corresponding increase of two in the number of deaths from trauma, stress asphyxia in labour, and cord entanglement, and an increase of three in the "premature, cause unknown" group. The number of deaths due to antepartum haemorrhage (unrelated to hypertension and pre-eclampsia) has not altered.

In the induced group a relatively large number of foetal deaths were attributed to maternal hypertension and pre-eclampsia. However, the number was no higher than would be expected as a result of the high incidence of these conditions in women who were induced.

Fig. 2 shows that the overall foetal death rate has remained virtually static, despite the marked increase in the induction rate. The combined stillbirth and neonatal death rate in the induced group fell gradually until, in 1955, it was actually lower than the total figure for all deliveries. No doubt this fall is due to the increasing number of inductions performed for minor indications; nevertheless the conditions for which induction was performed constitute a distinct danger to the baby. It may be misleading to draw any firm conclusions from this trend, but a balance sheet can be drawn up summarizing the points which have been made for and against induction.

For Induction	*Against Induction*
1. Reduction of the stillbirth and neonatal death rate in the induced group to that of the whole group.	1. Overall stillbirth and neonatal death rate has not apparently improved.
2. The overall caesarean section rate has not increased.	2. 10–15% risk of caesarean section after induction.
	3. Slightly increased morbidity rate.
	4. Psychological trauma.

Until the placental reserve can be measured, a large number of women with adequate placental function will be induced to save a few infants from placental insufficiency. A number of hospitals have reported induction rates of over 20%. They have achieved caesarean section rates after induction of under 5% by allowing the latent period to exceed 72 hours in many cases. They are thus submitting many infants to a danger far greater than that of allowing pregnancy to continue. Once surgical induction has been performed, delivery should be effected within three days.

Summary

An analysis has been made of the effect of the sevenfold increase in the rate of surgical induction of labour at Hammersmith Hospital during the period 1951 to 1956. The risk to the mother is that of caesarean section. The caesarean section rate after induction was 14.5% against an overall rate of 5.4%. Caesarean section was carried out when labour was not established within 72 hours. In spite of this policy and the rising induction rate, the overall caesarean section rate did not increase.

The incidence of puerperal pyrexia was 9.1% against the overall rate of 5.3%. This increase was entirely associated with the higher caesarean section rate.

The increased induction rate has not apparently effected a reduction in the overall foetal mortality during the period under review.

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TUBELESS GASTRIC ANALYSIS

BY

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Gastric test-meal examinations are now carried out mainly for two purposes. One is to see whether the patient is capable of secreting free hydrochloric acid, as in the diagnosis of pernicious anaemia and carcinoma of the stomach. The other is to see whether the patient secretes free hydrochloric acid in excessive amounts or concentrations, as in the study of duodenal ulcer and stomal ulceration. Segal *et al.* (1950a, 1950b) introduced a method of tubeless gastric analysis depending on the use of cation exchange resins which are dissociated in the presence of free hydrogen ions in the stomach, so that the cation is absorbed and appears in the urine. Two compounds have been used, both marketed under the trade name "diagnex." Quininium is used as the exchange cation in the one method, and the dye azure A in the other. This paper reports our results with the quininium and azure A resins used as screening tests for achlorhydria. We have compared the results with those of histamine test meals on the same patients.

Patients Studied.—We investigated 124 patients. The majority were in-patients requiring gastric analysis who had been admitted to the Radcliffe Infirmary under the care of one of us (L. J. W.). The remainder had diagnex tests as out-patients and were admitted to hospital for the histamine meal, usually for one morning only. In the latter group there was a high incidence of achlorhydria, since the patients were being investigated as part of a study of the relation between achlorhydria and anaemia.

