dard disc procedure; (c) the strong synergistic effects inside the zone where the two antibiotics are simultaneously present.

Results are easy to read, as are those obtained with penicillin G or other aminoglycosides (amikacin, gentamicin, streptomycin). Although less easy to read, similar results have been obtained by using the Kirby Bauer disc diffusion method (instead of the triple layer technique), penase solution being then directly set on the ampicillin disc after 5 h incubation.

A technique based on this principle has been recently published by Lee and Komarmy (1975).

It is highly probable that microorganisms situated inside the zone of synergism are killed; definite confirmation of this, however, would be brought about only by simultaneous inactivation of the two

antibiotics; an aminoglycoside-destroying enzyme, unfortunately, is not yet commercially available.

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A modified rack for the LKB Sample Processor

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The LKB Sample Processor (2071) is a programmable unit that can be adapted to many different tests in the laboratory. Racks carrying samples in disposable tubes are fed through a sampler unit. From here serum may be aspirated (in duplicate if desired) and dispensed with reagent or diluent into a second set of tubes in racks fed in parallel through the main unit. Both sets are moved by cogs that engage holes in the side of the racks. The tubes, projecting above the upper surface of the rack, activate a micro-switch, and operation ceases if no tube is present. Further reagents may be added by dispensing pumps to which reagent containers are attached.

The versatile nature of the system and the speed of operation (sampling speed of 400 per hour) recommends it as a radioimmunoassay sample processor and we have used it as such for over a year. There are two main problems. Many reagents for radioimmunoassay are bought in kit form: in the case of antisera and labelled antigen the volumes

supplied are small, often 5 or 10 ml, and just sufficient for the number of tests indicated. If these expensive reagents are dispensed through the pump, the deadspace of pump, tubing, and container may amount to 20% or more of the reagent with undesirable waste. A second problem is that one is reluctant to pass radioactive and proteinaceous material through a system with possible resultant contamination. The latter can, however, be overcome by thorough washing through after use.

Both of these disadvantages would disappear if one could repetitively aspirate the reagent from a container in the sampling position and dispense, with buffer, into the reaction tubes. The sample processor cannot be programmed to do this as the sampling mechanism will only operate if a sample rack, containing tubes, is in position and moves in parallel with the rack of recipient tubes.

We have overcome this problem by using a Teflon rack identical in length and width with the sample rack but with the following differences (figure):

1. It is as high as a rack loaded with tubes. This activates the tube-detecting microswitch.
2. Three cavities, of 5, 10, and 20 ml capacity, to contain reagents take the place of the holes for tubes.
3. At the level of the holes normally engaged by the cogs there is a full-length groove; thus the cogs of the sample operate but do not engage and move the rack.

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Figure Diagram of segment of standard LKB sample rack (left) and modified rack (right). Note the extra height, longitudinal groove, and reagent cavity of the modified rack.

The operating procedure is simple. For addition of antiserum or labelled antigen, the reagent is placed in one of the cavities of the Teflon rack. The pumps are primed with buffer and the programme is initiated. The recipient tube racks are fed in automatically and, as the sampler cogs begin to turn,

the Teflon rack is pushed into the sampler position by hand. The sampler now operates repetitively to aspirate and dispense reagent with buffer into the recipient tubes as they move past normally. At the end of the run the Teflon rack is pushed out, again manually.

With this system only the sampler tip comes in contact with the reagent, and cleaning is easy and rapid. One possible problem is that the cavities in the rack might become contaminated and affect subsequent reagents. This could be avoided by using disposable plastic liners or containers in the cavities. We have found cleaning with a detergent, for example, Contrad (Hickman & Kleber; SA) to be adequate.

Another point to consider is whether or not significant evaporation occurs from the cavities. The mass of 20 ml of water in the large cavity (surface area $\pm 8.5 \text{ cm}^2$) at 22°C decreases by $\pm 0.2\%$ over 1 hour. As all the reagents used are aqueous and the processing time of 200 tubes is 30 minutes this does not create a problem.

All but $\pm 0.3 \text{ ml}$ of reagent is recovered from this rack. The reproducibility of sampling depends on the pumps and will not be affected by this modification.

Letter to the Editor

Unusual Megaloblastic Anaemia

Saary *et al* (1975) describe two cases of unusual megaloblastic anaemia and review the relevant literature. In discussing the mechanism of the changes they suggest that folic acid deficiency may have made a minor contribution to the blood abnormalities but they consider that some other disturbance in erythropoiesis is responsible for the bizarre blood and bone marrow appearances.

We have recently described two cases of rapidly developing megaloblastosis in our intensive therapy unit (Ibbotson *et al*,

1975). In addition, we have seen other patients who developed a similar though less florid megaloblastosis during intensive therapy. The syndrome has been associated with major surgery or trauma, renal failure and dialysis, and severe infection with the use of antibiotics. In three cases, megaloblastosis was diagnosed within three weeks of admission of previously healthy patients.

Diagnosis has been difficult because of a lack of macrocytosis, most of the patients having been transfused. Thrombocytopenia has been a constant feature and has been very severe in two cases. The white cell changes of megaloblastosis have been present in some cases but these could be attributed to renal failure (Hampers *et al*,

1967). Vitamin B12 and folic acid assay have been inhibited by antibiotics. One patient developed a leucoerythroblastic anaemia with circulating megaloblasts, as in Saary's cases, but the striking feature in common has been the morphology of the bone marrow megaloblasts including multilobed nuclei and basophilic stippling (figure, see page 1008).

In our two published cases we were able to give an adequate course of folic acid and both responded within seven days, the platelet count returning to normal and the bone marrow becoming normoblastic. We therefore feel that folic acid deficiency plays a major role in this problem but the aetiology of the deficiency remains uncertain.