BRITISH ASSOCIATION OF DERMATOLOGY.

FORTY-FIFTH ANNUAL MEETING.

THE Forty-fifth Annual Meeting of the Association was held in Bristol on 8, 9 and 10 July 1965 under the Presidency of Dr. Clifford Evans. The business and scientific meetings were held in the auditorium of the newly built Medical School. The following Executive Committee was elected to serve during 1965–66.

President	Dr. H. R. Vickers
Immediate Past President	Dr. Clifford Evans
Vice-President	Dr. R. M. B. MacKenna
Hon. Treasurer	Prof. J. T. Ingram
Hon. Secretary	Dr. S. C. Gold
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Dr. M. Feiwel	Dr. J. S. Pegum	Dr. O. L. S. Scott
Dr. P. W. Hannay	Dr. E. Ritter	Dr. E. Waddington

Professor J. T. Ingram was elected an Honorary Member. Dr. P. de Graciansky (France), Prof. F. Latapi (Mexico) and Dr. F. Sagher (Israel) were made Honorary Foreign Members. The election of Drs. T. Allen and K. Georgouras (New South Wales) as Overseas Members was confirmed as was the election of the following as Ordinary Members.

Dr. J. O'D. Alexander	Dr. C. F. H. Vickers
Dr. H. W. Chadfield	Dr. J. F. Wilkinson
Dr. A. F. McKenzie	Dr. E. Wilson Jones

It was resolved that the B.A.D. Scholarship should be called the Dowling Fellowship. It was announced that the Gray Medal for outstanding service to British Dermatology had been awarded to the retiring Secretary, Dr. D. I. Williams. The meeting also decided that from January 1966 the annual subscription to the Association should be £2 and to the Journal £5. The next Annual Meeting will be held in Oxford, combined with the Anglo-French Reunion, on 20–23 July, 1966 : living accommodation will be available at Lady Margaret Hall.

Summaries of the papers read appear in this issue. The clinical cases were seen in the Outpatient Department of Southmeads Hospital, an illustrated brochure being available. The President and Mrs. Evans held a reception for members and guests in the Senate House of Bristol University. The social programme also included a visit to Clifton Zoo, an expedition to Berkeley

Castle and a dinner at the Royal Hotel attended by about 180 people. The Dowling-McCaw Cup was won for the third year in succession by Dr. Eric Waddington and the Bowers-Sneddon Trophy by Dr. Carslaw.

The Association is grateful to Dr. Evans, Dr. Warin and Dr. Harman (Local Secretary) for an excellently organized meeting, urbane yet exciting like Bristol itself.

Summaries of Papers.

(Those marked with an asterisk will be subsequently published in full.)

Degranulation of Mast Cells.—G. I. Horsfield (M.R.C., Birmingham).

The changes occurring in rat peritoneal mast cells during the action of five histamine-releasing reagents have been studied by cine-photomicrography and electron microscopy. Compound 48/80, rabbit anti-rat gamma globulin serum, and horse serum on cells from sensitized animals, produce degranulation but the antihistamine, promethazine hydrochloride, and the antiheparin, protamine sulphate, do not produce degranulation.

The response of mast cells to the degranulating agents is characterized by the formation of large vacuoles within the cell, pores in the surface membrane, and by the discharge of granules *via* these pores. The large vacuoles are formed by the fusion of numerous small vacuoles around individual granules. Electron microscopy has shown that the membranes around individual granules fuse together forming a membrane bounding the cytoplasm and continuous with the outer cell membrane at the edges of the pores. During the action of Compound 48/80, three phases can be recognized : a lag phase lasting 1 second, a phase of vacuolation and pore formation lasting 4 seconds, and a phase of degranulation lasting 20 minutes. During the antigen-antibody reactions the lag phase is prolonged for at least 30 seconds and the second and third phases occur concurrently. However, despite these differences in timing, the morphological changes which occur are essentially the same in all three cases.