Procedure of Diagnex Tests

The basis of the two tests is similar. The patient is requested to fast overnight for at least eight hours. He then empties his bladder, discards the urine, and takes a capsule containing caffeine sodium benzoate, 500 mg., as gastric stimulant. One hour later he again empties his bladder, this time saving the urine as a control sample. Immediately afterwards he takes 2 g. of granules by mouth —a carbacrylic cation exchange resin, "amberlite RXE-96," in reversible combination with either quininium or the orthoquinoid salt of azure A. Free hydrogen ions in the stomach liberate quininium or azure A, which is then absorbed into the blood stream and excreted in the urine. Maximum excretion normally occurs within two hours. The total urine passed in the two hours after the granules have been taken is analysed for its content of quininium or azure A.

The time limit of two hours is imposed to avoid errors due to later displacement of the test cation in the intestine by cations such as magnesium, sodium, or potassium. Drugs such as kaolin, alkalis, barium, and magnesium salts should for the same reason not be taken for 24 hours before the test.

Methods of Estimation

Urinary quininium is estimated by an ether/sulphuric acid extraction method (Kelsey and Geiling, 1942). The control urine serves as a check on any extraneous fluorescent substances present. The urine specimens are made alkaline and

diluted with distilled water to 300 ml.; 120 ml. of this is extracted with 60 ml. of anaesthetic ether; 32.8 ml. of the ether layer, which contains the quininium, is separated off and fluorescence developed by shaking well with 20 ml. of N/10 sulphuric acid. The quininium is then estimated quantitatively in a suitable fluorimeter. We used a Hilger spectrophotometer. Previous workers (Segal *et al.*, 1950b; Shay *et al.*, 1954) have shown that the presence of 15 μg. or less of quininium indicates achlorhydria, whereas more than 25 μg. indicates "free acid." Intermediate values were reported as "low free acid," and in these cases tests were repeated if possible.

In the *azure A method* the test urine is again diluted to 300 ml. with distilled water, and its colour compared with two known dye standards, supplied by the manufacturers, representing 0.3 mg. and 0.6 mg. of azure A per 300 ml. Previous *in vivo* and *in vitro* (Segal *et al.*, 1955; Sievers and Gieselman, 1956) studies have suggested that a test-urine colour more intense than the 0.6 mg. standard indicates the presence of "free gastric acid," while a colour less intense than the 0.3 mg. standard indicates achlorhydria. Intermediate values are, as in the quininium test, considered to indicate "low free acid." If the colour is less intense than the 0.3 mg. standard the specimen is acidified (one drop of 6 N hydrochloric acid per 100 ml.), placed in a boiling water-bath for 10 minutes, and allowed to cool for one hour. It is then again compared with the standards. Boiling will liberate dye from a colourless conjugated form often present in urine. We used a simple comparator block and placed the control urine behind the dye standard to compensate for the greenish hue produced by urochromes.

Tests Used for Comparison.—The quininium resin test was checked against the single-dose histamine test meal. A Ryle tube was passed and the resting juice aspirated. "Free acid" was titrated in the conventional way with Töpfer's reagent as indicator. If "free acid" was detected there was no need to go any further. If "free acid" was absent 0.5 mg. of histamine acid phosphate was injected subcutaneously and the stomach aspirated completely every 15 minutes for one hour. Later in the series the augmented histamine test meal (Kay, 1953) was introduced to check the azure A test. Histamine, 0.4 mg. per 10 kg. body weight subcutaneously, was used as gastric stimulant and covered by an antihistaminic drug (mepyramine hydrogen maleate, 100 mg. intramuscularly) to counteract the systemic effects. The gastric contents were aspirated continuously for three successive 15-minute intervals.

Results

In 73 subjects quininium resin tests and single-dose histamine test meals were performed (Table I). Good correlation between the tests was evident, disagreement occurring in only two out of the 73 cases. In three patients equivocal "low free acid" results were obtained.

