JOINT SUMMER MEETING 1976

Liverpool University

British Transplantation Society	July 14
British Society for Immunology	July 15,16
British Society for Allergy and Clinical Immunology	July 17

Saturday Afternoon

Chairman: A.W.Frankland

2.00p.m. R.MUNRO FORD (Adelaide, Australia)

'Drug trials in allergic diseases'

2.30p.m. M.L.H.FLINDT (Manchester University)

'Alkalase - the end of the story?'

3.00p.m. Tea

GENERAL NOTES

Accommodation

Single rooms are available at the Carnatic University Halls for those who have booked. Car park facilities are available at the Halls and next to the Central Lecture Building (cf. enclosed map). Please inform the car park attendant - if any - that you are attending the BTS/BSI/BSACI Meetings.

Meals and Refreshments

Tea and coffee will be available at the indicated times on the First Floor of the Lecture Building and should be prepaid. Additional tickets may not be available on the day of the meetings. Lunches will be available at the Students' Union (sign-posted from the Lecture Hall) and should also be prepaid.

Social Functions

A Civic Reception (free) will be held at the Town Hall on the Thursday evening and a University Reception (free) on the Friday evening with the Dinner afterwards at the Carnatic Hall. Coaches will convey guests to and from the Halls to the Lecture Theatre Block. Exact times of the above will be announced at the meeting.

Future Meetings

An Autumn Meeting, for BSI and BTS jointly, will be held at the Wembley Conference Centre on 21st and 22nd October. Dr Howard C.Goodman and Professor Paul Russell will be the speakers on the morning of the 21st. Open papers will be presented on Thursday afternoon and Friday morning, and on Friday afternoon there will be a Poster Session. (see May BSI Newsletter)

Spring Meeting 1977 of the BSI will be held on 21st and 22nd April at Imperial College, London. There will be a Symposium entitled "Inflammation and Initiation of Immunity' on the 21st.

ABSTRACTS

British Transplantation Society (not for publication)

The influence of anatomical variations in donor kidneys on the success of renal transplants

J.R.SANSOM

Queen Elizabeth Hospital, Birmingham B15 2TH.

In a review of 250 consecutive human cadaveric kidney transplants the primary failure rate of donor kidneys with an anatomically abnormal blood supply was found to be 36.7% as compared with 16.2% for kidneys with a single artery and vein ($p<0.001$). The incidence of primary failure due to renal vascular thrombosis was 24.2% in the abnormal group as compared with 4.1% in the normal group ($p<0.001$). The rate of thrombosis was to some degree related to the type of vascular anomaly encountered but not influenced by the type of anastomosis performed. The incidence of thrombosis was not related to the side from which the donor kidney was obtained (right or left).

A significantly greater incidence of anastomotic haemorrhage (8%) was associated with anomalous vessels into donor kidney as compared with kidneys with a single artery and vein (1%, $p<0.01$), irrespective of the type of vascular anastomosis used.

Ureteric leaks requiring surgical correction, occurred in 8.0% of abnormal kidneys as opposed to 2.3% of normals ($p<0.05$).

In view of these findings it seems questionable whether donor kidneys with an abnormal vascular supply should be used in human cadaveric renal transplantation.

Rejection of HL-A identical related kidney grafts

J.R.SALAMAN

Renal Transplant Unit, Royal Infirmary, Cardiff.

An HL-A identical related kidney transplant offers the best chances of success when transplanting someone with chronic renal failure. Rejection episodes are observed from time to time but they are seldom insurmountable and 80% of these grafts can be expected to be functioning one year after transplantation. Our recent experience with three HL-A identical grafts is perhaps unique in that all three rejected, two irreversibly.

Each of the three recipients received a kidney transplant from a brother who was not only HL-A identical but M.L.C. non-reactive. The immunosuppressive regimen used was the same as that employed for cadaver grafts. One patient who was diabetic had not received prior dialysis. Of the three patients, one suffered severe rejection episodes during the third and seventh

weeks which were reversed, although full function was never regained. The other two rejected their grafts completely and these were removed. The diabetic patient developed cytotoxic antibodies which could not be characterised, but were not active against the donor. Serum prednisolone and azathioprine levels were checked but these were not reduced nor were they lower when the patients took antacids at the same time, as had been their practice.

This experience would emphasize that the major histocompatibility locus is not the only system governing the fate of kidney transplants in man.

Management of 117 renal graft rejection episodes

C.MOISEY and M.FOX

Royal Hospital, Sheffield.

The mechanism of rejection following renal transplantation remains unclear and treatment constitutes a continuing problem for which many regimes have been suggested. In recent years high dose steroid pulse treatment has been employed and it is the results of this management with or without additional anti-coagulants, Actinomycin-C and local irradiation which are compared with those of lower doses of steroids. Survival and function of the graft are also compared with age, number of rejection episodes, time relation after grafting and complications.

