, acetoacetate, beta-hydroxybutyrate and isopropyl alcohol is routinely performed in our facility in Lausanne, along with determination of vitreous glucose, blood glycated hemoglobin and numerous other biochemical parameters. On the other hand, the systematic application of postmortem biochemical investigations in general, and the application of analyses pertaining to glucose and free fatty acid metabolism specifically, in conventional and alternative postmortem samples, allowed us to obtain interesting data that proved useful in the postmortem diagnosis of death by hypothermia and alcoholic ketoacidosis. Biochemical investigations performed in samples collected during autopsy also enabled the determination of diabetic ketoacidosis as the main cause of death in previously unsuspected diabetics to be made as well as the identification of diabetic ketoacidosis-related deaths in situations with apparently conclusive autopsy and toxicology findings (Palmiere *et al.*, 2013a,b).

We would like to thank Professor Thomsen and his research team, firstly, for having demonstrated that alcoholic ketoacidosis should always be considered a possible cause of death in chronic alcohol abusers with otherwise unascertained causes of death, and secondly, for having shown that postmortem biochemical investigations can allow the conclusion of alcoholic ketoacidosis as the cause of death to be reached, thereby allowing alternative causes of death to be excluded.

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