

became weaker but was not completely removed even after 60 minutes.

Lack of any tissue staining was a disadvantage, and a further section was taken to 70% alcohol and then stained in Cole's haematoxylin⁹ for 30 seconds, rinsed in tap water for 10 seconds, dehydrated, cleared, and mounted. This provided adequate nuclear staining, and the crystals (Figure) and red fluorescence were unaffected. Using this method, inclusions and fluorescence were demonstrated in two other old paraffin blocks of liver tissue from patients with PCT. Neither inclusions nor fluorescence had been observed in the earlier examination of routinely prepared paraffin sections from this material.

It is suggested that failure to demonstrate needle-like inclusions in cases of PCT may be due to the treatment of sections with water. Of interest was the persistence of typical porphyrin autofluorescence in sections from routinely fixed and processed paraffin blocks stored for several years.

It is well known that contact with water must be avoided to preserve optimum autofluorescence in fresh cryostat sections:¹ prolonged contact with water during paraffin wax processing and slide preparation should also be avoided to preserve the characteristic inclusions of PCT. Although frozen sections of fresh tissue are the method of choice to demonstrate autofluorescence, these are not essential, and satisfactory results can be obtained with paraffin-embedded tissue provided sections are left unstained or are stained in the way described above.

A punch for Guthrie papers

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Although there are numerous punches for removing small discs from Guthrie papers^{1*} we needed a punch to remove the whole of the square section containing the blood spot (Fig. 3c). On each Guthrie card we require four circles to be filled with the

*See HM (69) 72 para 7 request form/filter paper (form HMR 101/6).

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blood; a maximum of two are required for the amino acid screen technique² for the detection of excess phenylalanine in phenylketonuria. We added thyroid stimulating hormone (TSH) estimation to the screen for the diagnosis of hypothyroidism in the newborn. The case number of the patient is written on each of the last two squares. They are punched from the Guthrie card and sent to the regional assay laboratory for TSH estimation. This punch speeds up the preparation of the squares.

The machine

The punch consists of a frame of aluminium alloy (Fig. 1). Above the frame is a perforated table with a backstop. The table is raised above the base plate

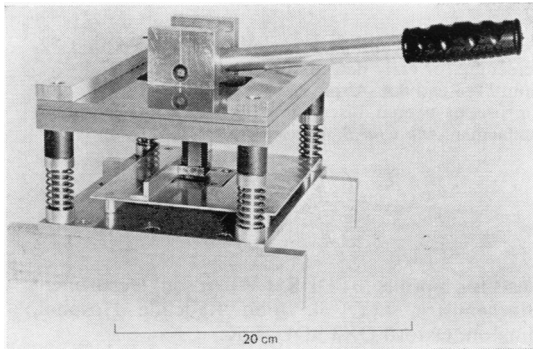


Fig. 1 *The punch for Guthrie paper squares.*

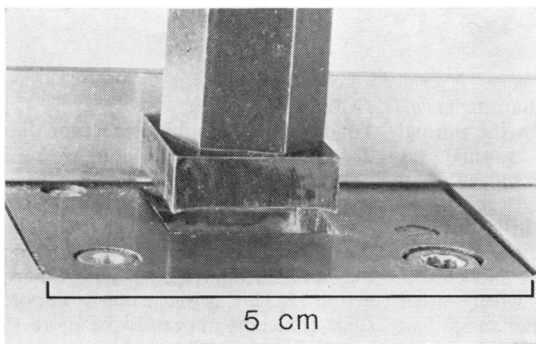


Fig. 2 *Detail of punch plate with cutter above.*

to facilitate the removal of the punched out squares. The punch plate is made of hardened steel with a central square hole of 18 mm (Fig. 2). The cutter (Fig. 3a) is a square of hardened steel, the face of which is spherically concave to a depth of 1.5 mm and the edges are slightly concave along their length (radius of curve is 38 mm). It is carried on a steel column attached to a top plate. The top plate is carried on four spring-loaded guides so that it moves with an accurate vertical motion. Above the top plate is a frame secured to the vertical guides. This carries a cam, which depresses the top plate and the punch. Raising the handle depresses the punch and cuts a square from the Guthrie card. The square which bears the same number as the Guthrie card can be recovered from under the punch table. It is quite possible to punch 80 cards in 10 minutes.

A considerable time was taken to design the cutting mechanism. It was difficult to obtain a clean cut with the standard Guthrie card of heavy absorption paper. The critical points of the apparatus lie in the clearance between the cutter and the cutter plate (Fig. 3b) and the shaping (in a concave direction) of the cutter (Fig. 3a),

Discussion

In many situations it will be necessary to separate the analysis of squares containing the blood spots from Guthrie cards. In our case, it was because the