Reversal was achieved in 86% in the first, 67% in the second and 54% in the 3rd and 4th episodes. It was easier to reverse rejections below 39 years (81.5%) than after (74.5%). Reversal of the first rejection was more difficult to accomplish if it occurred in the first two weeks (80%) than from the second to the 12th weeks (89%).

Treatment consisted of Methyl Prednisolone 1 gm daily i.v. from one to five daily doses either alone or in combination with Actinomycin-C. or D. for 3 doses, Heparin 20,000 units per day for 3 to 5 days, 150r local irradiation to the kidney on alternate days x3. There was no statistical difference in the results between any of these courses or in 16 cases when 200 mg Prednisolone was given orally for 3-5 days with or without Actinomycin and/or Heparin. The only significant finding was that a single dose of 1 G Methyl Prednisolone was not as effective (70%) as 2 to 5 doses (82-84%). Two doses were as effective as four or more.

Complication rates were compared between the various regimes. The only notable one was that of urinary fistulae the incidence of which increased with larger total steroid treatment given.

The prediction of upper gastro-intestinal haemorrhage in patients suffering from chronic renal failure

J.A.CRAPP, A.G.JOHNSON, E.M.GORDON and GRANT WILLIAMS

Department of Surgery, Charing Cross Hospital Medical School and Renal Transplantation Unit, Charing Cross Hospital, London.

Gastric acid secretion, upper gastro-intestinal radiology, and symptomatology were studied in 117 patients undergoing intermittent haemodialysis for chronic renal failure. Forty-nine had abnormal maximum acid output, 38 had abnormal X-rays, and 21 suffered from dyspepsia. Seven patients had prophylactic vagotomy because of high acid output, but in the remaining 110 patients, 11 bled from the upper gastro-intestinal tract. Of the three parameters used to define those at risk from haemorrhage, epigastric pain was the most discriminating feature between the group which bled and that which did not, and occurred in the presence of either abnormal acid secretion or abnormal barium meal significantly more often in the former group. None of 41 patients who had three normal parameters bled and the presence of any abnormality occurred significantly more often in the group which bled. Patients with chronic renal failure should have all three investigations routinely prior to renal transplantation to identify those patients with peptic ulceration or a predisposition towards it. Highly selective vagotomy is recommended for those patients with a duodenal ulcer diathesis. Of seven patients with gastro-duodenal bleeding after renal transplantation, some or all of these three parameters were abnormal.

Lymphocyte dependent antibody in renal transplantation

Keryn WILLIAMS, D.OLIVER and P.J.MORRIS

Nuffield Department of Surgery, University of Oxford, Radcliffe Infirmary, Oxford.

Serial serum samples from 25 patients before and after a cadaveric renal transplant were assayed for the presence of lymphocyte dependent antibody (LDA). 154 dialysis sera, including the immediate pretransplant samples, from these 25 patients were screened retrospectively against a panel of 10 lymphocyte donors. The target lymphocytes were chosen to include any mismatched donor HLA antigens of the A and B series. Lymphocytes from a single donor were used as effector cells. The definition of a positive reaction was based on ^{51}Cr release by the target cells using a more stringent definition than that of other workers. 21 of 25 patients (84%) gave a positive reaction for LDA before transplantation. Of these 4 grafts were removed for irreversible rejection and 1 died of infection associated with immunosuppression, while 16 are functioning at 2 to 12 months after transplantation. 4 of the 25 patients were negative for LDA and of these there were 2 failures. There was no correlation between rejection episodes and the presence of specific LDA before

transplantation. In addition, 280 postgraft serial serum samples were tested for LDA but no correlation was noted between positive reactions and rejection. These results do not suggest that the presence of LDA before transplantation is indicative of a poor graft prognosis, nor that the presence of LDA after transplantation is associated with rejection, as suggested by Ting and Terasaki (1975) and Jeannet, Vassalli and Botella (1975).

Ting, A. and Terasaki, P.I. (1975) Lancet, 1, 304-306.

Jeannet, M., Vassalli, P. and Botella, F. (1975) Transplantation Proceedings, 7, 631.

In vitro monitoring of DNCB sensitivity

D.N.H.HAMILTON, V.LEDGER and A.A.DIAMANDOPOULOS

Department of Surgery and Renal Unit, Western Infirmary, Glasgow.

Skin testing with DNCB is the most valuable single test of levels of cell-mediated immunity (CMI). However, quantitation of it is difficult and it cannot be repeated frequently. An in vitro measurement of the CMI to DNCB would be valuable.

