

Letters to the Editor

Comments on Oxoid Signal blood culture system

We were interested to read the description of the Oxoid Signal blood culture system.¹ We have had the opportunity to evaluate about 400 bottles in clinical trials, and these showed some inadequacies and unfavourable features.

Two trials were conducted. The first, on febrile neutropenic haematology patients, compared the Oxoid system with the Roche Septi-check bottles and our own (MRI) method. The second trial was on unselected patients, comparing the MRI bottles with the Oxoid Signal system. The MRI bottles comprise a Casteneda slope of Columbia agar with Difco bacto-tryptose broth, trisodium citrate, and Difco penase, together with a second bottle containing 80 ml Oxoid thioglycollate USP (CM 173).

During our work with 100 haematology patients many false positive signals were noted at 37°C, which showed reversal after 10-15 minutes at room temperature. Although many theories for this phenomenon were postulated and tested, the reason was never ascertained. A general tendency to slower isolation and failure to grow some organisms were noticed. These occurrences prompted the second trial of blood cultures on unselected patients when 135 blood culture sets (MRI and Oxoid Signal) were returned to the laboratory. Thirteen of 135 bottles grew organisms in the MRI system that were considered to be clinically important.

Seven of these organisms were not isolated at all in the Oxoid bottles (two *Klebsiella* spp two *Candida albicans*, one *Pseudomonas* sp, one *Staphylococcus aureus*, and one *Acinetobacter anitratus*). Of the remaining six; two gave no signal but showed visible growth in the bottle (coagulase negative staphylococci), two gave "late signals" (one and six days after growth in the MRI bottles for *Escherichia coli* and coagulase negative staphylococci, respectively), and two gave equal results (both *Staphylococcus aureus*). It is also worth noting that the latter isolates required subculturing for further laboratory tests, whereas growth on the Casteneda slope was available immediately in the MRI system. There were no instances of clinically important isolates in the Oxoid bottles which did not grow in our own.

Our final concern is that of laboratory safety. The system is far from being "user-friendly" as quoted, with the handling of 70 mm needles representing a particular hazard. One medical laboratory scientific officer sustained a needle stick injury during insertion of the needle, and dismantling of the autoclaved bottles is made difficult by the buckling of the plastic signal component.

With all these points in mind we would conclude by saying that while Oxoid have the basis of a good idea, individual laboratories should conduct their own clinical evaluations before accepting it in preference to their own or other commercial systems.

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References

- 1 Sawhney D, Hinder S, Swaine D, Bridson EY. Novel method for detecting micro-organisms in blood cultures. *J Clin Pathol* 1986;39:1259-63.

Drs Bridson, Hinder, Sawhney, and Swaine comment:

"The authors' poor results in their trial suggest that the importance of early insertion of the Signal chamber into the bottle after adding blood and adequate agitation during the first day of incubation were insufficiently emphasised. This would be particularly relevant for the *C albicans*, *Pseudomonas* sp, and *Acinetobacter* sp, which the authors failed to isolate.

All the comments made in the early clinical trials were noted and action taken. Following initial studies with prototype Signal chambers, they are now fabricated in polycarbonate to prevent buckling in the autoclave, and the design of the chamber has been changed twice.

False positive reactions with the Signal system are rare; where they have arisen the cause would seem to be some transitory effect in the laboratory or incubator, which invariably disappeared.

The term "user friendly" is overworked computer jargon but it succinctly describes the enthusiasm displayed by most laboratory staff towards the system. The insertion of the 50 mm needle (not 70 mm) obviously requires care, particularly to avoid contaminating the needle shaft. The potential danger from this operation, however, is much less than the injection of blood into any blood culture system, when using hypodermic needles and syringes.

The authors are right to recommend prudence to laboratories contemplating changing their blood culture systems. Large scale trials and routine use in both UK and overseas laboratories show, however, that the signal system compares favourably with other blood culture systems.

It is to be hoped that the authors will re-examine the Signal device, using the amended protocol, as they seem to like the basic concept of the system.

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Corynebacterium CDC group D2 bacteraemia

Coryne bacterium CDC D2 is a pathogen of the urinary tract¹ (Soriano F, *et al.* Abstract presented at 26th Interscience Conference on Antimicrobial Agents and Chemotherapy 1986) but has not been reported as causing bacteraemia or sepsis.¹ We report the isolation of this organism on three occasions from the blood of a renal transplant recipient.

A 24 year old woman was receiving chronic haemodialysis for renal failure secondary to hypertension. She received a cadaver kidney in March 1984 after which she developed a chest infection that was treated with ampicillin, with good clinical results. There was poor urine output, and the donor kidney was surgically explored five days postoperatively, showing signs of acute rejection. Haemodialysis was restarted via an arterio-ventricular fistula. In April a subclavian line was inserted for further haemodialysis at a time when the patient was receiving azathioprine, her white cell count being $1.5 \times 10^9/l$. The following day she developed a fever. Blood cultures taken on three occasions over the subsequent seven days grew *Corynebacterium* CDC D2. Blind antibiotic treatment with cefotaxime 1g, twice daily, intravenously, and oral metronidazole 400 mg, thrice daily, was given at the onset of fever, and a transplant nephrectomy of the "necrotic, septic-looking" donor kidney was subsequently performed. Postoperatively her temperature returned to normal and she remained well. She was subsequently started on continuous ambulatory peritoneal dialysis.