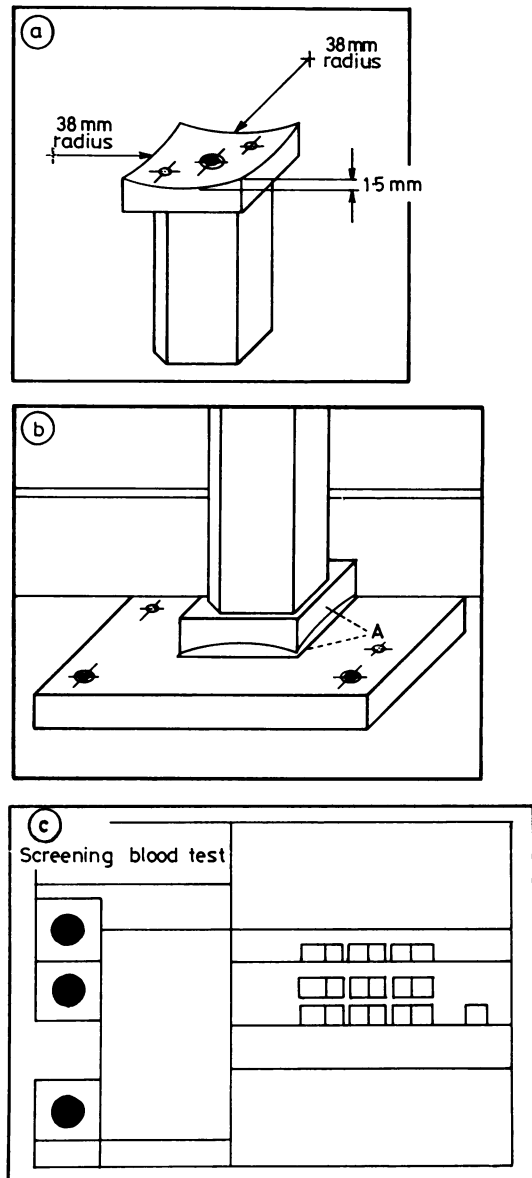


Fig. 3 (a) *Isometric drawing of punch showing curvature of face.* (b) *Isometric drawing of punch and plate showing critical clearance 'A'.* (c) *Guthrie paper with square excised.*

regional assay laboratory was placed at a distance from the baby screening laboratory. In some instances, it will be necessary, as other screening procedures are developed, for the squares to be sent over greater distances to specialised laboratories. This punch took some time to develop because of the peculiar properties of the paper, which caused the difficulty in punching squares quickly from the Guthrie paper. It is a robust piece of apparatus and has proved acceptable to the operators.

We thank the Engineering Section of the Department of Anaesthetics for the use of their facilities.

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Letters to the Editors

Analytical goals in clinical biochemistry

In their paper 'A clinical view of analytical goals in clinical biochemistry' (*J Clin Pathol* 1979;32:893-6) Barrett *et al.* express the hope that their report will stimulate discussion. Having performed a study similar to the one described,^{1,2} I would like to enter this discussion.

They, like Skendzel,³ fail to recognise that there are two main—essentially different—areas of medical decision making:

(a) the diagnosis—the physician has to distinguish the diseased individual from the normal population;

(b) the follow-up of a patient—the physician considers subsequent laboratory results in one patient to follow the course of the disease.

If one studies desirable precision of laboratory results from the clinician's point of view by questioning the physician on the subject of a medically significant change in a patient (situation *b*), one has to be very careful in selecting the initial value. As I pointed out in response to Skendzel's paper,⁴ the physician's answers are bound to be ambiguous if the initial value is chosen within the normal range. Many physicians will indicate that the value passes a limit of normal or a limit of action rather than a change. In this situation it becomes irrelevant where in the normal range the initial value was chosen, and the difference between the initial value and the value compatible with a significant change is not necessarily indicative of desired precision.

This is the case for, for example,

calcium and cholesterol. Barrett *et al.* chose an initial value within the normal range, and the limit of normal (as apparent from my study) was given as an answer (Table 1).

I contend that the answers in the study of Barrett *et al.* would have been 2.66 mmol/l and 7.0 mmol/l for calcium and cholesterol, respectively, also when other starting values in the normal range had been chosen, for example, 2.55 mmol/l for calcium or 6.1 mmol/l for cholesterol, leading to entirely different conclusions with respect to desired precision.

In those cases where Barrett *et al.* chose an initial value outside the normal range the results correlate well with the results of my study where physicians were confronted with an initial value in the near abnormal range and were asked to indicate a medically significant change

(Table 2).

To determine desirable precision in the decision range between normal and just abnormal, the diagnostic situation (*a*) has to be considered and other criteria should be sought, such as, for example, the difference between limit of normal and the level prompting the physician to action.^{1,2} This is particularly important since clinicians appear to be more strict in the diagnostic situation.^{1,2}

There are a number of unwarranted or careless statements in the paper that appear to need reconsideration:

1 'This study is thus a baseline assessment of current clinical opinion for use in concurrent and future research.'

Irrespective of the question whether 62 physicians provide enough information to set such a baseline, the ambiguous set-up of the project interferes with the

Table 1

	Barrett <i>et al.</i>		Elion ¹
	Initial value	Medically significant change	Median limit of normal
Calcium (mmol/l)	2.60	2.66	2.67
Cholesterol (mmol/l)	6.5	7.0	7.1

Table 2

	Barrett <i>et al.</i>		Elion ¹	
	Initial value	Medically significant change	Initial value	Medically significant change
Sodium (mmol/l)	130	→	125 (5)	→
Potassium (mmol/l)	3.0	→	2.7 (0.3)	→
Chloride (mmol/l)	115	→	120 (5)	→
Urea (mmol/l)	9.0	→	11.4 (2.4)	→
			14.0	→
				11.5 (2.5)