We have used the haptene made by mixing DNCB with human RBC as the antigen in a leucocyte migration-inhibition assay. Patients who developed full sensitivity to DNCB 14 days after sensitisation showed 45% inhibition of leucocyte migration by this RBC-DNCB antigen and control leucocytes showed only 8% inhibition. The variable factors in the test have been studied and the optimal concentration of DNCB in preparation of the haptene was found to be 2.5% The optimal dose of antigen was 40,000 RBC-DNCB haptene protein equivalents.

This test may be valuable in continuous in vitro monitoring of CMI.

Allogeneic priming of H-2 restricted T-cell mediated responses to H-Y

R.D.GORDON and Elizabeth SIMPSON

Transplantation Biology Unit, Clinical Research Centre, Harrow, Middlesex.

The target cell specificity of in vitro generated T-cell mediated secondary cytotoxic responses to H-Y antigen is restricted by the H-2 complex (1) suggesting that H-Y antigen cannot be detected on allogeneic male cells. However, it has been previously reported that in vivo responder females primed with allogeneic male cells give a second set response to a subsequent syngeneic male graft (2). We here report that C57BL/10 (B10)

females primed in vivo with an allogeneic (CBA or BALB/c) male graft, and challenged in vitro with irradiated syngeneic (B10) male cells, lyse syngeneic (B10) but not allogeneic (CBA or BALB/c) male target cells. This suggests that at least some component of H-Y is detected on allogeneic cells during primary sensitization and that the second set T-cell mediated response to H-Y is not necessarily restricted by the H-2 haplotype of the primary sensitizing strain. Furthermore, preliminary data indicate that (CBA x B10)F_1 females primed in vivo with male cells of one parental haplotype and challenged in vitro with male cells of the other parental haplotype fail to lyse male target cells of either parental haplotype. This makes it unlikely that a shared helper determinant is responsible for primary sensitization to H-Y using allogeneic male stimulating cells.

These observations are difficult to reconcile with either the intimacy (dual recognition) or the altered self (interaction) hypotheses for H-2 restricted cell-mediated cytotoxicity (3). It may be that the helper T-cell subset generated during in vivo priming to non-self (allogeneic) H-Y is capable of helping secondary responses to altered-self (syngeneic) H-Y by H-2 restricted cytotoxic effector cells generated in secondary MLC.

1. Gordon, R.D. et al. (1975), J.Exp.Med., 142, 1108.

2. Silvers, W.K. and Yang, S.L. (1973) Science (Wash.D.C.), 181, 570.

3. Zinkernagel, R.M. and P.C.Doherty (1974), Nature (Lond.), 251, 547.

Studies on the mechanism of immunoinhibition by linoleic (C18:2) and arachidonic (C20:4) acids

C.J.MEADE, J.MERTIN, Ruth HUNT and Jinan SHEENA

Transplantation Biology Section, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ.

C18:2 and C20:4 prolong skin allograft survival. How?

The early effects of C18:2 and C20:4, injected according to schedules known to prolong allograft survival, resemble those of allograft induced 'immunostimulation'. Uptake of ^{125}IudR by peripheral lymph nodes, spleen and bone marrow is increased. The lymphocytes of the spleen and lymph nodes, and in the spleen, also metamyelocytes, can be shown by autoradiography to be the principal cells stimulated to divide. These results will be discussed in relation to the reported increase in membrane phospholipid C18:2 and C20:4 minutes after mitogen-lymphocyte interaction (Resch and Ferber, 1975).

Longer C18:2 treatment considerably reduces the ability of lymph nodes, thymus, bone marrow and spleen to respond (as measured by increased ^{125}IudR uptake) to challenge by allografting. Could earlier 'sterile activation' of

lymphocytes, by forestalling other immunological commitments, contribute to immunoinhibition?

Prolonged C18:2 or C20:4 treatment causes destruction specifically of lymphoid organs, particularly the spleen.

Splenectomy considerably reduces the ability of C18:2 to prolong survival of C3H allografts on CBA mice. Evidence will be presented that the spleen not only acts as a target for C18:2 action, but also can modulate the C18:2 effect on other organs.

Resch, K. and Ferber, E. (1975) The role of phospholipids in lymphocyte activation. Immune recognition. pp.281-312. Academic Press, N.Y.

British Society for Immunology (not for publication)

Affinities of different IgE-s for receptors in chopped human lung

R.C.GODFREY

Faculty of Medicine, Southampton University.

The amount of specific IgE antibody to allergens can be measured in serum by means of the in vitro chopped human lung test system. By allowing competition for binding sites to take place between the allergen-specific IgE antibody and IgE from another source, it is possible to compare the affinities of different IgE-s for tissue receptors. The evidence so far suggests that individual patients produce IgE of either high or low affinity. The biological and clinical implications of this finding will be discussed.

