# Direct measurement of low-density lipoprotein in diabetic patients with end-stage renal failure

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Calculation of serum low-density lipoprotein (LDL) from the Friedewald equation is used commonly in UK laboratories. However, a fasting triglyceride sample is required for the Friedewald equation to apply, which can be difficult in diabetic patients. Moreover, the equation cannot be used with triglyceride values >4.5 mmol/L.

In order to obviate these problems, direct assays for LDL are available and have been shown to correlate well with the calculated method.[1] The assays have not been tested in patients with end-stage renal failure, but the structure of LDL is known to be affected by uraemic serum.[2]

This brief study used routine monthly blood samples from 40 diabetic patients receiving maintenance haemodialysis to test the correlation between measured and calculated LDL in uraemia. The results are shown in Figure 1.

The two methods correlated well (r=0.97), but there was a consistent bias, with the 95% confidence interval (CI) falling outside the line of identity. The calculated values were 10–15% lower than the measured values across the measured range (1.0–4.3 mmol/L). The results cannot be explained by hypertriglyceridaemia, as the mean triglyceride value was 1.5 mmol/L (range 0.5–3.8 mmol/L).

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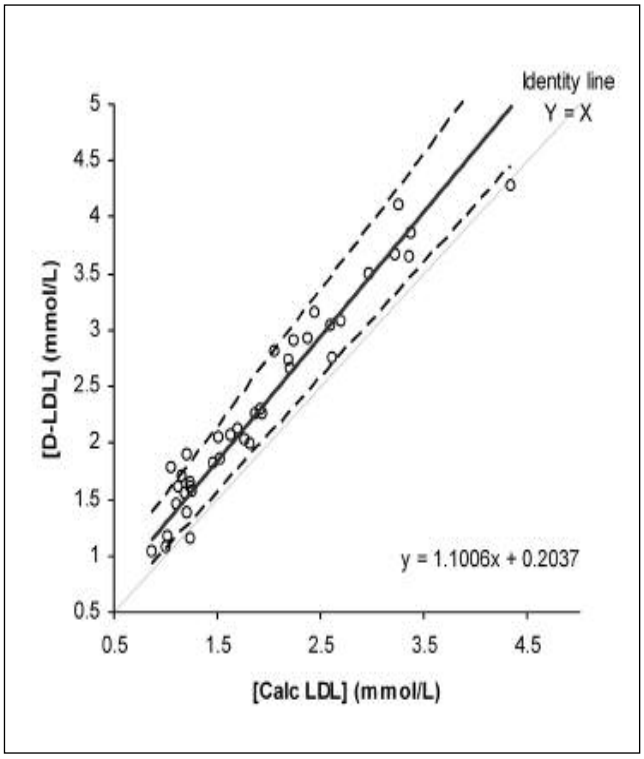


**Fig. 1.** Correlation between measured and calculated LDL in 40 diabetic patients on maintenance haemodialysis.

Abnormalities of the LDL molecule in uraemia include variations in the proportion of cholesterol and apolipoproteins,[2] and it is possible that these structural changes are responsible for the results presented here. They might also be explained by unidentified retained substances in uraemia interfering with the assay. Whatever the explanation, the discrepancy may have clinical significance as this group of patients has a very high risk for cardiovascular disease.[3]

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# Endocarditis due to a nutritionally variant streptococcus: a lesson in recognition and isolation

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A 40-year-old man with a history of a corrected tetralogy of Fallot was referred by his GP with a six-month history of malaise, lethargy and night sweats. Clinical examination revealed an ejection systolic murmur (grade 4/6) and early diastolic murmur (grade 2/4) in the pulmonary region; however, no old notes were available for comparison with previous examinations. He had a normocytic anaemia (haemoglobin [Hb] 10.7 g/dL, mean cell volume [MCV] 89.5 fL) and a raised C-reactive protein (CRP) of 73 mg/L.

Four sets of blood cultures detected Gram-positive cocci in chains within 24 h (BACTEC 9240 Standard Anaerobic/F and Standard/10 Aerobic/F culture vials, Becton Dickinson, Sparks, MD, USA). A trans-oesophageal echocardiogram showed thickened, hypermobile aortic valve cusps consistent with endocarditis, and the patient was commenced on penicillin and gentamicin.

