inflammatory properties. Since reduction of complement results in suppression of acute inflammatory reactions, our in vitro experiments show that the involvement of a hepatic process is not required for the anti-inflammatory action of ITF. Further, there is uncertainty whether the tissue factor which we recovered is identical with that found by BILLINGHAM.

Zusammenfassung. Bei Ratten wurde aus entzündetem Gewebe ein Hemmer für das Komplementsystem extrahiert, welcher die durch Carrageenin oder Kaolin erzeugten Entzündungen zu unterdrücken vermag.

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The Migration of Lymphoid Cells in Malignant Disease

Circulating sensitized lymphoid cells do not attack malignant homografts. Their lack of cytotoxicity, in vivo, has been attributed to certain serum factors: antibodies[1], antigens[2] or antigen/antibody complexes[3]. These are thought to block lymphocyte/tumour target cell interaction. Tumour produces a soluble substance which inhibits cellular adhesion and pseudopodia formation[4] and impairs the migration of leucocytes[5]. It is suggested that this substance paralyses all manner of lymphocyte locomotion: diapedesis, directional migration and attachment to target cell and that it is this paralysis, and not blocking by antibody, which enhances tumour growth.

Materials and methods. White Wistar outbred rats, weanlings of 80–100 g and adults of 150–180 g were obtained from Messrs. Tuck & Son, Rayleigh.

Tumour: A transplantable tumour, originally induced in the rat uterus[6] was maintained by serial passage and used in these experiments.

Two plastic millipore discs, 25 mm in diameter, pore size 6 nm, from Messrs. Millipore, London, were heat-sealed to form a cell impermeable diffusion chamber. Accessible lymph nodes were excised, minced in an aliquot of saline and centrifuged until the supernatant was clear. The latter was discarded and the sediment only used.

Tumour fragments of 0.2–0.3 cm^3 were grafted into the left flank of an adult animal. About 12 days later, when the tumour had reached a diameter of 10–15 mm, a piece was excised and divided into 3 portions of 0.2 cm^3 each.

One portion was grafted into the right flank of the donor. The second fragment was sealed into a millipore chamber and the third portion was enclosed in a chamber together with 0.2 ml of packed lymphoid cells. The 2 chambers were placed into the abdominal cavity of the donor animals and left in situ for 7 days. At the end of this period, the chambers were again removed, the tumour fragments taken out and implanted s.c. into weanling rats.

In a control series a similar procedure was adopted using tumour free animals and homologuous tumour.

Liver fragments of 0.3 cm^3 were implanted s.c. and full thickness skin allografts of 10 mm diameter were sewn to the anterior chest wall of adult rats.

Grafts, their substrate and the draining lymph nodes were excised at various intervals after implantation, fixed in formol saline and stained with haematoxylin eosin or methyl green pyronin.

Results. Non-malignant homografts induced a progressive accumulation of mononuclear cells at the graft site, culminating in the rejection or destruction of the graft, usually by the 10th-13th day.

There was a similar accumulation of mononuclear cells at the implantation site of malignant homografts, and also a blastic response in the regional node. However, the peritumoral white cell reaction reached a peak on the 2nd post-implantation day and from then on gradually subsided to completely disappear by the 6th day.

The Table shows that tumour fragments in millipore chambers remained viable but lost their viability and transplantability when exposed to lymph node cells, particularly to lymphocytes from the tumour bearing host. Close contact with tumour for a period of 7 days also conferred a certain degree of cytotoxicity to non-sensitized lymphocytes.

Cytotoxicity was not affected by serum factors penetrating the pores of the chamber, even though the host carried 2 subcutaneous tumours, one of which 19 days old and about to cause the death of the animal.

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Growth of tumour fragments enclosed for 7 days in an intraperitoneal diffusion chamber and thence grafted into weanling rats

Content of Chamber			
Tumour and nonsensitized lymphoid cells	Tumour and sensitized lymphoid cells	Tumour only	Control Tumour autograft
Number of tumour bearing weanlings			Adults
6/12	1/14	26/26	14/14

Discussion. The foregoing results confirm that there is no white cell reaction in and around established tumour but that serum factors do not affect lymphoid cell cytotoxicity. However, such cytotoxicity is only effective when lymphoid cells and tumour target cells are brought into close contact as in the millipore experiment.