The addition of promethazine hydrochloride produces an immediate swelling of the cell with the formation of a few vacuoles. 30 seconds later there is a sudden alteration in refractility of the granules which can be attributed to cell death and fixation. High concentrations of protamine sulphate have a similar effect but the successive addition of low concentrations (0·1 mg./ml.) produces a progressive increase in the number of vacuoles around individual granules accompanied by swelling and finally rupture of the cell.

When degranulation occurs, and also when vacuolation is produced by promethazine hydrochloride, the electron microscopic appearances of the individual granules are changed from the normal pattern of densely packed fibrils and particles to an open network of fibres. From these studies it would appear likely that vacuolation of the cell and the electron microscopic changes in the granules are associated with histamine release and that degranulation is not essential for histamine release.

*Lymphoblast in Transformation in Sulphonamide Sensitivity.**—G. A. Caron and I. Sarkany (Royal Free Hospital, London).

Peripheral leucocytes maintained in tissue culture are transformed into blast cells with the capacity to undergo mitosis by the addition of phytohaemagglutinin and to a lesser degree by substances to which the leucocyte donor is sensitive, such as vaccinia virus and old tuberculin.

We have now demonstrated that this transformation depends on the lymphocytes themselves and not on any plasma factors. We have used this method in an investigation of a patient with sulphonamide sensitivity and have shown lymphoblast

transformation of the patient's lymphocytes in the presence of soluble sulphonamide. After six days' incubation the percentage of transformation was 7% in the sulphonamide sensitive patient compared with no transformation in two control subjects. Confirmation of the degree of blast transformation was obtained by autoradiography using triated thymidine. Other antigens, such as tuberculin and vaccinia virus produce lymphoblast transformation of a similar order.

*Investigation of Nodular Vasculitis by Means of the Fluorescent Antibody Technique.**—W. E. PARISH and E. L. RHODES (King's College Hospital, London).

Biopsy specimens of nine cases of nodular vasculitis were examined for gammaglobulin using the fluorescent labelled antibody technique. Gammaglobulin was found in and around the vessel walls of two patients only, one of whom had developed her leg lesions two weeks after a quinsy.

The nine cases were then examined for streptococcal complexes with rabbit antistreptococcal serum of both group A and group D streptococci, tracing any fixation of this serum with a fluorescent labelled goat anti-rabbit serum.

Fluorescence with the streptococcal group A antigen was found only in the section of the patient who had had a quinsy and then in the areas where gammaglobulin had previously been found. Sections were also examined for tubercle antigen using rabbit anti-human tubercle serum and tracing fixation with fluorescent goat anti-rabbit serum. Specific fluorescence indicating tubercle antigen was found in the sections from two patients—both of whom had active tuberculous glands in their necks.

The lesions on the legs in all nine patients looked very similar.

Mitogenic Effect of Phytohaemagglutinin on Human Skin in Organ Culture and Guinea-pig Skin in vivo.*—I. SARKANY and G. A. CARON (Royal Free Hospital, London).

It is established that phytohaemagglutinin (PHA) has a mitogenic effect on peripheral lymphocytes in tissue culture. However, there are no reports of the effect of PHA on epithelial cells.

Using Colcemid to arrest mitotic division, we have shown that PHA stimulates mitosis in epithelial cells of adult human skin in organ culture. After four days' incubation, up to 23% of basal cells showed mitotic figures. This mitogenic effect was confirmed by autoradiography which showed the incorporation of tritiated thymidine into a high proportion of the basal cells. This compared strikingly with control cultures in which only occasional mitoses were seen.

Following injection of PHA into the skin of guinea-pigs, a similar increase in mitotic activity of the epidermis occurred. This lead to a striking degree of acanthosis which was proportional to the dose of PHA.

The mechanism of action of PHA is discussed in the light of these observations.

*A Brief Review of Some Conditions Affecting the Hair, up to the 17th Century.**—BETHEL SOLOMONS (Chelmsford and Essex County Hospital).

