an absolute-pressure gauge or a mercury manometer can be relied on for this purpose. Even if the prevacuum is adequate, leaks can allow sufficient air to be readmitted between the prevacuum and steaming stages to prevent rapid penetration of the load.[1] The manufacturers of sterilisers are aware of these difficulties: they and others are known to be actively seeking technical ways to overcome them.

I have personally investigated the analytical control of Browne's tubes and I am satisfied that, if correctly stored and used, they are a reliable guide to efficient sterilisation. (This was also the opinion of the Medical Research Council working party on pressure-steam sterilisers [2]). A failure to change a type-II tube by a high-temperature high-prevacuum steriliser should never be ignored but should be the signal for a critical appraisal of the steriliser and of the way it is being used with, if necessary, assistance by the manufacturer.

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THE INDUSTRY IT DESERVES?

SIR,—Dr. Schmeidler (Nov. 11) asserts that "there often elapses a long period of time before the drug is officially given a generic name". Assuming that he writes from the viewpoint of practice in this country, "occasionally some time" would be more accurate than "often a long period".

Most drugs are introduced into this country from overseas, and even if the British Pharmacopœia Commission has not officially recognised a generic name when a drug is first marketed here, either a W.H.O. non-proprietary name or an American N.N.D. name is usually available to any manufacturer who really wishes to convey the information. The example quoted by Dr. Schmeidler draws our attention to the "anti-inflammatory" steroids, a series of compounds which illustrate the point nicely. Incidentally, I believe that his example has been known as prednisone (or Δ' cortisone) since its introduction into British medicine. In support of Dr. Laurence, we might quote another example from the same series. Most doctors prescribe 9α-fluoro- 11β, 17α, 21— trihydroxy- 16α-methylpregna-1, 4-diene-3,20-dione as dexamethasone (originally an American N.N.D. name and available long before the drug's introduction here), realising that to use any of the names 'Decadron', 'Dexacortisyl', 'Millicorten', 'Dextelan', or 'Oradexon' would be to make a rod of confusion for their own backs. The only example to date of a compound of this type not being introduced from abroad had an approved name from the first—betamethasone.

It seems to me that Dr. Schmeidler's point (while valid in a few cases if amended as I have suggested) is used by some manufacturers as an excuse for withholding information, and to give their proprietary name an exaggerated importance.

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HALVING THE DRUG BILL

SIR,—Tony and John are identical twins, born in 1956, and bed-wetters. They are invariably dry or wet, as the case may be, on the same night, though they sleep in separate beds. They are never out of step. Last year, they both were given some tablets for the enuresis, and both improved for a while—still in step. A month ago, John was started on amphetamine, 2·5 mg. at bedtime. Tony has no pills. Now they *both* are dry much more often than before—still invariably in step.

Waroona,
Western Australia. PAUL MESTITZ.

1. Fallon, R. J. *J. clin. Path.* 1961, **14**, 505.
2. *Lancet*, 1959, i, 425.

URINARY EXCRETION OF UROCANIC ACID IN MEGALOBLASTIC ANÆMIA

SIR,—Dr. Knowles (Nov. 18) finds that "under controlled experimental conditions the excretion of formiminoglutamic acid after a histidine load can be significantly increased in folic-acid-deficient patients but not in normals". The following figures show the excretion in the urine of formiminoglutamic acid in 4 medical students given increasing oral doses of histidine:

Histidine (*g.*)	*Urinary formiminoglutamic acid* (*mg. in 8 hours*)			
5	1	<1	1	<1
10	3	6	4	4
15	9	8	8	5

Increased amounts of histidine derivatives appear in the urine with regularity after adequate histidine loading both in normal subjects and in many disease states. These results emphasise that in carrying out critical studies a sensitive and quantitative method for estimating histidine derivatives is essential. Methods that depend on ninhydrin staining may prove useful in the clinical laboratory but give too many false negative results to be reliable as a research tool.

We have now studied a number of patients with megaloblastic anæmia in whom only urocanic acid was excreted after histidine loading. The clinical value of these observations is self-evident.

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I. CHANARIN.

LATEST THOUGHTS ON THE CARDIA

SIR,—Referring to your leader of Oct. 7, I would like to record my investigations of the closing mechanism of the cardia.