The positive blood cultures were not taken via the subclavian line but by periph-

eral venepuncture, and thus a true bacteraemia was present rather than just colonisation of the line. Subsequent culture, however, of the subclavian tip showed no growth. The most probable cause of the seven day fever was the necrotic donor kidney which, unfortunately, was not sent for culture. This hypothesis is supported by the fact that the subclavian line was still in situ following the fall in temperature.

CDC D2 coryneforms, like the "JK" diphtheroids, have multiple resistance to antibiotics. This organism was found to be highly resistant to cefotaxime, (MIC to cefotaxime >32 mg/l). The bacteraemia, therefore, seemed to have been self limiting.

This organism is considered to be a nitrate negative variant of *Corynebacterium pseudodiphthericum*. Using the identification scheme of Hollis and Weaver³ *Corynebacterium* CDC D2 shows the following reactions: Gram positive rod; catalase positive; motility negative; nitrate negative; urea positive; no oxidation or fermentation of glucose; citrate negative; and mannitol negative.

The colonies are small (less than 1 mm at 24 hours) and non-pigmented. Blood or serum containing media is required for growth. By disc testing, the organism showed resistance to cefuroxime, cefotaxime, and trimethoprim, but was sensitive to gentamicin, netilmicin, vancomycin, and erythromycin. As far as we know this is the first case of bacteraemia with *Corynebacterium* CDC D2. We have subsequently isolated *Corynebacterium* CDC D2 from another patient who had also had a renal transplant; the organism was found colonising both an intravenous cannula and cannula skin entry site.

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Proposed relation between expression of interleukin-2 and transferrin receptors in B lymphocyte chronic lymphocytic leukaemia

We report the preliminary findings of a study of two receptors on cells from patients with B lymphocyte chronic lymphocytic leukaemia (B-CLL). The two receptors, interleukin-2 receptor (IL-2R) and the transferrin receptor (TfR), were identified using monoclonal antibodies anti-TAC (courtesy of Dr T Waldman, USA) and B3/25 (courtesy of Dr I Trowbridge, USA), respectively.

Blood films from 49 patients with B-CLL were examined, and membrane phenotypes were determined using a panel of monoclonal antibodies, as previously reported.¹ Assessed thus, the B-CLL's appeared as a homogenous group. When examined morphologically, however, it was apparent that the group was more heterogeneous than was suggested by the conventional membrane marker results. When IL-2R and TfR were determined the B-CLL's were also found to exhibit heterogeneity in the expression of these two receptors, (table), and it seemed that the morphological appearances correlated with the expression of the IL-2R and TfR. "Typical" B-CLL's were negative for both receptors, but the cases where prolymphocytes were evident showed expression of IL-2R and TfR, or just TfR alone.

Previously reported studies of the TfR have suggested that the appearance of this receptor is a prerequisite for cells to proceed from G₁ phase to S phase in a cells DNA cycle.² Neckers and Cossman reported that the IL-2R needed to be expressed on phytohaemagglutinin in assay stimulated lymphocytes before the TfR could be expressed.³ Work by Bettens *et al*⁴ on lymphocytes stimulated by phytohaemagglutinin in assay showed that interleukin-2 is required to convert G_{1a} (middle RNA content) into G_{1b} (high RNA content).

There could, therefore, be an evolutionary link between the two receptors. This may correlate with the cycle when the cells in G₀ phase may fail to express the receptors, IL-2R is expressed in early G₁ phase, TfR and

IL-2R in intermediate G₁ phase, and the sole expression of the TfR occurs in late G₁ phase. A study of the TfR expression, prognosis, and histological class in non-Hodgkin's lymphoma indicated that positive expression of the receptor could, in certain cases, be of prognostic value.⁵

We suggest that the expression of IL-2R and TfR may be of value in predicting which B-CLL's will transform into a more aggressive polyclonal phase, and we are presently engaged in further investigation into this area.

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- 5 Habeshaw JA, Lister TA, Stansfield AG, Greaves MF. Correlation of transferrin receptor expression with histological class and outcome in non-Hodgkin's lymphoma. *Lancet* 1983;i:498-500.

Table IL-2R and TfR distribution in B-CLL

Total No of cases	Cases negative for IL-2R and TfR	Cases expressing IL-2R alone	Cases expressing IL-2R and TfR	Cases expressing TfR alone
49	22	9	13	5

All fluorescence was exhibited in weak density when examined using indirect immunofluorescence techniques.

References

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