The historical background was outlined, and followed by descriptions of alopecia, hirsuties, pili incarnati, tinea capitis, hair-dyeing, and the first use of the microscope in studying the hair.

Literary references were made to Assyrian medical texts, the views of Hippocrates, Galen, Mercuria, Naldius, Paré, Hooke, and other worthies.

Electron Microscopy of Pre-terminal Nerve Fibres in Vitiliginous Skin.—A. S. BREATHNACH, S. BOR and L. M.-A. WYLLIE (St. Mary's Hospital Medical School, London).

The fact that the lesions in vitiligo appear to have a dermatomal distribution, or to be limited to the area supplied by individual cutaneous nerves, suggests that the

condition may be due to some disturbance of a normal nervous control of melanogenesis. This is a view which is widely held, and in apparent confirmation, some workers using light microscopic techniques claim to have discovered dystrophic changes in nerve fibres supplying depigmented areas in vitiligo. However, these techniques have been criticized on the ground that artifacts of preparation may mimic pathological changes, and be interpreted as such. The preparative techniques employed for electron microscopy are known to involve much less distortion of tissues.

Skin from six subjects with vitiligo was examined, and biopsy specimens were taken from the centres of lesions of varying duration, as well as from marginal areas, both pigmented and non-pigmented. The great majority of pre-terminal nervous elements encountered in this material appeared essentially normal. What might be described as degenerative changes of minimal degree were seen in marginal areas of some lesions, but it seems doubtful that they could be sufficient to account for the fundamental morphological and functional changes in the melanocytes.

The Direction of Epithelial Growth.—Dr. T. J. RYAN (Radcliffe Infirmary, Oxford).

The terms " outward migration ", " movement outwards " and " pushed outwards " are frequently applied to epidermal cells in explanation of their exfoliation.

The forces promoting the growth and organization of the epidermis emanate from the dermis and the epidermal cell provides little to encourage its own survival. The term " migration outwards " implies that the cell directs itself away from such forces which is unlike cell behaviour in general.

It is suggested that the epidermal cell strives habitually to preserve contact with its source of nourishment and " chief promotor " and that " movement outwards " is due to separation of cells from the dermis by more fortunate cells jostling themselves into a position of optimal nourishment; thus deprived, the separated cells degenerate.

Inward growth may lead to the passive inclusion of dermal constituents within the epidermis and during a proliferative phase cells undergoing mitosis tend to be left behind the advancing basal cells and are found at a higher level in the prickle-cell layer.

Epidermal cells grow in the direction of their blood supply throughout life, as in embryo. Thus the direction of nail growth should be viewed as proximal towards the horizontally disposed vessels.

Skin Window Study of Inflammation in Psoriasis and Lichen Planus.—R. R. M. HARMAN (Bristol United Hospitals).

A new method of studying leucocyte functions *in vivo* was described by J. W. Rebuck and J. H. Crowley in 1955[1]. Here this technique has been applied to examine the cytology of inflammation caused by trauma. Skin studied has been in a group of control patients, in psoriatic plaques and in uninvolved skin of psoriatic inpatients, and in a small number of subjects with widespread lichen planus.

Cover-slip preparations of inflammatory cells were gathered at 3, 6, 9, 12, 24, 36 and 48 hours from the test sites. These were stained by the May-Gruenwald-Giemsa method, mounted as permanent preparations and differential counts of the cell types were made.

In the control group an almost exclusively neutrophil migration occurred first and slowly gave way to an inflex of mononuclear cells which predominated 24 hours after trauma. In the apparently normal skin of psoriatics, migration of identical cells occurred but to a different timetable. The mononuclear influx was more rapid and this cell type predominated 9 hours after the trauma. In psoriatic plaques a similar pattern was found. In uninvolved skin of patients with lichen planus, no departure from the normal occurred.

