

spontaneous regression, but "florid" and "infiltrative" tumours have an appreciable morbidity and mortality. Lymphocyte transformation in Ugandan patients with this tumour has been studied using iodo-uridine (¹²⁵I.U.D.R.) uptake as a measure of lymphoblast formation.³ Normal Ugandan males provided blood for controls. In 9 of 23 patients the P.H.A./control uptake ratio was below 20, compared with 1 of 15 control patients ($P < 0.001$). 2 patients died during the period of study and lymphocytes from both of them showed a poor response to P.H.A. stimulation. However, in general the morphological type of tumour and course of this disease were less clearly defined by this method of investigation than by lymphocyte transformation in response to culture with mitomycin-inhibited autologous tumour cells. Cutaneous delayed hypersensitivity responses using dinitrochlorobenzene sensitisation and subsequent challenge⁴ are also impaired in patients with invasive forms of this sarcoma.⁵

In order to determine the relevance of P.H.A.-stimulated lymphocyte transformation to clinical events, further immunological studies of human sarcomas are required utilising a variety of in-vitro and in-vivo techniques simultaneously. The question of whether defective blastogenesis is related to the pathogenesis of the tumours or is the result of tumour progression may be answered by repeating the tests during the course of the disease.

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ACHILLES TENDON RUPTURE

SIR,—You remarked (Jan. 27, p. 189) that it is doubtful whether surgical repair in closed ruptures of tendo Achillis can still be justified. I, too, am concerned about the need for surgery in these ruptures. We have just completed a study of 130 patients treated surgically by orthopaedic surgeons at the Hospital for Special Surgery in New York City. There was a 15% wound-to-complication rate in this large series; however, there were no reruptures. There was one method of surgical repair that gave the best functional results without wound complications. 50 of these patients had their tendon repair objectively evaluated on the Cybex isodynameter.

The Cybex isodynameter tests musculotendinous function through an isokinetic principle. In the isokinetic loading technique the muscle encounters no external resistance until it reaches a pre-set velocity of contraction. The force levels generated by the muscle are monitored by an external load cell and are recorded on a strip chart recorder. By this means the strength of contraction in foot-pounds can be easily determined, but, more important, the power potential in foot-pounds per second. The measurements of power are analogous to walking and running, where weight must be moved in required time intervals.

The operated leg was compared with the normal leg, and these results indicated that there was a 101% recovery of strength and 85% return of power after operation, even in those patients in whom a wound complication had occurred. We noted that, in the 50 patients evaluated, there were 4 patients with rerupture of a tendo Achillis after conservative treatment—that is, treatment in a plaster cast for 8 to 12 weeks. These patients did not do as well after tendon reconstruction.

We are now evaluating on the isodynameter a large number of patients treated conservatively. If these patients

do as well as the patients after surgical repair, and if the problem of rerupture can be solved, then surgical repair will not be the treatment of choice. However, until the objective data are available there is no evidence that operation is not the treatment of choice.

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ALLERGY AND CANCER

SIR,—An immune reaction is believed to control the body's rejection of most developing malignant cells.¹ This is thought to be a function of the cell-mediated thymus-dependent immunological system that also controls delayed hypersensitivity and graft rejection. However, vasculocellular damage follows the development of immediate hypersensitivity caused by immunoglobulins of the IgE class, and the idea that people with immediate hypersensitivity (who apparently produce excess IgE) are less likely to develop cancer has attracted some attention. A practitioner of yoga² mentions the negative association between allergy and cancer. Jacobs and his colleagues found comparatively low IgE levels in patients with malignant disease.³ Several surveys⁴⁻⁷ indicate that cancer is less common in allergic people. One report,⁸ however, suggests that cancer patients are more likely to have allergic disorders, and another⁹ describes similar IgE levels and skin-prick results in patients both with and without cancer.

DISTRIBUTION OF ASTHMA OR HAYFEVER AMONG PEOPLE WITH AND WITHOUT CANCER

Patient group	Age-group (yr.)												Total	
	30-39		40-49		50-59		60-69		70-79		80 +			
	M	F	M	F	M	F	M	F	M	F	M	F		
Without cancer (553)														
With allergy	5	2	1	3	4	18	12	15	6	10	5	2	83 (15.0%)	
Without allergy	9	12	10	31	35	75	65	76	63	60	18	16	470 (85.0%)	
With cancer (546)														
With allergy	0	2	1	1	2	3	4	7	3	1	3	0	27 (4.9%)	
Without allergy	12	12	13	38	37	86	72	81	63	70	17	18	519 (95.1%)	

We have studied the frequency of allergy, as manifested by asthma or hayfever, in 546 cancer patients and 553 non-cancer subjects matched for sex, age, and area of residence.

The cancer patients were attending the radiotherapy department, and the non-cancer patients were visiting various surgeons, geriatricians, and general practitioners. 4.9% of the cancer patients claimed to have had asthma or hayfever, compared with 15% of the non-cancer subjects (see table). Statistically, the difference is highly significant ($\chi^2 = 29.8$, $P < 10^{-7}$).

