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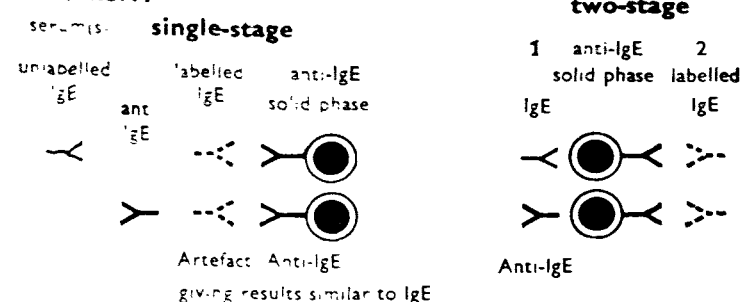
MICHAEL J. K. HARPER.

CIRCULATING IgE LEVELS IN PATIENTS WITH CANCER

SIR,—I wish to comment on the letter by Dr Hourri and others (March 1, p. 530) in which my name was quoted in one of the references¹ to the methods which were used to establish the nature of the artefact(s) which led to the incorrect conclusions reported by Jacobs et al.² that serum from patients with lung and other cancers contained an IgE inhibitor. These original findings were not confirmed by Dr Stanworth (Jan. 11, p. 64) nor by Dr Merrett and his collaborators (March 1, p. 530).

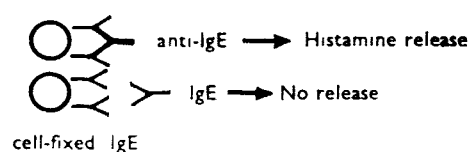
The reference to my name was put in the following words: "These sera were shown, by a variety of procedures, to contain antibodies of the IgG class, directed against IgE, which . . . caused excessive histamine release from sensitised leucocytes" (my italics).¹ This was part of my own efforts to establish the explanation for the paradoxical findings reported in the 1972 paper—namely, the existence of antibodies against IgE (which I originally thought to be endogenous and not exogenous, as it turned out to be) in the serum of patients showing very high levels of what seemed to be serum IgE, as estimated by the radioimmunosorbent technique (R.I.S.T.), and a paradoxically low IgE as measured by single radial immunodiffusion (modified Mancini technique). It was also due to my interest in looking for anti-IgE antibodies in certain diseases—e.g., intrinsic asthma—especially if they have biological activity in terms of the effects described below, and thus are distinguishable from IgM antibodies against IgE, which have been detected in some allergic patients, and after hyposensitisation, but which did not release histamine from

A R.I.S.T.



B

Histamine release from IgE-coated leucocytes



C

Single radial immunodiffusion

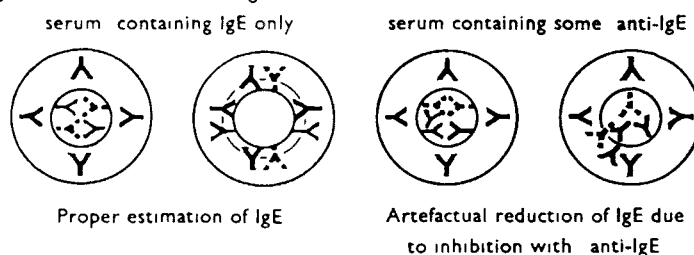


Fig. 2—Artefacts produced by the presence of anti-IgE antibodies on the assay of serum total IgE by the radioimmunosorbent technique (R.I.S.T., A; 'Phadebas' IgE kit, Pharmacia), and by the single radial immunodiffusion technique (C).

The possible existence of anti-IgE in the serum in question can be ascertained by incubating it with IgE-sensitised human leucocytes (obtained from patients with immediate-type allergy), as shown in test B. Note that the artefact in R.I.S.T. can be avoided by a two-stage test procedure.

1. Assem, E. S. K., McAllen, M. K. *Br. med. J.* 1970, ii, 504.
2. *Lancet*, 1972, ii, 1059.

- Goat anti-E chain specific serum
- Sheep anti-IgE serum (W.H.O.)
- ▲ Goat anti-IgE estimated by R.I.S.T.