These results support the work of Holti,[2] Ross,[3] Weddell *et al.*,[4] and others and point to an abnormality of " normal " skin in psoriasis.

REFERENCES.

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2. HOLTI, G. (1964) *Brit. J. Derm.*, **76**, 503.
3. Ross, J. B. (1964) *Brit. J. Derm.*, 511.
4. WEDDELL, G., COWAN, M. A., PALMER, E., and RAMASWAMY, S. (1965) *Arch Derm.*, **91**, 252.

Small Bowel Disease in Rosacea.—W. C. WATSON, ESTHER PATON and D. MURRAY (Glasgow Royal Infirmary).

Small bowel histology, serum alkaline phosphatase, calcium, phosphorus and protein levels, and blood groups were investigated in 60 patients with rosacea. Weights were compared with a control group attending at the same clinic. Detailed clinical and family histories were taken.

The jejunal biopsies were graded by carefully selected criteria into 5 groups, ranging from normal (1), through provisionally normal (2 and 3) to frankly abnormal (4 and 5). Thirty-three per cent of the biopsies were in groups 4 and 5. At least 4 of these patients have adult coeliac disease. Thirty-seven per cent are more than 14 pounds below their expected average weight, and the group as a whole is significantly lighter than the control group. Twenty-seven per cent had a history of chronic intermittent diarrhoea, and 57% of dyspepsia. There were family histories of rosacea, pernicious anaemia and coeliac disease.

Additional data were presented and certain aetiological considerations discussed. We believe that rosacea is a systemic, and perhaps hereditary, disease.

(This paper has appeared in full in *Lancet*, ii, 47 1965.)

*The Influence of Vehicles, Solvents and Particle Size on Percutaneous Absorption of Corticosteroids.**—I. SARKANY, J. W. HADGRAFT, C. W. BARRETT and G. A. CARON (Royal Free Hospital, London).

Using a new quantitative method for application of ointment to the skin, we have studied the role of vehicles in skin penetration. The influence of the four main types of vehicles in general use was investigated by observing the vasodilatation produced by methyl nicotinate and by assessing the vasoconstriction produced by fluorinated steroids.

The absorption of these marker substances was affected by the type of vehicle. Fluocinolone acetonide and betamethasone-17-valerate differed markedly in their absorption from macrogol ointment. We screened the effect on topical steroid absorption of a series of solvents including tetrahydrofurfuryl alcohol, acetdimethylamide and dimethyl sulphoxide. By altering the vehicle for hydrocortisone alcohol and acetate their vasoconstrictive properties were strikingly increased but the clinical efficacy was only partially improved.

A study of micronised fluocinolone acetonide showed that reducing the particle size enhanced the vasoconstrictive and clinical efficacy. This could be further improved by incorporating propylene glycol in the vehicle.

*Intermittent Infusion of Low Molecular Dextran in the Treatment of Systemic Sclerosis.**—G. HOLTI (Royal Victoria Infirmary, Newcastle upon Tyne).

Twelve patients with systemic sclerosis and seven patients with Raynaud's phenomenon of late onset were treated by intravenous low molecular dextran (Rheomacrodex) at intervals of 5–8 weeks during the winter. The majority of these patients showed a very satisfactory and long lasting improvement of their advanced digital ischaemic changes. Their improved blood flow was measured at varying intervals after treatment by skin thermometry under set experimental conditions. Two litres of Rheomacrodex were given during 48 hours at each treatment. No undue side effects were observed.

It is suggested that the beneficial effect of Rheomacrodex upon the skin circulation is due to its ability to reduce intravascular cell aggregation, to lower blood viscosity

and to increase capillary flow and tissue perfusion. Its long lasting effect may be related to its ability to adhere firmly to circulating red cells and to vessels with intimal damage.

Some Recent Observations on the Presentation, Behaviour and Pathology of Malignant Melanomas.—D. C. BODENHAM and O. C. LLOYD (Frenchay Hospital, Bristol).