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The results of this inquiry suggest that a person who does not have an allergy, as defined, is at least 3 times more likely to develop cancer than one who does. Allergic people respond in a special way to some antigens, and it seems possible that they might react in a similar way to the antigens by which malignant cells differ from their non-malignant cells of origin. In many people this reaction may involve only the cell-mediated immune system, and neoplastic cells would then be attacked by a process related to graft rejection. However, if tumour-specific IgE is produced, cells might also be destroyed after vascular damage by the release of histamine-like substances from activated mast-cells. In any event, the highly significant difference demonstrated in the frequency of allergy between those with and those without cancer lends weight to the idea that immunological mechanisms are important in suppression of malignancy. It also suggests that a person's ability to react by the production of immediate hypersensitivity to a new antigen at the surface of malignant cells may be important in securing the destruction of such cells. This might be in addition to, or instead of, the graft-rejection response.

I thank a number of my colleagues for generous cooperation in completing questionnaires on their patients.

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DIARRHŒA RESEMBLING CHOLERA INDUCED BY ESCHERICHIA COLI CULTURE FILTRATE

SIR,—We write to correct an error in our letter of March 24 (p. 677) and to give some additional information. The NaCl concentration of the test solution was 150 mmole per l., not 300.

Since our letter we have conducted additional neutralisation studies in dog jejunal loops. Sera were collected from rabbits before and after immunisation with purified Wyeth 001 cholera toxin. Preimmunisation sera had no detectable vibriocidal antibody titres. Preimmunisation and post-immunisation sera from 3 rabbits were incubated with cholera toxin and also with *Escherichia coli* toxin of the type described in our letter. Paired pre and post immunisation sera mixed with *E. coli* toxin (2 loops) and cholera toxin (2 loops) were placed in 4 adjacent loops in each of 3 dogs for 10 minutes and were then rinsed out. 2 additional control loops in each dog were treated with the toxins alone. Net fluid accumulation in the dog loops was measured over the following 6 hours.

Premixture of *E. coli* toxin or *Vibrio cholerae* toxin with preimmunisation sera did not prevent fluid accumulation, which began 2–3 hours after exposure to toxin-sera mixtures.

Sera from rabbits immunised with cholera toxin neutralised both *E. coli* toxin and cholera toxin and prevented fluid accumulation in the loops. *E. coli* or cholera toxin given alone caused fluid accumulation in both control loops. Sera from rabbits immunised with *E. coli* toxin have not yet been tested.

These results are consistent with the idea that cholera antitoxin can neutralise *E. coli* enterotoxin of the type we have described, and suggest that the two toxins share antigenic determinants or possibly are identical. These observations agree with a previous study in which whole-cell lysates were used instead of supernatant filtrates.¹

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AUSTRALIA ANTIGEN IN BLOOD-DONORS

SIR,—May I record the results of studies of Australia antigen in asymptomatic volunteer blood-donors at this hospital? The work began in mid-1971, and during the rest of the year 2400 donors were tested. 10 were positive (an incidence of 0.41%). In 1972, 5615 donors were tested and 10 (0.17%) were positive. The method used was Spectra's counter electrophoresis. Sera from 977 donors were studied both by counter electrophoresis and Abbott's radioimmunoassay. 7 positive sera were detected by radioimmunoassay and none by counter electrophoresis. The radioimmunoassay-positive sera were repeated again by counter electrophoresis and all the sera were negative.

Technical assistance was provided by Lieut. JG S. Sessions, HMC C. Hightower, HM1 W. E. Alston, Jr., and HM2 J. W. Burmeister.

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ABNORMALITY OF SEPARATE SUBUNITS OF FACTOR VIII?

SIR,—The interesting letters of Professor Hougie and Mr Sargeant (March 17, p. 616) and Dr Bloom and his associates (March 24, p. 661) prompt me to write briefly of some of the findings and ideas which have evolved during immunological studies of hæmophilia and von Willebrand's disease carried out at University College Hospital.

In general, disorders of protein synthesis fall into two main categories: (a) those in which there is reduced or absent synthesis of the protein; and (b) those in which there is synthesis of an abnormal inactive protein. In the case of hæmophilia where there are low or absent levels of factor-VIII activity, immunological studies using human antibodies against factor VIII have shown that factor-VIII-related antigen is present in normal amounts in only 10–15% of hæmophilic patients.^{1,2} When testing is carried out using rabbit antibodies raised against human factor VIII, normal amounts of factor-VIII-related antigen are found to be present in the plasmas of most^{3,4} or all^{5,6} of the patients tested. In contrast, patients with von Willebrand's disease have been shown to possess an amount of factor-VIII-related antigen comparable to their levels of factor-VIII activity,^{5,6} although exceptions to these findings have been reported.^{7–9} As a result of these various observations it has been postulated that hæmophilic patients synthesise an abnormal, inactive factor-VIII-(like) protein^{3–6} and that von Willebrand patients manifest a true deficiency of factor VIII.

Certain observations have, however, raised the question of what is being measured by rabbit antiserum. For example, in two antibody-neutralisation experiments carried out in this laboratory to compare human and rabbit antisera it was shown that rabbit antibody was capable of measuring normal levels of factor-VIII-related antigen in (a) normal plasma which had been depleted of factor-VIII activity by incubation for 5 days at 37°C and

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