TABLE I.—*Comparison of Quininium Test with Single-dose Histamine Test*

Quininium Excreted	Single-dose Histamine Test		Total
	Free HCl	No HCl	
>25 μg.	29	1	30
15–25 ,, ...	2	1	3
<15 ,, ...	1	39	40
Total ..	32	41	73

TABLE II.—*Comparison of Azure-A Test with Augmented Histamine Test*

Azure A Excreted	Augmented Histamine Test		Total
	Free HCl	No HCl	
>0·6 mg.	6	2	8
0·3–0·6 ,, ...	6	8	14
<0·3 ,, ...	3	26	29
Total ..	15	36	51

Fifty-one patients underwent the azure A test and an augmented histamine test meal (Table II). It was found that of 15 patients with "free" hydrochloric acid in the gastric juice, three were missed by the azure A method; and of 36 cases with no "free acid" two were misdiagnosed by the latter method. One patient with undoubted pernicious anaemia gave a positive result in the azure A test, though the presence of achlorhydria was confirmed by the histamine test meal. In 14 patients equivocal results were obtained—six in the free acid group and eight among the achlorhydrics.

Discussion

Segal and Miller (1955) summarized the available literature on exchange-resin gastric analysis and reported as follows: (1) Quininium method: nine false negatives among 832 patients with proved "free gastric acid" on test meal and 12 false positive among 285 patients with achlorhydria. (2) Azure A method: two false negatives among 208 patients with "free acid" and two false positives among 57 achlorhydrics.

Since then literature, on the azure A method in particular, has accumulated (Goldbloom *et al.*, 1955; Sievers and Gieselman, 1956; Sievers and Fischer, 1957; Poliner *et al.*, 1957; Bolt *et al.*, 1957; Fentress and Sandweiss, 1957; Rechtshaffen *et al.*, 1957; etc.). Among 412 patients investigated with this test, 95 were achlorhydric on intubation and there was agreement with the dye test in all but two subjects. In 317 patients with "free gastric acid" on intubation, the azure A test gave a false-negative result in 43 instances. However, it should be noted that the percentage disagreement varies widely in the different series—for example, Poliner *et al.* (1957) report the high incidence of 75% false-negative results, while Goldbloom *et al.* (1955), at the other extreme, noted a 100% agreement between dye test and intubation results.

An occasional false negative is not of much consequence if these methods are used as screening tests for achlorhydria. Subsequent gastric analysis will reveal that "free acid" is in fact being secreted. The likeliest cause of a result of this kind is inefficient gastric stimulation by caffeine benzoate. However, Poliner *et al.* (1957) have pointed out that certain pathological conditions are apt to give negative resin-test results, whatever the gastric secretion. Pyloro-duodenal obstruction, malabsorption syndromes, and severe diarrhoea may lead to defective cation absorption. Renal disease, bladder-neck obstruction, and possibly liver disease may lead to delayed excretion; few data have been published on this aspect of the subject (Behr and Lawrie, 1955; Bolt *et al.*, 1957).

If the aim is to detect achlorhydria, false positives will invalidate the test. Fluorescent substances in the urine, notably found after riboflavine or nicotinic acid has been taken by mouth, are a theoretical cause of incorrect results with the quininium method. In practice, routine analysis of the control urine obviates this difficulty. Strong cation displacers like magnesium, iron, aluminium, barium, calcium, and kaolin should not be taken by mouth for two days before the test.

Gastric operations may affect the results in various ways (Galambos and Kirsner, 1955; Poliner *et al.*, 1957). Resin granules may pass through the stomach remnant so rapidly that proper cation exchange is not possible. Alkaline intestinal juice regurgitating through an operation stoma may neutralize gastric acid. Abnormally rapid gastric emptying may result in premature liberation of dye or quininium by intestinal cations.

Our own findings with the quininium resin revealed satisfactory correlation with the single-dose histamine meal, comparable with the findings of other workers (Segal *et al.*, 1955). The azure A method, on the other hand,

although simpler to perform, has given too many equivocal results to be satisfactory. It has also given more false positives and false negatives than the quininium test. It is true that we checked it against the much more stringent augmented histamine test, but this would not explain the false positives.

There is evidence that if tubeless gastric analysis is repeated in cases in which an equivocal result has been obtained, a definitive result may be obtained in the second test (Flood *et al.*, 1953; Galambos and Kirsner, 1955; Sievers and Gieselman, 1956). It has also been suggested that histamine should replace caffeine benzoate as the gastric stimulant in tubeless gastric analysis. Indeed, Galambos and Kirsner (1955) found only one false positive and one false negative among 104 patients using betazole hydrochloride ("histalog") instead of caffeine in the azure A test. We are, however, interested in a simple test for achlorhydria which can be performed at home by the patient, and the introduction of parenteral histamine would take tubeless gastric analysis out of the category of screening tests.

