

THE relation between cancer and allergy has been the subject of several studies. Most have indicated that cancer is less common in people with a history of allergy than in non-allergic individuals. Thus, Mackay ¹ found that significantly fewer women with cancer gave a family or past history of allergic disorders than did matched controls, and Fisherman ² recorded that a history of allergy was four times more common in patients without cancer than in those with malignant disease. Ure,³ in an investigation of gynæcological patients, presented evidence that allergic and neoplastic disorders were mutually exclusive, while Gabriel et al.⁴ reported that only 2% from a group of male cancer patients admitted to an allergic history, compared with 14% in a control group. Conversely,

McKee et al.⁵ found no significant difference in the incidence of allergy in cancer and non-cancer patients, and Logan and Saker⁶ reported that cancer patients were more likely to have allergic disorders.

The development of sensitive and specific assays for immunoglobulin E (IgE) may help elucidate these apparently contradictory findings. Circulating levels of IgE are raised in patients with allergic disorders,^{7,8} so we decided to determine IgE levels in patients with a variety of neoplasms.

Patients, Volunteers, and Methods

Serum samples were collected from 100 healthy individuals with no clinical evidence of allergy or cancer, from 200 untreated patients with advanced neoplasms, and from 200 patients with cancer who had been treated with cyclophosphamide. About 50% of the patients had bronchial carcinoma, the remainder having a variety of malignant diseases, including myeloma and cancer of the prostate or breast. We could not match exactly the treated and untreated groups, and, in general, the disease was more advanced in the untreated group. A group of 50 patients with a variety of allergic disorders was also studied.

IgE levels were measured both by a solid-phase radioimmunoassay ('Phadebas IgE Test', Pharmacia Ltd., London) and by a modification of the single radial immunodiffusion method.⁹ The amounts of IgE are given in terms of the British research standard 68/341. The radioimmunoassay detects 20 units per ml. or more, and its coefficient of variation for between-batch precision in four separate assays, using different batches of reagents,

was 7%. The sensitivity of the radial immunodiffusion method (250 units per ml.) did not enable it to separate normal and subnormal IgE values.

Results

Radioimmunoassay

Values in the controls ranged from 85 to 740 units per ml. (see figure), with a mean of 215 units per ml. Increased circulating levels were found in most allergic patients, the mean value being 1060 (range 101–10,000 units per ml.). In contrast, levels of IgE in patients with cancer receiving cytotoxic drugs were significantly reduced, ranging from 20 to 680 units per ml., with a mean of 125. According to radioimmunoassay, patients with untreated cancer could be divided into two groups of approximately equal size—one with low IgE values and one with apparent values in excess of 100,000 units per ml.

Radial Immunodiffusion and Other Studies

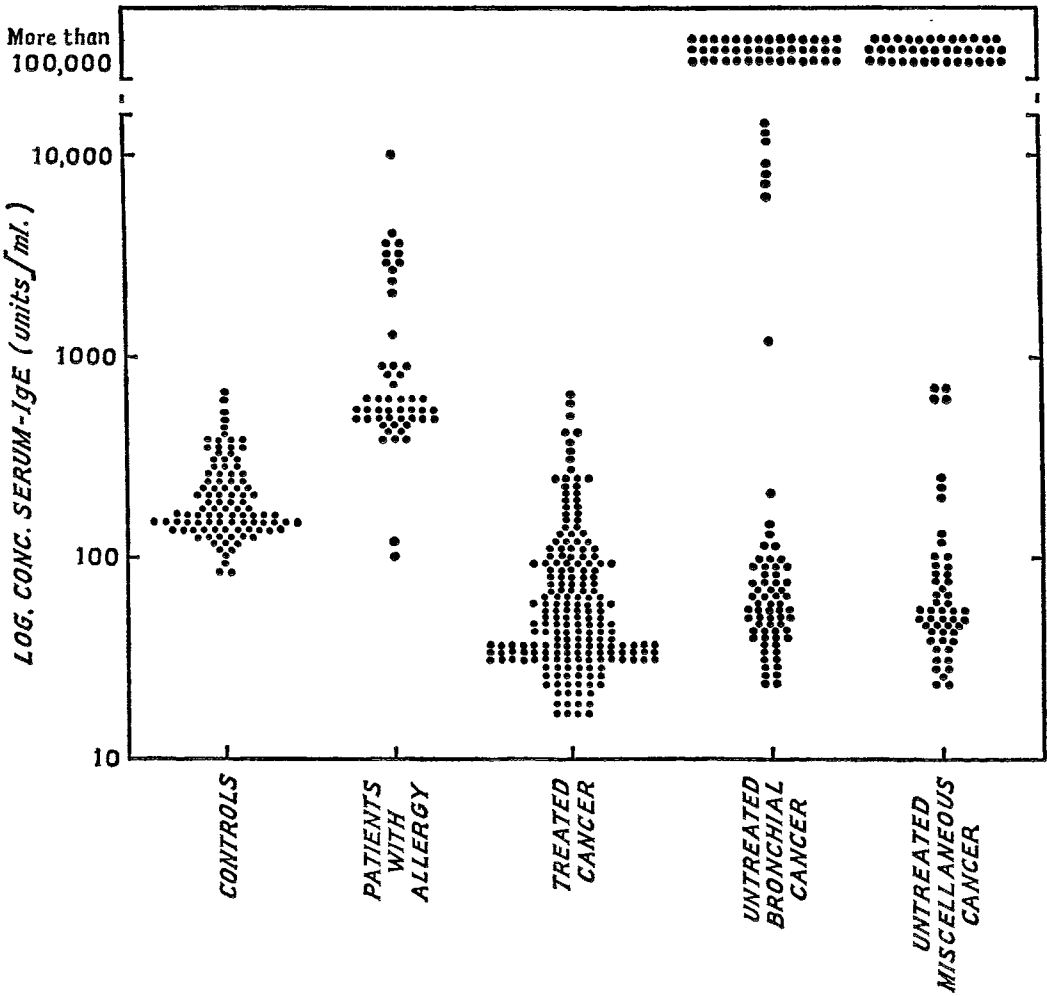
There was good agreement between the results obtained by radial immunodiffusion and radioimmunoassay in controls ($r=0.96$) and allergic patients ($r=0.99$) and in patients receiving cytotoxic drugs ($r=0.98$). In contrast, there was no agreement between the results obtained in untreated patients with high levels, as determined by radioimmunoassay, almost all of whom had undetectable values using the radial immunodiffusion technique. Further-