The measurements given below were made in anæsthetised dogs, and all figures are averages of several measurements in mm. Hg. In the first series of experiments the "yield pressure" (Y.P.) of the cardia to the passage of fluids, in both directions, was determined, by progressive filling of the stomach and œsophagus, and was recorded at the moment of reflux:

Dog	*Œsophagus-stomach*	*Stomach-œsophagus*	*Remarks*
1	10	10	Thoraco-laparotomy
2	13	13	Diaphragm intact
3a	10	10	Abdomen and thorax open
3b	10	10	Same animal with thorax open and spontaneous respiration

These results show the Y.P. of the cardia to be the same in both directions.

If, as manometric experiments indicate, the cardiac sphincter is situated in the intra-abdominal part of the œsophagus, it is possible that the closing of the cardia will be affected by the intra-abdominal pressure, and that when this is raised a higher intragastric pressure will be required if reflux is to occur. It was decided to investigate the possibility that reflux will only occur when the intragastric pressure exceeds the Y.P. of the cardia by an amount equal to the intra-abdominal pressure; in other words that the Y.P. of the cardia can be calculated as the difference between the intragastric and intra-abdominal pressure at the moment of reflux.

To test this hypothesis 4 dogs were anæsthetised, and intragastric (I.G.P.) and intra-abdominal pressures (I.A.P.) were measured during progressive filling of the stomach until reflux occurred. These experiments were performed with closed and widely opened abdomen. Again all figures are averages of several measurements in mm. Hg:

	Abdomen closed			*Abdomen open*		
Dog	*I.G.P.*	*I.A.P.*	*Y.P.*	*I.G.P.*	*I.A.P.*	*Y.P.*
1	36	18	18	18	0	18
2	34	15	19	19	0	19
3	19	10	9	10	0	10
4	17	5	12	8	0	8

These results seem to demonstrate the validity of the hypothesis.

When the cardia is situated in the thorax, as with a sliding hernia, it will no longer be subject to intra-abdominal pressure. It was decided to investigate the effect of the "negative"

intrathoracic pressure in such cases; a partial thoracic stomach was produced in dog 1 from the second series, and, after a lapse of several weeks, the experiment was repeated:

Abdomen closed		*Abdomen open*	
I.G.P.	*I.A.P.*	*I.G.P.*	*I.A.P.*
8	5	9	0

This experiment shows that reflux was produced at approximately the same intragastric pressure with closed and open abdomen. The Y.P. of the cardia must now be calculated as the difference between the intragastric and intrathoracic pressure at the moment of reflux. Assuming the latter, during quiet respiration, to be of the order of 10 mm. Hg, the Y.P. will be 8− (−10)=18 mm. Hg—i.e., the same as for the same dog in the second series of experiments.

I think these findings support the views of Creamer et al., and are strong evidence in favour of the existence of a functional cardiac sphincter.

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Holland. J. H. MEISS.

LATE APPEARANCE OF LEG SYMPTOMS IN PULMONARY EMBOLUS

SIR,—I think the test mentioned by Dr. Churcher (Nov. 11) is liable to give false impressions.

Many elderly people have a distinct aversion to having " the fingers pressed very firmly into each belly of the gastrocnemius . . ." On the other hand, palpation between the two heads of the muscle over the popliteal vein at the lower end of the popliteal fossa elicits tenderness even in cases where the calf muscles are painless to pressure. This form of palpation is not resented, a very important point.

Being pulmonary-embolus minded, for many years I have habitually examined the legs of all elderly chest patients and other suitable cases, and I can confirm that embolism is common.

Just occasionally it may be very difficult to distinguish an embolus from a small cardiac infarct; but serial E.C.G.S, in conjunction with the serum transaminase, lactic dehydrogenase, and bilirubin, resolves most problems. To be pulmonary-embolus minded is the greatest help of all.

Barnet, Herts. G. RIDDELL ROYSTON.

ULTRASONICS AS AN AID TO DIAGNOSIS

SIR,—Your leading article of Oct. 28 comes as a welcome sign to one who has laboured for over eight years to interest other radiologists in the possibilities of ultrasound both diagnostic and surgical.

Though I read a paper on the uses in neurology and neurosurgery at the Symposium Neuroradiologicum of 1955, and this year read a paper to the Ophthalmological Society of the United Kingdom on the diagnostic use in the eye and orbit, interest has been aroused among clinicians much more than among radiologists.