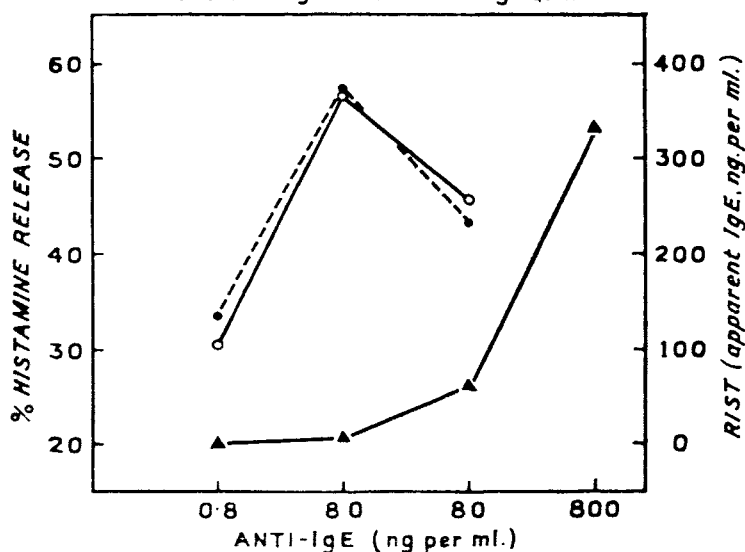


Fig. 1—Use of IgE radioimmunosorbent test (▲) and histamine-release test on isolated IgE-sensitised human leucocytes for standardisation of anti-IgE sera and measurement of anti-IgE antibodies in general.

● and ○ = leucocyte test on goat anti-ε chain and sheep anti-IgE (W.H.O.) sera.

IgE-sensitised leucocytes.³ We have had extensive experience in these tests, including the biological test procedure known as "reversed leucocyte anaphylaxis", where different concentrations of sera suspected to contain these antibodies are incubated with IgE-sensitised human leucocytes obtained from allergic donors, and histamine release is measured. A serum containing anti-IgE antibodies induces histamine release greater than the spontaneous one because of the bridging by anti-IgE of adjacent cell (basophil)-fixed IgE, which is similar to the antigen-induced response.

We have also used these techniques in the past four years for the standardisation of anti-IgE sera raised in experimental animals. Since these sera contain relatively large amounts of anti-IgE, when they are used in high concentrations (containing excess anti-IgE in relation to the amount of cell-fixed IgE) histamine release drops below the maximum. This does not occur in a cytotoxic reaction. Anti-IgE sera when used in the single-stage R.I.S.T. give readings which are related to serum concentration (fig. 1)—i.e., results similar to IgE-containing sera, but the latter do not produce histamine release from sensitised leucocytes. On the other hand, in the Mancini technique anti-IgE serum alone does not give any readings, and if mixed with IgE, it gives a lower figure for the latter (fig. 2), which may be called "inhibition". I obtained similar findings in 12 of 20 sera from the patients with cancer

3. Williams, R. C., Jr., Griffiths, R. W., Emmons, J. D., Field, R. C. *J. clin. Invest.* 1972, 51, 955.

reported by Jacobs et al.⁴ In some of these 12 samples the amount of anti-IgE detected could explain the high level of "apparent" IgE (R.I.S.T.) previously reported, but in other samples the amount of anti-IgE detected could not have been the sole factor to account for the colossal apparent concentration of "IgE".

Twelve sera from a second group of patients with cancer were sent to me by Dr Merrett, where the earlier results could not be confirmed (Dr Hourì and others, March 1, p. 530) and did not behave like the original group in our tests. One or two seem likely, however, to contain minute amounts of anti-IgE antibodies, which are detectable only by reversed leucocyte anaphylaxis, and which I wish to believe are endogenous.

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E. S. K. ASSEM.

DESIGN OF ANÆSTHESIA APPARATUS

SIR,—Professor Clutton-Brock (June 21, p. 1376) remarks that a fresh approach to the design of anæsthetic machines is long overdue. I should like to add that a branch of psychology known as human factors engineering can make an important contribution to the design of equipment (not only anæsthetic), so that erroneous use is less likely. Long ago the value of this approach was established in the aircraft industry, where the incidence of misread instruments and accidentally operated controls has been reduced. At present there is a special danger when an anæsthetist works abroad with equipment which is superficially similar to his own but differs dangerously in detail—e.g., colours of gas cylinders, relative position of flowmeters. It is therefore important that improvements in anæsthetic safety are internationally agreed upon and enforced.

