MELBOURNE PATHOLOGY
Quality is in our DNA

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Fasting for lipids/glucose

Insight – February 2014

- As chylomicrons have ten times more triglyceride in them than cholesterol, fasting for less than 12 hours will result in triglyceride levels that are 50% to 250% higher.
- There is evidence that short fasting periods, for example after a large and late supper, may lead to elevated morning glucose levels.
- Similarly there is evidence that prolonged fasting, such as taking fasting glucose levels in the afternoon, will lead to half of the undiagnosed diabetics being missed.

The forms and virtues of fasting

Fasting is the act of willingly abstaining from some or all food, drink or both. Implied is a sense of benefit to the individual which may be religious, general health or improving the reliability of medical procedures. We should first distinguish between fasting for surgical and diagnostic procedures.

When we ask patients to fast for surgical procedures, the purpose is to empty the stomach in order to avoid pulmonary aspiration.

Emptying the stomach may take two hours for clear liquids and 6 hours for light meals. In the diagnostic procedure of the urea breath test, a procedure that also requires an empty stomach, we similarly aim for 6 hours of fasting. Other surgical and diagnostic procedures aim to start with the rest of the gastrointestinal tract empty (eg. glucose or lactose tolerance tests and hydrogen breath tests) and require a longer fasting period of 8 to 12 hours.

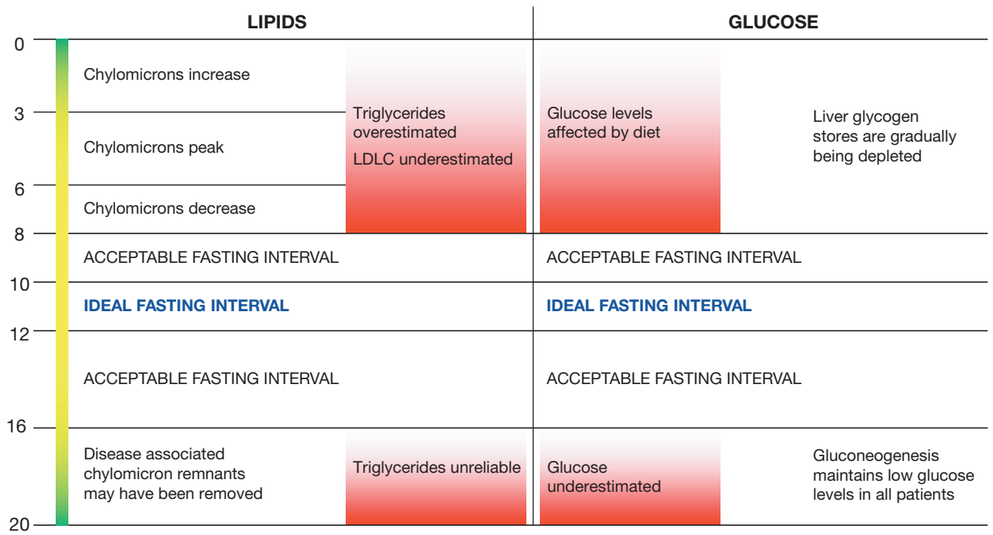

Figure 1. Ideal fasting interval

Fasting for lipid studies

For lipid studies (cholesterol, triglycerides, HDLC), the aim is not to ensure that the gut is empty but that the blood is free of chlyomicrons, the lipoprotein particle that is involved in the absorption and distribution of dietary fat. Australian researcher Prof Paul Nestel was a pioneer in understanding the fate of chylomicron after a meal[1]. Levels of chylomicrons peak 3 to 6 hours after a meal and it normally takes over 8 hours for the chylomicron remnants to be completely removed[2]. While very healthy patients, such as athletes can have a fast chylomicron clearance[3], national authorities in the US recommend fasting studies[4] of at least 12 hours duration[5] and this has been supported by scientific studies[6]. Unfortunately the definitions of fasting usually still vary from laboratory to laboratory and even research studies usually do not define fasting accurately[7].