Histamine and histidine uptake by basophil leucocytes

J.STEWART, D.G.JONES and A.B.KAY

University Departments of Respiratory Diseases and Biochemistry and Blood Transfusion Service, Edinburgh.

Purified bone marrow leucocytes from the guinea-pig were examined for their ability to take up radiolabelled histamine and its precursor L-histidine. The uptake of ^{14}C-L-histidine was five to fifteen times greater than that of histamine. The incorporation of both compounds correlated with the basophil content of the preparations used, as did the amounts of extractable endogenous histamine. Time course studies

indicated a rapid uptake of both compounds during the first 60 minutes. Histamine uptake continued steadily over the following 5 hours, whereas over the same period very little histidine was incorporated. Neither compound was taken up in significant amounts by purified preparations of other guinea-pig leucocytes, including eosinophils, neutrophils and mononuclear cells. The significance of these observations will be discussed in terms of the regulation of histamine stores by basophils and its possible alteration following anaphylaxis.

Eosinophil accumulation and mast cell degranulation in the skin of a non-human primate

Lindsay W.TURNBULL, D.P.EVANS and A.B.KAY

University Departments of Pathology and Respiratory Diseases, Blood Transfusion Service, Edinburgh and Imperial Chemical Industries Ltd., Macclesfield.

Marmoset skin could be prepared with IgE-containing serum for the antigen-induced accumulation of eosinophils. Increasing concentration of antibody was associated with increased eosinophil infiltration and apparent degranulation of mast cells. The acidic tetrapeptides Val-Gly-Ser-Glu and Ala-Gly-Ser-Glu (ECF-A), also evoked eosinophil infiltration but there was no difference in the mast cell counts between the peptide-treated skin site and controls.

Histamine alone did not promote eosinophil accumulation and when combined with Val-Gly-Ser-Glu or Ala-Gly-Ser-Glu abrogated the eosinophil promoting properties of these peptides. These studies suggest that the ECF-A peptides have the capacity to recruit eosinophils in vivo by a mechanism apparently independent of mast cell disruption.

Eosinophils as regulators of repair following anaphylaxis

A.B.KAY and D.G.JONES

University Department of Respiratory Diseases and Blood Transfusion Service, Edinburgh.

A monospecific antiserum against guinea-pig eosinophils (AES) has been prepared in the rabbit. AES did not agglutinate neutrophils, mononuclear or red cells in vitro and selectively depleted eosinophils from the site of passive cutaneous anaphylactic reactions (PCA). The effect of AES on histamine depletion and re-accumulation following PCA reactions were studied.

AES or control rabbit serum (NRS) and antigen was injected i.v. into guinea-pigs in which skin sites were previously prepared with IgG_1. Following challenge, skin sites were excised, histamine extracted and the levels compared with the contra-lateral control sites. At 1 hour, with NRS, there was approximately 55% depletion but histamine stores were not fully replenished until 48 hours. With AES there was a comparable histamine depletion at 1 hour but levels were fully restored by 9 hours. These studies suggest that eosinophils may have a regulatory role in repair mechanisms following anaphylaxis by inhibiting the restoration of histamine and possibly other chemical mediators.

Purification of normal human eosinophils from peripheral blood

Poh-Chun TAI and Christopher J.F.SPRY

Department of Immunology, Royal Postgraduate Medical School, London.

Normal human eosinophils do not possess Fc receptors for the altered Fc piece of rabbit IgG, unlike normal blood neutrophils which have this receptor. Using this difference, we have been able to separate eosinophils from neutrophils, by exposing mixtures of cells containing eosinophils and neutrophils to Ag-Ab complexes coated onto plastic dishes. Neutrophils adhered to these complexes via the Fc receptors, leaving the non-adherent cells in the supernatant, 90% of which are eosinophils. 30-60% of the eosinophils are recovered by this method of separation.

Studies on the structure and function of normal eosinophils prepared in this way will be compared with stimulated or altered eosinophils which are found in the blood of patients with an eosinophilia.

Demonstration of two antigenic surface determinants on rat macrophages and their relation to Fc receptors

O.Förster, Angelika Boltz and G.Nitulescu

Institute of Experimental Pathology, University of Vienna, Austria.

Differences in the titres of anti-rat macrophage sera on rat alveolar (RAM) and peritoneal (RPM) macrophages have been reported. The conclusion by some authors of the existence of separate antigens specific for RAM and RPM could not be confirmed by our studies. Exhaustive absorptions of anti-RAM and anti-RPM sera with RAM or RPM lead to a complete disappearance of antibody activity. Transiently, however, some specificity of anti-RAM sera for RAM and of anti-RPM sera for RPM was observed. This was interpreted as being caused by a different epitopic density of at least two

different antigens on the surface of the two macrophage populations.