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M. E. WILSON.

CARE OF HANDICAPPED CHILDREN

SIR,—Most of the 8000 mentally and physically handicapped children at present in hospital in this country (June 14, p. 1326) are not likely to find foster parents outside hospital, especially in those parts of the country where there is difficulty in fostering normal children. However, there is hope for them. Most of these children are in hospitals for the mentally handicapped, and in these hospitals there are ample "foster parents" waiting to look after them. These are the adult patients in the hospitals, kind, sympathetic and well able, with some nursing help, to look after these children. Up to the present they are deprived themselves. Most of them never sit a child on their knees, help to teach a child to dress or feed himself, take a child for a walk or to school; and yet these are all things they are capable of doing and love to do.

What we should be fighting for is to abolish all children's wards by putting the children in with the adults. Where this is done, both benefit. The children receive security, affection, and constant care by one or two people; bad practices are abolished; and in consequence the children improve. The adults improve too, for they now have at long last someone to look after and love. The job of the nurse in this situation is to train the adult for these new duties and responsibilities. Anyone who attempts to do this will have to face the displeasure of the Department of Health, which blandly says—without giving any reason—

that mentally handicapped children should not be mixed with adults, and pædiatricians, to whom the practice is anathema. They will, however, have the whole-hearted support of the parents of these children who, in my experience, when they have once had a child in a ward with adults absolutely refuse to have him put back in a children's ward. Moreover, this enormous enrichment of the life of child and adult can be achieved without additional staff, buildings, or money.

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J. GIBSON.

BACTERIAL CULTURE OF JEJUNAL MUCOSA IN CHILDHOOD CÆLIAC DISEASE

SIR,—We were interested in the paper by Dr Tomkins and others (Jan. 11, p. 59) describing bacterial culture of the proximal jejunal mucosa in patients with acute tropical sprue. These authors found 4 species of *Enterobacteria* in the mucosa of 11 of their 16 patients. They suggested that these organisms were responsible for persisting jejunal abnormalities and were not merely markers of mucosal pathology. There are histological similarities between the jejunal lesions of tropical sprue and untreated celiac disease, but no comparable bacteriological study has been made of the celiac enteropathy.

We have cultured jejunal mucosa and intestinal juice from 3 children with untreated celiac disease whose biopsies showed total villous atrophy. 4 children whose jejunal biopsies were normal but who were investigated to exclude a gluten-sensitive enteropathy were also studied.

The intestinal biopsy specimens were taken with a pædiatric Watson capsule. Tissue handling, transport,

BACTERIAL COUNTS IN CÆLIAC PATIENTS AND CONTROLS
(Mean log₁₀ viable counts per g. mucosa or per ml. luminal fluid)

		Mean total viable count (log ₁₀ /g. or /ml.)	No. of sterile specimens	Total species of bacteria	Enterobacteria isolations
Celiac patients (n = 3)	Mucosa	8.6	1	5	0
	Luminal fluid	5.8	1	4	0
Control patients (n = 4)	Mucosa	7.6	2	3	0
	Luminal fluid	5.7	2	4	0

and culture techniques were exactly the same as those used by Tomkins et al.

Total viable bacterial counts in the mucosa and fluid of the 2 groups of patients are shown in the accompanying table. There were no differences between the celiac patients and the control group, and *Enterobacteriaceæ* were not isolated. Bacterial counts were higher in the mucosal specimens; only one organism was isolated from the mucosa (*Staphylococcus albus*) without also being present in the paired intestinal juice. 2 of the controls and 1 celiac patient had sterile biopsies. *Streptococcus viridans*, *Neisseria*, and *Hæmophilus* species were the commonest aerobic organisms cultured. A species of *Veillonella* was the only anaerobic organism isolated, and was found in 1 control and 1 celiac patient.

These results suggest that there is no single bacterial

4. Jacobs, D., Hourì, M., Landon, J., Merrett, T. G. *Lancet*, 1973, ii, 1059.