The concept of a non-specific 'lymphocyte migration paralyzing agent' produced by tumour would explain various phenomena observed in a tumour bearing host. As the tumour grows, there is increasing production of this agent and this would account for: the initial development[7] and subsequent loss[8] of concomitant immunity, the immunological stimulation, followed by immunological paralysis in the nodes draining the tumour[9,10], the evolution of generalized, non-specific allergy[11] and the inhibition of tumour by any (non specific) measure which promotes the infiltration of lymphocytes into tumour tissue[12,13]. All these are independent of serum factors viz. specific antibody.

Non-malignant homografts e.g. organ transplants equally induce humoral and cellular immunity – but fail to secrete paralyzing agent, hence the progressive monocytic infiltration which leads to the rejection of the graft[14].

As to the nature of the paralyzing agent produced by tumour, it is conceivable that it is an enzyme which inactivates prostaglandin. The prostaglandins are ubiquitous tissue hormones which participate in inflammatory[15] and allergic[16] reactions, promote the diapedesis[17] and migration[18] of leucocytes and enhance the cell mediated immune response[19].

The inactivation of prostaglandin by tumour would account for the (cell mediated) immunological unresponsiveness in the tumour bearing host[20].

Zusammenfassung. Experimenteller Nachweis, dass fortschreitendes Tumorwachstum nicht Serumfaktoren (Antikörpern) zuzuschreiben ist, sondern offenbar geschwulsteigenen Substanzen mit Lokomotionshemmung der Leukozyten.

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Skeletal Muscle and Tumour Metastasis

Muscle can undergo sarcomatous changes. It is an immunologically privileged tissue which can accept malignant and non-malignant homografts[1]. There are no mechanical factors to impair the haematogenous dissemination of tumour emboli into skeletal muscle[2].

It would therefore appear that neither the 'soil'[3] nor the 'haemodynamic'[4] hypotheses could offer an adequate explanation for the paucity of blood borne metastases in voluntary muscle. In the present communication a third hypothesis to account for this phenomenon, is put forward.

Materials and methods. Animals and tumours were used as in the previous communication.

Preparation and administration of tumour suspension. 1 volume of tumour was suspended in 2 volumes of saline and homogenized in a MSE homogenizer at 10,000 rpm for 90 sec. 4 groups of 10 rats received an infusion of 0.3 ml of tumour suspension: group A into the left femoral artery, group B into the left thigh muscles, groups C and D into subcutaneous and intradermal sites respectively.

Method of immunization. Amounts of 0.5 ml of tumour suspension were injected into the right flank. After 10–12 days, when the tumour had reached a diameter of approximately 15 mm, it was excised. The animal was challenged with 0.4 ml of intradermal tumour 3 weeks after extirpation of the immunizing growth. Animals which rejected the challenging tumour were considered to be immune and were used for the second part of these experiments.

Histological methods. Skin biopsies taken at various intervals after tumour challenge and muscle biopsies, taken at day 2, 7 and 10 after i.m. tumour inoculation into immunized and non-immunized animals, were fixed in formol saline and stained with methyl green-pyronin.

Results. Tumour took in 8 out of 10 animals of group A. This intraarterial infusion gave rise to a diffuse tumour growth in the whole lower limb. The i.m. inoculum, which took in all recipients, was confined to 1 muscle group only. Cutaneous grafts also took in all animals and grew into round, ulcerating nodes. Similar experiments, repeated with immune recipients resulted in tumour rejection in all instances. However, the rejection mechanism varied in each group.

Intradermal and s.c. tumour caused a localized induration of no more than 10 mm in diameter which subsided after 4–6 days. Histologically there was an accumulation of leucocytes, including immunoblasts, in the affected area. Intraarterial infusion did not cause palpable thickening though the limb appeared to be tender for several days after the infusion.

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