To get some insight into the functional significance of these antigens, the effect of our antisera on the formation of rosettes of RAM and RPM with IgG-antibody coated rat-RBC was investigated. In this test a significant difference in rosette inhibition between RAM and RPM was observed only for anti-RAM and not for anti-RPM sera. This seems to be due to a difference in the spatial relation of the antigens to the Fc-receptor.

Structural studies of human IgD. Denaturation of tFcδ on mild acid and heat treatment

R.JEFFERIS, J.B.MATTHEWS and P.BAYLEY*

Department of Experimental Pathology, University of Birmingham Medical School, Birmingham B15 2TJ; * National Institute for Medical Research, Mill Hill, London NW7.

Limited amino acid sequence studies indicate that IgD has more homology with IgE than the other immunoglobulin classes. We have investigated other physical and biological properties of IgD to investigate further possible similarities in behaviour. These studies include circular dichroic spectra of intact IgD and Fabδ and Fcδ fragments and mild acid and heat denaturation of the tFcδ fragment. Certain physical and structural features of IgD are shown to more closely parallel the behaviour of IgE than the other immunoglobulin classes.

Electron spin resonance spectroscopy (ESR) studies on antigen-antibody interactions

R.C.CONNOLLY*, N.S.HARGREAVES and L.H.SUTCLIFFE

Department of Anatomy*, and Department of Inorganic, Physical and Industrial Chemistry, Liverpool University.

Spin label studies on plasma proteins derived from both human and non-human sources have yielded characteristic spectra. Information on both the primary and quarternary structure of the proteins has been derived from incorporation and immobilisation spectra.

Complex-formation of these proteins with both homologous and cross-reacting antisera produce modifications to the label-spectra. Analysis of these and equivalent spectra of labelled complexes give information on the changes induced in the molecular environment by antibody-antigen interaction and the localisation of antibody attachment to the antigen molecule.

Antibody-facilitated digestion and the consequences of its failure

D.L.J.FREED and F.H.Y.GREEN

Department of Bacteriology and Virology, University of Manchester, Manchester, M13 9PT.

Many common foodstuffs are antigenic to the gut, but are nonetheless efficiently absorbed from it. We propose that the antibodies they stimulate, far from decreasing the uptake of antigenic foods, facilitate it, the small-intestinal epithelial cell acting in the manner of a macrophage. The theory has several implications, if true, for the aetiology of coeliac disease and several other gut affections, and also for their treatment.

Chromium release assay for measuring phagocytic killing of C.albicans

M.YAMAMURA, Jill BOLER and H.VALDIMARSSON

Department of Immunology, St Mary's Hospital Medical School, London W2 1PG.

Methods hitherto used for measuring candidacidal activity of leucocytes and serum depend on counting colony forming units on agar or microscopic evaluation of stained versus unstained organisms. In the first yeast clumping is a major problem, whilst the latter is liable to subjective errors. We have devised a technique in which the release of ^{51}chromium is used for measuring killing of C.albicans.

The amount of chromium released from the organisms correlates with their viability as determined by other methods. Standardization of the assay will be discussed and optimal conditions for its clinical application described.

The assay is objective, easy to perform and requires small amount of blood.

Objective method for measuring phagocytosis of C.albicans

M.YAMAMURA, Jill BOLER and H.VALDIMARSSON

Department of Immunology, St Mary's Hospital Medical School, London W2 1PG.

Yeast incorporates large amounts of uridine during the log phase of its growth. There is a linear relationship between yeast number and rate of uridine incorporation. However, yeast replicating within phagocytic cells in vitro does not take up uridine from culture medium. Neither do phagocytic cells incorporate significant amounts of uridine in short term cultures.

Inhibition of ^{3}H-uridine incorporation into yeast can therefore be used as an objective and sensitive index of phagocytic function. Standardization and suitable assay conditions for measuring phagocytosis of C.albicans will be described.

Application of enzymo-immunoassays (E.L.I.S.A.) to the serodiagnosis of human candidiasis and aspergillosis

M.HOMMEL*, D.E.BIDWELL** and T.T.KIEN***

* Liverpool School of Tropical Medicine; ** Nuffield Institute for Comparative Medicine, London; *** Laboratoire de Parasitologie, Strasbourg.

The application of ELISA to the serodiagnosis of aspergillosis using whole antigen and a purified fraction is described. A good correlation was observed with clinical information and with other serological techniques (Immunofluorescence and gel precipitation with demonstration of specific enzyme bands). In the case of candidiasis a satisfactory correlation was observed with other techniques, but the relation to disease is still difficult to assess. This new assay is a useful addition to the existing battery of serological techniques for the diagnosis of deep mycosis.