The blood cultures were subcultured on blood, chocolate, MacConkey and fastidious anaerobic agar (FAA). At 72 h the only growth present was on FAA, with scanty (<0.5 mm

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diameter) non-haemolytic, greyish colonies present. The colonies were catalase-negative. Gram stain confirmed Gram-positive cocci in chains. A confident identification could not be obtained with commercially available biochemical identification kits (Rapid ID 32 Strep and API 20 Strep, bioMérieux, Marcy l'Etoile, France).

The isolate was identified as *Granulicatella adiacens* by the Streptococcus and Diphtheria Reference Unit (SDRU) at the Health Protection Agency, Colindale. Further testing in the author's laboratory confirmed satellite growth of the organism around a *Staphylococcus aureus* streak on blood agar, and very scanty growth at six days on chocolate and cysteine lactose electrolyte deficient (CLED) agar.

The patient received intravenous penicillin and gentamicin for six weeks and made a full recovery, with a normal aortic valve appearance on repeat echocardiogram.

The difficulties in isolating nutritionally variant streptococci (NVS), such as the isolate reported here, have been well documented since their first description in 1961.[1] Their fastidious growth requirements have led to suggestions that their prevalence as a cause of infection in humans may be underestimated. They have been implicated as one of the causes of culture-negative endocarditis,[2–4] and have also been associated with bacteraemia, septic arthritis, central nervous system (CNS) infection, otitis media, osteomyelitis and ophthalmic infections.

Isolation of NVS requires media containing pyridoxal, pyridoxamine, cysteine or other thiol compounds. The blood culture system in the author's laboratory uses broths containing 0.10% (w/v) thiols in the anaerobic bottle and 0.001% (w/v) pyridoxal hydrochloride in the aerobic bottle. The thiol and pyridoxal supplemented broths have both been shown to be effective in the recovery of NVS strains.[5–8] In addition, there is evidence that isolation is improved if the blood culture is subcultured on solid media within two days, as in this case.[6,7] These conditions should be attainable in all laboratories.

The first detectable growth observed in the present case was on FAA (Bioconnections, Leeds, UK), which was inoculated routinely in processing of the blood culture. Here, cysteine in the FAA permitted a slow but detectable growth. Transfer of pyridoxal or thiols from the blood culture broth was unlikely to be significant as the isolate grew after several subcultures on FAA.

To the author's knowledge there have been no reports of isolation of NVS on FAA to date, and feels that this is an important observation. Nutritionally variant streptococci may not be considered in an initial assessment of growth on FAA. However, if the clinical details correlate and initial growth is compatible with a slow-growing streptococcal species, then NVS should be considered.

Indeed, it is important to remember that initial growth of an NVS in routine processing is unlikely to be on a pyridoxal-supplemented medium or on one streaked with a helper organism, as these may not have been inoculated routinely. Blood and chocolate agar can also be variable in their ability to support growth of NVS. The rapid acquisition of sufficient organisms for identification and sensitivity testing is vital in endocarditis, where speciation and minimum inhibitory concentration (MIC) tests are helpful in instituting timely appropriate therapy.

The most easily modifiable factor in specimen processing is the solid medium on which the blood culture is subcultured. The most widely recognised solid medium used in the isolation of NVS strains is blood agar supplemented with 0.001% pyridoxal. Other suitable media include those supplemented with pyridoxamine, cysteine,[1,9] blood agar with a 'helper' streak of *S. aureus/epidermidis*[10] or chocolate agar.[5]

Published cases of *G. adiacens* endocarditis have reported isolation on chocolate agar,[4] and satellite growth around *Enterococcus faecium* on blood agar.[11]

Although it was not possible to identify the present isolate using commercially available biochemical identification systems, other authors have identified NVS successfully to species level using the Rapid ID 32 Strep system (bioMérieux).[4,12]

This case demonstrates the importance of careful scrutiny of any unusual growth on media containing thiols or pyridoxal. Of more general importance, however, is the fact that an awareness of the constituents of routine, as well as more specialised, media will aid in the interpretation of early growth in such specimens.

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