The work of Douglass Howry, of Boulder, Colorado, goes back twenty years, and it is only recently that he has begun to be recognised as the great pioneer he is. In association with J. H. Holmes, of Denver, using a technique of multiple scans very similar to that of Donald, he has extended the diagnostic use of ultrasound to the liver, spleen, kidney, neck, and limbs. It is astonishing that his demonstration of metastatic deposits in the liver has not been hailed as epoch-making.

I have organised two discussion groups on the medical uses of ultrasound: the first, on the destructive uses in Ménière's disease and in neurosurgery, has had two meetings; and the other, on the diagnostic uses, had its first meeting on Nov. 23 at the Royal Society of Medicine.

Those wishing to receive the summary of the proceedings of either group are asked to let me know.

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91, Dean Street, London, W.1. DOUGLAS GORDON.

ANTINUCLEAR FACTORS AND SYSTEMIC LUPUS ERYTHEMATOSUS

SIR,—In their letter of Sept. 9, Dr. Ansell and her colleagues reported that they had found antinuclear factors in the serum of only 4 of 81 first-degree relatives of patients with classical systemic lupus erythematosus, and this incidence is considerably less than that reported by us last year.[1] Since our preliminary communication was published, full details of the method we used have been given,[2] and our studies have also been considerably extended.

The method which we use differs from that of Dr. Ansell and her colleagues in the following respects:

(1) Fresh, unfixed human buccal mucosal-cell smears were used as the source of the cell nuclei, rather than alcohol-fixed frozen sections of fœtal thyroid tissue.

(2) Serial dilutions of serum were used in the test on every serum, rather than a single 1 in 10 dilution of serum.

We have not worked with fœtal thyroid tissue, but early in our studies on the antinuclear factors, we found that frozen *unfixed* sections of rat kidney tissue were a less sensitive source of cell nuclei than were unfixed human buccal mucosal cells.[2] In fact, we tested 97 sera on both rat kidney tissue and human buccal mucosal cells. We found that the tests on 32 sera were positive and on 38 sera were negative with both tissues. However, 26 sera were positive with buccal mucosal cells and negative with rat kidney, whereas the reverse occurred in only 1 instance.[2] Also, we showed that when serial dilutions of sera were compared, higher titres were found with buccal mucosal cells on 14 sera, whereas a higher titre was observed only once with rat kidney tissue. For these reasons, we elected to use human buccal mucosal cells as the test tissue in our future experiments. Clearly, in order to compare Dr. Ansell's results with our own, it will be necessary to compare the same sera in both test systems.

We have also given our reasons [2] for accepting as a positive test specific nuclear fluorescence with serum diluted 1 in 4. In the past year our studies on control subjects, as well as on patients with S.L.E., have been extended, and we believe that our data justify the assumption that a positive test is one in which nuclear fluorescence is obtained with serum diluted 1 in 4. The following data summarise our observations to date on healthy subjects, patients with diseases unrelated to S.L.E. and other collagen diseases, and on relatives:

	No. of tests	*Serum diluted 1:4*		*Serum diluted 1:8*	
		Positive	*Negative*	*Positive*	*Negative*
Healthy subjects	63	1	62	0	63
Patients with disorders " unrelated to S.L.E." . .	195	8	187	6	189
Patients with S.L.E. (total no. of sera)	325	298	27	286	39
Relatives:					
First-degree relatives of S.L.E. patients . .	109	47	62	32	77
Second-degree relatives of S.L.E. patients . .	45	10	35	5	40
Relatives of healthy propositi matched for age, sex, and race with S.L.E. patients . .	23	0	23	0	23

These figures justify our earlier conclusion [1] that antinuclear factors do in fact occur frequently in first-degree relatives of patients with S.L.E. If 1 in 4 is taken as the critical level, then 47 of 109 first-degree relatives had positive tests. If we re-examine our data in terms of a serum dilution of 1 in 8—thus approximating the dilution used by Dr. Ansell and her colleagues—then we still conclude that 32 of 109 first-degree relatives had a positive test for antinuclear factors.

In addition, we find it difficult to accept that the incidence of antinuclear factors in relatives can be as low as that found by Dr. Ansell and her colleagues because, in the course of our studies, we have already encountered 3

1. Pollak, V. E., Mandema, E., Kark, R. M. *Lancet*, 1960, ii, 1061.
2. Mandema, E., Pollak, V. E., Kark, R. M., Rezaian, J. *J. Lab. clin. Med.* 1961, **58**, 337.