

release chuck designed to accept both metal and lint-capped bottles. To overcome the out-of-balance load of the bottle, the chuck is fitted with a flexible coupling allowing the bottle to precess around its dynamic centre while spinning. For loading and unloading the spinners a horizontal bar is fitted above the cabinet on which the spinners can hang.

Details of the design are shown in the sectional diagram (Fig. 2). With this equipment the times for freezing solutions starting at room temperature were as follows: 100 ml of solution in a standard 540 ml transfusion bottle three minutes or, in a 250 ml bottle five minutes; 400 ml of plasma in a 540 ml bottle 15 to 20 minutes.

We wish to thank Mr I. C. Costar for the diagrams.

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## CORRECTION

In Figure 1 of the paper by Helen McCullough, 'Semi-Automated method for the differential determination of plasma catecholamines' (*J. clin. Path.*, 21, 759), showing the flow system the waste tube (no. 10) should pass through the pump once only. Reagents for the various tubes and tube diameters in inches should be shown as follows: (2) Sample (0.045); (4) Acetate-Ferricyanide (0.065); (6) Air (0.056); (8) 2.5N NaoH (0.045); (9) Stabilizing reagent (0.030); (10) Waste (0.065).

## Letters to the Editor

## THYROID FUNCTION TESTS

I was most interested in the paper by Thomson, Boyle, McGirr, Macdonald, Nicol, and Brown (1968)<sup>1</sup> in which they describe difficulties they have experienced in the interpretation of some thyroid function tests. I feel, however, that their conclusions are too dogmatic, and shall appreciate space to reply to some of their statements.

Thyroid function tests fall into two groups, first those which aim to determine 'thyroid status', and secondly those directed at specific thyroid disorders independent of thyroid status. The commonest example of the second group is the diagnosis of Hashimoto's disease by demonstration of high titres of specific antibodies to thyroid components in the peripheral blood. A patient with Hashimoto's disease may be euthyroid, hypothyroid or, rarely, thyrotoxic, but the antibody findings are quite independent of this aspect. It is useful, when considering and comparing tests of thyroid function, to separate the two groups of investigations to avoid confusion.

The authors state in their synopsis that 'an uptake test and estimation of the serum protein-bound radioactive iodine (PB<sup>131</sup>I), supplemented as required by the protein-bound iodine (PBI), remain the best routine tests of thyroid function'. This conclusion is not based on a comparison with the variety of newer tests now available, of which they used only the triiodothyronine resin uptake in a few cases. Although their statement might have been valid between 1963 and 1965, when the work was done, it does less than justice to the many authors who have published studies since then.

Recent work on the determination of thyroid status has largely been concerned with the direct measurement of levels of thyroid hormone in blood. Ekins (1960) and Murphy (1965) developed specific thyroxine assay techniques based on the saturation analysis principle and Nauman, Nauman, and Werner (1967) described a method for the determination of serum triiodothyronine also based on this technique. These methods eliminate inaccuracies inherent in PBI measurements by being specific for the hormones themselves. Following the extensive development by Robbins and Rall (1957) of the concept of protein-binding of thyroid hormones in blood, it has been recognized that thyroid function is most closely related to the concentration of unbound hormone. This level is dependent on the concentrations of thyroxine-binding globulin (TBG) and thyroxine-binding prealbumin (TBPA), as well as on the level of total thyroid hormone. Free thyroxine can be measured directly by equilibrium dialysis or ultrafiltration, and indirectly by methods derived from that of Hamolsky, Stein, and Freedberg (1957) which reflect the concentration of thyroxine-binding proteins. These have been well

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reviewed recently in your own columns by Osorio (1967) and Clark (1967).

If thyroid scanning is required, better pictures may be obtained with a lower dose of radiation to the patient by using technetium ( $^{99m}\text{Tc}$ ) instead of  $^{131}\text{I}$ . Although the  $^{131}\text{I}$  thyroïdal uptake remains a convenient and valuable technique, especially in centres where the newer methods are not yet available, these more specific and radiation-free tests of thyroid status appear likely to replace it, as it previously replaced the measurement of basal metabolic rate.

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#### SIMPLIFIED METHOD OF FILLING THE WELLS ACCURATELY IN GEL IMMUNODIFFUSION PLATES

Precise measurement of very small volumes of biological fluids and their accurate application to immunodiffusion gels can be greatly facilitated by the use of Microcaps (Drummond Scientific Co., Broomall, Pa., USA). These are micropipettes so manufactured from fine capillary glass tubing that their inherent error is of a remarkably low order (less than 1%).

Microcaps can be filled very easily by capillary action, and may be emptied by use of the rubber-bulbed auxiliary pipette attachment supplied by the makers with each packet. The contents are thus delivered by squeezing the bulb after occluding its vent with a moist finger tip. However, full control of delivery when using the auxiliary

pipette requires an almost inhumanly nice delicacy of touch. Warming the auxiliary pipette barrel between two fingers of the other hand allows better control than does compressing the bulb, but even so it is difficult for the most exact of operators to avoid occasional bubbles and overflow when filling small wells, especially with the smaller Microcaps.

A different method of discharging these micropipettes has been found which, compared with the auxiliary pipette technique, has proved at once much simpler, less laborious and time consuming, and at least as accurate and reliable.

After cutting out the pattern of wells as usual, the immunodiffusion plate is replaced precisely under the mask, and the two are clamped or otherwise fixed together so that the mask apertures and corresponding gel wells remain in accurate alignment. The tip of each charged Microcap is then guided into its particular gel well via the corresponding mask aperture. The Microcaps are left standing thus supported by the mask in a more or less vertical position, and the whole apparatus is placed in a moist chamber at room temperature. Over the subsequent two or three hours absorption by the gel leads to complete emptying of the micropipettes. Development of the precipitin patterns may then proceed as usual and, unless the mask is required again for immediate use, the empty micropipettes need not be removed until the plate is examined for reading.

The success of this method depends upon adequate absorptive capacity of the agar gel. It has been found that the minimum adequate agar concentrations are 2.2% for Ionagar no. 1 (Oxo Ltd, London, EC4) and 1.6% for Ionagar no. 2. At these concentrations and in gel layers of 1/16 in. thickness as much as 10 microlitres of neat serum is completely absorbed within three hours, while smaller volumes or dilutions are taken up even more rapidly.

The simplicity of the method is such that a previously inexperienced operator can achieve maximum accuracy and avoid all artefacts after only two or three days' practice.

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