The exchange-resin methods have no value as quantitative tests of gastric acidity, as the amounts of cation displaced from the resin, absorbed from the intestine, and excreted in the urine are not directly proportional to the amount of hydrochloric acid secreted by the stomach (Segal *et al.*, 1955; Galambos and Kirsner, 1955; Sievers and Gieselman, 1956). The resins are therefore of little use in the study of hyperchlorhydria and peptic ulceration. Their role is in the detection of diseases associated with achlorhydria, such as pernicious anaemia and gastric carcinoma.

Summary

The literature on tubeless gastric analysis is briefly reviewed and the circumstances under which such tests are likely to be unreliable are mentioned.

The quininium resin test was compared with the single-dose histamine test meal in the recognition of achlorhydria; agreement was satisfactory.

The azure A resin was compared with the augmented histamine test. The results were unsatisfactory, as there was too high a proportion of equivocal results. In addition, false positive and false negatives were more frequent than in the quininium test.

The quininium test is a valuable method of screening patients for achlorhydria, but the azure A method, although simpler to perform, cannot be recommended.

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A NEW EXAMPLE OF THE Rh ANTIBODY, ANTI-C^x

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This paper records the finding and investigation of the rare antibody, anti-C^x, in the serum of a patient and the investigation of a number of persons who were thereby shown to carry the corresponding antigen.

Present Investigation

The patient, Mrs. T., was born in 1911; she had two children, born in 1938 and 1940. The first of these died at the age of 1 week from a cause which it is now almost impossible to ascertain owing to the lapse of time. There is no record of any other pregnancy, of any transfusion, or of any injection of blood prior to the test in which the abnormal antibody was discovered.

In January, 1957, the patient was found to have an adenocarcinoma of the caecum, and was admitted for operation to the Hospital of St. John and St. Elizabeth, London. As it was anticipated that a blood transfusion would be needed she was grouped, and found to be group O, Rh(D) positive; two bottles of group O, Rh-positive packed cells (each from two donors) were then tested for compatibility with her serum. One bottle was found to be incompatible both by saline and by albumin tests. Further tests with her serum showed no agglutination of 13 other donor samples examined, or of seven samples from the transfusion centre staff, selected as covering a wide range of antigens. In all, blood from 11 donors was transfused uneventfully. The two donors who had contributed to the incompatible bottle of packed cells were recalled for further investigation.

At the Blood Group Reference Laboratory the patient's serum was tested against red cells from both these donors and from a selected panel of 22 other bloods, including known examples of the antigens Wr^a, Mi^a, V^w, and one other "family" antigen, so far unpublished. Tests were carried out in saline and albumin at 37°, 18°, and 4° C., and by the indirect anti-human-globulin method; the serum was also tested by Löw's method with cystein-activated papain, and against trypsin-treated cells. All the results were negative except in the case of the blood from one of the two contributors to the incompatible bottle, Mrs. W., which reacted in all the tests except at 4° C. in saline.

The red cells of this donor's father and sister, but not those of her mother, were also found to be agglutinated by the serum; those of the patient herself, her husband, and her surviving son were unagglutinated.

The cells of the donor, Mrs. W., were grouped as fully as possible with available standard sera. They were tested also with reagents for the antigens Wr^a, Mi^a, V^w, V, Diego, C^x, E^w, f, Be^a, R$_m$, U, Vel, and Tj^a, and for two other rare "family" antigens at present under investigation, and were found to react only with anti-C^x, anti-U, anti-Vel, and anti-Tj^a, the last three of which react with nearly all known bloods. This result strongly suggested that the patient's antibody was anti-C^x. Through the kindness of Dr. F. Stratton, who had supplied the known anti-C^x used in the tests, we received a sample of known C^x-positive