As chylomicrons have 10 times more triglyceride in them than cholesterol, fasting for less than 12 hours will result in triglyceride levels that are 50 to 250 percent higher[8]. Furthermore as VLDL particles, which are also triglyceride rich particles, have to compete with chylomicrons for access to cellular lipoprotein lipase, VLDL also increases after meals further contributing to elevated triglyceride levels[9].

Some patients have long delays in the clearance of chylomicrons[10,11]. Remnant removal disease is due to the apolipoprotein E2/2 gene and after a standard fast triglyceride levels are still elevated[12]. Diabetes also leads to impaired chylomicron and VLDL clearance[13] probably through impaired lipoprotein lipase activity. Prolonged fasting (eg. 18 hours) may allow many of these patients to eventually clear the remnant particles and appear normal on blood testing.

The laboratory usually calculates LDLC using the 'Friedewald' calculation and an overestimation of triglyceride due to the abnormal presence of chylomicrons may lead to a 20 percent underestimation of LDLC. Total cholesterol and HDLC levels actually don't change (although some older methods for HDLC underestimated their presence after a meal.) While non-fasting samples are less reliable for triglyceride and LDLC, they are reliable for total cholesterol and HDLC and therefore still useful for cardiovascular risk prediction[14].

An important point in fasting for lipid studies is that many patients conduct a dry fast and the resultant dehydration causes an elevation in the concentration of many blood tests, including lipids which may increase by 10 percent or more[15]. Patients should be advised to drink water in the morning of such a fast, which also makes phlebotomy significantly easier. In general, our laboratory data show that most routine blood tests do not differ on fasting while a few differ slightly and our reference intervals usually take this possible variation into account (see table 1).

Analyte	Effect of fasting
Potassium, Bicarbonate, Anion Gap, Creatinine, GGT, ALT, AST, AST/ALT, Total Protein, Albumin, Calcium, Phosphate	No significant change
Sodium, Chloride	1 mmol/L higher in elderly
Urate	0.02 mmol/L higher
Urea	0.5 mmol/L lower in elderly
ALP, LD	5 IU/L lower
Bilirubin	2 IU/L higher

Table 1

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Fasting for glucose studies

During feeding blood glucose is derived principally from the diet. After a meal, glucose levels are elevated for about 2 hours then normally fall for up to 10 hours[16] as liver glycogen stores are consumed. Glucose levels usually then rise slightly after the morning cortisol peak (around 10 – 12 hours)[17]. During fasting, glucose is released by the liver by glycogenolysis and gluconeogenesis which are processes controlled primarily by endocrine factors[18]. In diabetes, increased hepatic glucose production, mainly through gluconeogenesis, contributes to fasting hyperglycaemia.

There is evidence that short fasting periods, for example after a large and late supper, may lead to elevated morning glucose levels[19]. Similarly there is evidence that prolonged fasting, such as taking fasting glucose levels in the afternoon, will lead to half of the undiagnosed diabetics being missed[20]. For these reasons it is generally recommended that fasting glucose levels be taken between 8 to 16 hours after a meal.

While fasting measurements of lipids or glucose are the usual approach to vascular risk assessment, recent studies also suggest that post-prandial lipids[21] or glucose[22] are also independently correlated with risk — however it may be even harder to standardize a meal compared to a fast[23]. Finally, as HbA1c is now approved as a diagnostic test for diabetes[24], and is unaffected by meals, HbA1c measurement avoids the need for fasting to make a diagnosis of diabetes.

Concluding remarks

There are many more diagnostic procedures that require full fasting (eg. gastrointestinal hormones such as gastrin, insulin and glucagon, bone turnover markers, homocysteine, amino acids, bile acids) or selective fasting (eg. avoiding bananas, pineapple and nuts before a 24 hour urine 5HIAA).

The reasons for fasting during any diagnostic procedure vary and the duration and nature of fasting should vary correspondingly.

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A graduate of the University of Melbourne, A/Prof Sikaris trained at the Royal Melbourne, Queen Victoria, and Prince Henry's and Heidelberg Repatriation Hospitals. He obtained fellowships from the Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists in 1992 and 1997 respectively.

A/Prof Sikaris was Director of Chemical Pathology at St Vincent's Hospital in Melbourne between 1993 and 1996.

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