The effect of sensitised pig lymph node cells in reducing pulmonary metastasis formation in mice

Sarah PRICHARD-THOMAS and M.O.SYMES

Department of Surgery, University of Bristol.

Pulmonary metastases were produced in A-strain mice by intravenous injection of 1×10^{6} cells from A-strain mammary carcinomata. Their number was counted on day 14 following fixation of the lungs in Bouin's fluid.

Pig mesenteric lymph nodes were sensitised by implantation of fragments from the same tumours into the mesentery. Non sensitised nodes were obtained from disconnected portions of the same node chains.

Combination of tumour cells and sensitised pig cells in ratios of 1:10 and 1:60 prior to injection reduced the number of metastases observed 14 days later. Non sensitised cells were ineffective.

Treatment of mice with either type of pig cell 7 days after injection of tumour was ineffective.

However, if splenectomy was performed 1 day before injection of sensitised cells metastasis formation was reduced. Sensitisation against A-strain mouse tumour or skin was equally effective, but pig cells sensitised against a human colon carcinoma did not reduce metastases.

Non-specific immunity in mice infected with a variant of murine leukaemia (Friend)

Gillian A.HURST and K.E.K.ROWSON

Department of Pathology, Institute of Laryngology and Otology, 330 Gray's Inn Road, London WC1X 8EE.

Friend virus causes an erythroleukaemic in Balb/c mice. A variant of this virus produces an early acute phase which proves lethal one month post-infection, due to haemorrhage into the spleen.

Studies have been carried out on the non-specific immunity of infected mice and the effect of treatment to boost this. Corynebacterium parvum has been shown to stimulate macrophages. This organism also has an inhibitory effect upon the growth of some tumours in several species including mice. The effect of Corynebacterium upon the survival times of infected mice was looked at and it was found that there was no increase in survival of the treated mice as compared with untreated control animals. In vivo and in vitro tests of macrophage function in infected mice have been studied to see if there is any alteration of their activity in the early lethal phase in the disease caused by this strain of virus.

Cytolytic and cytostatic effector cells in alloimmune mice

B.JONES, Tina C.JONES and I.M.ROITT

Department of Immunology, Middlesex Hospital Medical School, London W1.

It is well established that T-cells arise in alloimmune mice with the ability to specifically lyse target cells of graft origin. The role of macrophages in cytotoxicity is more controversial. Whilst some workers report that macrophages can be armed specifically by soluble T-cell products (Lohmann-Matthes and Fischer, 1973), others fail to detect macrophage mediated activity in alloimmune mice (Brunner and Cerottini, 1971) or find that the factors are without immunological specificity (Pfizenmaier et al., 1975). The aim of the present study was to re-examine the alloimmune mouse to determine whether all the cytotoxic activity can be accounted for by T-cells.

In agreement with Brunner and Cerottini (1971) only effector T-cells could be detected in C57BL10 (H-2^b) mice immunized with the P815Y (H-2^d) mastocytoma using the ^{51}Cr-release assay for cytolysis. However, when cytostasis was measured using the ^{125}IUDr incorporation assay an additional population of T-independent adherent cells was revealed. Whilst the cytolytic T-cell was able to discriminate between the P815Y and EL4 (H-2^b) targets the T-independent population exerted activity against both targets. The question of whether this effector cell bears a receptor for antigen or whether it is non-specifically activated will be discussed.

Lohmann-Matthes, M.L. and Fischer, H. (1973) Transplant.Rev., 17, 150.

Brunner, K.T. and Cerottini, J.C. (1971) Progress in Immunology, 1, 385.

Pfizenmaier, K., Trostmann, H., Rollinghoff, M. and Wagner, H. (1975) Immunology, 29, 967.

The specificity of immunosuppression by alloantibody in the mouse

J.D.MILTON

Nuffield Unit of Medical Genetics, Department of Medicine, Liverpool University.

The ability of alloantibody to suppress the cytotoxic antibody response to alloantigens on lymph node cells was studied in relation to its specificity in two similar systems, one dependent on antibody only to some H-2 determinants on one haplotype and the other involving F1 cells with antibody directed against only one of the parental haplotypes. When CBA mice were immunised with C57 x DBA/2 F1 (CDF1) cells after treatment with CBA anti DBA/2 serum, which has some anti C57 cytotoxic activity, the cytotoxic antibody response to both C57 and DBA/2 was equally suppressed. Priming for a secondary response was also shown to be suppressed when the animals were immunised with CDF1 cells. When CBA mice were treated with C57 anti DBA/2 serum prior to immunisation with either CDF1 cells or mixed C57 and DBA/2 cells the antibody response to C57 cells was only suppressed when the antigenic determinants were presented on the same cells, namely on the CDF1 cells. These data suggest an afferent mechanism of antibody-mediated immunosuppression.