more, even after the addition of 5000 units of IgE to serum samples from patients in this group it was not possible to detect this immunoglobulin by the immunodiffusion assay in approximately half of the samples. The samples in which the added IgE remained undetected were, without exception, the same samples in which values in excess of 100,000 units per ml. were obtained by radioimmunoassay.

Preliminary studies were performed in which blood-samples were obtained from vessels draining tumours and from the peripheral circulation. These suggest that the apparently high values obtained in these patients by radioimmunoassay and the failure to detect large amounts of added IgE by radial immunodiffusion are due to the release of an inhibitor substance from the tumours which interferes with the binding of IgE by antibody.

Discussion

The function of IgE is uncertain. In general, atopic individuals have higher circulating levels than non-atopics (as we found), and it is thought that the immunoglobulin is absorbed on to tissue cells sensitised with



Circulating levels of IgE, as determined by radioimmunoassay.

In 100 healthy subjects, 50 allergic subjects, 200 patients with cancer being treated with cytotoxic drugs, 111 untreated patients with advanced bronchial carcinoma, and 89 untreated patients with a variety of other advanced neoplasms.

allergen and damages the cell membrane. It seems probable that IgE has functions other than as mediator of the allergic response, and Ure³ suggested that it might cause lysis of tumour cells. Gabriel et al.,⁴ in a recent survey, found that a statistically significant proportion of male patients admitted to hospital with cancer had a lower incidence of allergy than a control population, and suggested that an atopic individual may be able to protect himself against cancer with the aid of readily mobilised IgE. Furthermore, several workers have noted that allergic symptoms tend to subside with age, whereas cancer is a disease of later life—indeed this was a problem in trying to provide a matched group of allergic patients.

The present study is the first, of which we are aware, involving the assay of circulating IgE levels in a large number of patients with cancer. Circulating values were subnormal, as determined both by radioimmunoassay and by a radial immunodiffusion technique, in most patients who were receiving cytotoxic drugs. Immunosuppressive therapy might be expected to produce this effect, and Jameson et al.¹⁰ have recently reported that administration of a cytotoxic drug to two patients with bronchial asthma was associated with a fall in circulating IgE. It is tempting to postulate that the increased frequency of neoplasia noted in patients receiving immunosuppressant drugs following, for example, renal transplantation, might be due to a decrease in IgE.^{11,12} It should be noted, however, that the neoplasms that develop are often unusual.

Most of the patients with a variety of advanced, untreated neoplasms also had low or undetectable IgE levels as determined by radial immunodiffusion. This was confirmed by radioimmunoassay in about half. The remainder, who, in general, had the most advanced carcinomas, had apparent immunoreactive levels well above those ever recorded in allergic or any other conditions. This, together with the finding that large amounts of exogenous IgE added to these samples could not be detected by immunodiffusion, can best be explained by the presence of a circulating inhibitor that prevents the binding of IgE by anti-IgE sera. Thus inhibition of binding of labelled IgE in the radioimmunoassay can be misinterpreted as resulting from competition for available antisera by large amounts of unlabelled IgE, while the same effect in a radial immunodiffusion assay will prevent the formation of precipitation lines and be considered as indicating an absence of IgE.

Preliminary studies indicate that circulating IgE levels are also low in patients presenting with a variety of neoplasms in their early stages. Furthermore, an inhibitor can be detected in the venous drainage of some of these tumours before it can be detected in the systemic circulation. However, it would be wholly premature to postulate any link between IgE and IgE inhibitors and the aetiology of cancer.

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LOSS OF AMBULATORY ABILITY IN PATIENTS WITH OLD ANTERIOR POLIOMYELITIS

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Summary Lower-extremity involvement by anterior poliomyelitis in infants and children, thought to be a static neuromuscular impairment, may in later years, in the absence of new disease, yield increasing motor disability of such severity as to immobilise the previously mobile and remove the previously employed from the labour market. This picture is characterised by frequent falling, recurrent joint pain and instability, the need for additional bracing, change of employment and method of transportation, and long-bone fracture.

WE have been puzzling over the problem of functional deterioration in the middle-aged patient with a history of acute anterior poliomyelitis many years previously. We served as physical-medicine consultants to a pre-paid group-practice plan, caring for 32,000 people. Civil-servants and white-collar workers made up a major segment of the subscribers. Referred to us were a number of patients with old anterior poliomyelitis who had been functionally adequate until ambulatory ability suddenly or gradually deteriorated.

Over a period of 5 years, we saw twenty patients with lower-extremity impairment caused by anterior poliomyelitis. Some of these had a new neuromuscular complaint, and these will not be considered further. Subsequently we asked the group's family physicians about other patients, and we accumulated six cases where the major complaint was recent loss of ambulatory ability. We later heard of three other cases. All nine patients had had acute childhood poliomyelitis affecting the lower extremities and had a history of diminishing ambulatory ability in later adulthood (see table).

Each case had two or more of the following landmarks: joint pain or recurrent injury or instability;