Immunoglobulins and immunodepression in trypanosomiasis in mice

M.J.CLARKSON

Department of Veterinary Parasitology, Liverpool School of Tropical Medicine.

It is well-known that trypanosomiasis in man and animals results in a marked increase in serum IgM concentration. Immuno-depression to injected antigens, such as sheep red blood cells, also occurs in trypanosomiasis. The mechanism of IgM production and immuno-depression is not clear though it is believed that these are linked phenomena.

Mice of several inbred strains were infected with Trypanosoma brucei and serum immunoglobulin concentrations measured for up to 6 weeks after infection. There were great differences in the IgM response from virtually no increase to a 16-fold increase. Immuno-depression to SRBC occurred and did not appear to be linked with increase in IgM concentration.

Aspects of immunity in children with protein energy malnutrition

B.HEYWORTH

Department of Paediatrics and Tropical Child Health, Liverpool School of Tropical Medicine.

Young Gambian children given B.C.G. convert, when tested with PPD, according to their nutrition state at the time of vaccination. Subsequent retesting 12 and 18 months later showed anergy not related to nutritional status.

Lymphocyte transformation to PHA in children with PEM did not show an inherent defect in lymphocyte function. When cultured with autologous plasma, depression of lymphocyte transformation occurred, particularly in children who died. There was no correlation with low albumin or transferrin. Children with PEM had increased jejunal microflora. Secretory component was low, particularly in Kwashiorkor and Marasmic-Kwashiorkor but not well correlated with high bacterial counts.

Chicken paraocular glands and local immunity

I.D.AITKEN and B.D.SURVASHE

Sub-Department of Avian Medicine, Liverpool University.

The inter-acinar areas of the major paraocular glands (Harderian and lachrymal) of the domestic fowl are infiltrated by plasma cells, most of which are IgA-containing. Secreted immunoglobulin enters the collecting tubules and passes via the draining ducts on to the ocular surface and thence to the nasal cavity and oropharynx. In experiments with Newcastle disease virus, ocular

but not systemic infection greatly augmented plasma cell numbers and gland extracts acquired specific virus-neutralizing activity. Despite the development of high serum antibody titres no neutralizing activity was detected in the diminished lachrymal flow of birds whose glands had been destroyed or removed. These findings imply that the paraocular glands are active in defence of oculo-nasal mucosae.

A consistent light to moderate infiltration of plasma cells has also been encountered in the paraocular glands of 9 mammalian species surveyed.

Response of the Harderian gland of the domestic fowl to ocular infection with Newcastle disease virus

J.R.POWELL and I.D.AITKEN

Sub-Department of Avian Medicine, Liverpool University.

Following infection of 6-week old SPF chickens by eye-drop with the lentogenic Hitchner B1 strain of NDV specific haemagglutinin-inhibiting and virus-neutralizing antibodies appeared in extracts of perfused Harderian glands. Analysis of samples collected over 4 weeks revealed a close correlation between Harderian gland and serum antibody responses, each peaking on day 18. The early Harderian gland antibody accumulation phase was dose-dependent and, with a standard infecting dose, only minor differences were seen in birds aged 6, 12 and 18 weeks.

After a primary exposure at 6 weeks a second ocular infection at 10 weeks reactivated the Harderian gland response in a dose-dependent manner. Reinfection by the intramuscular or intravenous route did not affect Harderian gland antibody titre. Ocular reinfections up to 10^6 EID_{50} were apparently contained at the oculo-nasal level, but 10^8 EID_{50} resulted in systemic spread of virus.

Reaginic antibodies on basophils and mast cells demonstrated by a bead rosette test

R.AUGUSTIN*, N.ALAYE** and M.KING***

* Sub-Department of Immunology, Liverpool University; ** Instituto de Alergia e Immunologia, Universidad Nacional de Cordoba, Argentine; *** Department of Bacteriology, University of Sydney, Australia.

Particularized grass pollen allergen was prepared by covalent coupling of Dactylis glomerata protein concentrate to Sepharose beads. Human basophils were purified by gradient centrifugation and differential glass bead adherence and rat mast cells by gradient centrifugation.

Basophils from pollen allergic subjects rosetted around the allergen-coated bead surface by moulding to it in a manner so highly characteristic that false negatives were not encountered. Mast cells from rats sensitized with egg albumin (Ea) and B.pertussis and then reagin-potentiated by infection with N.brasiliensis interacted similarly with Ea-coated beads and there was no cross reactivity between the two systems. The obviously multivalent attachment of the basophils (mast cells) to the beads endorses visually the previously postulated requirements of receptor bridging as a condition for anaphylactic histamine release.

Histamine and white blood cells in severe acute asthma

A.SEATON*, S.J.WILLIAMS*, W.H.TAYLOR** and C.BRUCE**

* Asthma Research Unit, Sully Hospital, Penarth, Glamorganshire and ** Royal Infirmary, Liverpool.

Blood and plasma histamine and eosinophil and basophil counts were measured in control patients without chest disease and in 10 patients with severe acute asthma before and after high dose intravenous cortisone.

A simple device for deriving nasal airflow resistance

L.H.CAPEL

London Chest Hospital

Nasal airways resistance has been estimated and measured in many ways. It is now conventional to measure it from a simultaneous recording of post nasal pressure measured from the mouth and nasal airflow rate measured from a pneumotachometer, as proposed by J.C.Lilly in 1950. The original method of recording was from a slope recorded on an oscilloscope, with the coordinates of airflow rate and mouth pressure. A simple apparatus for deriving nasal airways resistance from the mouth pressure required to achieve a preset nasal airflow rate is discussed, and some practical applications in nasal disorder with airways narrowing.

Allergy to experimental animals amongst laboratory workers

A.NEWMAN-TAYLOR, Joan L.LONGBOTTOM and J.PEPYS

Department of Clinical Immunology, Cardiothoracic Institute, Brompton, London SW3.

Sensitivity to laboratory animals has been reported in more than 10% of those workers regularly handling them. We have investigated five laboratory workers, all of whom were exposed to rats and four of whom were exposed to mice. Inhalation testing with rat urine extract provoked an immediate reaction in all five; mouse urine extract provoked a similar reaction in the four exposed at work, but no reaction in the unexposed subject. Inhalation of rat serum provoked an immediate asthmatic reaction in three of the five workers; of mouse serum provoked a similar reaction in only one of the three tested.

A closer correlation of RAST's to specific animal exposure and inhalation test reactions was obtained with rat urine in five and mouse urine in four of the subjects than with rat or mouse serum.

Immunoelectrophoretic analysis of the mouse and rat urinary protein preparations, using rabbit antisera to both the sera and urine of each animal species showed the major component of the mouse urine to be a fast moving pre-albumin (not derived from serum) with several other distinct urinary proteins and trace amounts of serum protein also present. By comparison, the major urinary component of rat urine has an α-globulin mobility and is antigenically similar to a minor component found in mouse, but not in rabbit or guinea pig urine. Other specific urinary components are present in the rat as well as quite large amounts, varying with age and sex, of serum proteins.

These results suggest that the urine of rats and mice is an important source of the antigens responsible for sensitising those regularly handling experimental animals; these urinary antigens are not necessarily derived from the serum.

Steroid aerosols and oropharyngeal candidiasis

S.M.HARDING

Clinical Division, Glaxo Research Limited, Greenford, Middlesex UB6 0HE.

Candida albicans is frequently found in the oropharynx, but infections with this organism are rare in the healthy child or adult. With the use of steroid aerosols for asthma oropharyngeal candidiasis occurs in about 8% of adult patients, but further cases may go undetected since the condition is usually asymptomatic. The incidence of such infection seems greatest within the first three months of therapy and is related to the dose administered and to the topical activity of the steroid used. The wearing of dentures or related poor oral hygiene are probably the most significant predisposing factors in adults; this may explain why the incidence is far lower in children.

Although C. albicans may spread to the larynx, colonization of respiratory epithelium is uncommon. Hence, pulmonary infection is very rare and usually associated with obvious predisposing factors. No cases of pulmonary fungal infections have been reported following the use of steroid aerosols in a large number of patients over several years.

Treatment with a topical antifungal agent quickly clears oropharyngeal candidiasis, and a reduction in steroid aerosol dosage is recommended. Prophylactic measures to prevent infection are theoretically possible.

Asthma and aspirin-idiosyncrasy

J.C.DELANEY

Sefton General Hospital, Liverpool.

The clinical features of 50 patients with asthma and aspirin-idiosyncrasy are presented.

Only trace amounts of serum PGE_2 and $PGF_{2\alpha}$ were present during asthmatic attacks induced by aspirin challenge in 7 patients.

Measurements of circulating IgE, total haemolytic complement, and components C_4 and C_3 in 16 patients revealed IgE levels within normal limits and no differences in the complement levels between patients in this group and matched controls.

Alkalase - the end of the story?

M.L.H.FLINDT

Department of Occupational Health, University of Manchester.

Developments since the initial publication concerning respiratory illness in enzyme detergent workers will be reviewed and examples given of patterns of responses in affected individuals.