A continuous study during the last 18 years of a consecutive series of 483 malignant melanomas treated by the same team has resulted in a clearer picture of the pattern of the disease and led to a more rational approach to management.

There has been a 3/1 female overall predominance, but on the lower limb it is 11/1 with a peak age incidence of 40–45 years, on the face the peak is in the 70–80 age group.

Pregnancy has been studied in 20 cases of malignant melanoma, although it will require a large number of cases to be studied over a long period for any absolute conclusions to be drawn, there is no evidence in those cases so far studied that the pattern and prognosis of the disease is affected to a material extent.

The disease is progressive and prognosis is closely related to the stage at which treatment is carried out.

Stage I	Pre-invasive	100%	5-year survival.
Stage II	Early invasion of dermis	97%	5-year survival.
Stage III	Without obvious invasion of dermal lymphatics	65%	5-year survival.
Stage IV	With obvious invasion of dermal lymphatics	38%	5-year survival.

Prognosis for lesions affecting the leg and the face is more favourable than elsewhere, and females have a 10% advantage over males for five-year survival. Five-year survival rate for all treated cases is 52% and the ten year is 43%. Records show that the early lesion is often overlooked and the possibility of a " cure " thereby lessened.

Primary treatment is based on wide local excision and grafting. Trauma of any sort worsens prognosis, incisional biopsy is contra-indicated. If in doubt the diagnosis should be confirmed by excision and frozen section. The pathologist is an essential member of the surgical team, his report should confirm the adequacy of the excision or indicate further surgery and give a valuable guide to the prognosis of a particular case.

Many patients who are alive at five or more years have developed repeated recurrences, each one or group having been treated by further wide excision and in several instances have remained free of disease three and more years later. Treatment by chemotherapy and routine radiotherapeutic methods has proved disappointing, but similar methods used selectively at periods of natural or induced cyclical activity of the tumour, as shown by the P^{32} uptake tests developed in the Radiotherapy Department in Bristol, have shown a more favourable response. Treatment by endolymphatic injection of radioactive substances is not yet proven but may lead to improvement in the results in those early cases, involving a limb which have not developed lymphatic obstruction due to lymph node metastases.

Local excision with a margin of 5–15 cm. around the lesion must remain the basis of treatment for the forseeable future.

Basal-cell Carcinoma Survey : Combined Clinic 1959–64.*—D. I. MACCALLUM and P. D. C. KINMONT (Nottingham and Derby).

A combined clinic was established in the Nottingham–Derby area in August 1959, for discussion of problems of mutual interest to the dermatologist, radiotherapist, plastic surgeon and histopathologist and their junior staffs. Basal-cell carcinomata referred in the early days were mainly those that had recurred after previous treat-

ment, or those that were referred because of complication with regard to size, site or were referred because of complication with regard to size, site or multiplicity of the lesions. Since then the trend has been for more basal-cell carcinomata to be referred each year, and in 1964 the number referred was 222.

Various types of treatment have been prescribed during this 5½-year period. A recent check showed that the recurrence (failure) rate was 4·8% in a group of 617 patients with 728 basal-cell carcinomata. An analysis of data available on these cases has been undertaken, to determine why the recurrence rate has been so high, and to see what can be done to reduce it.

*Treatment of Rodent Ulcers by Curettage and Cauterization.**—J. R. SIMPSON (Royal Devon and Exeter Hospital).

In the past twelve years 495 histologically confirmed rodent ulcers have been treated by this method and followed up for at least two years. On these 35 have recurred, 23 (66%) within two years and three more than five years after treatment. The recurrence rate of 7% needs correction to allow for an expected increased by one-third for the cases followed up for less than five years but is still less than 10%. Of these 35 recurrences 22 have been treated again by the same method with no further incident, of which 15 have been followed for another two years. Only 13 have been referred for other treatment. No relationship was found between recurrence and the size of the lesion or its site, duration before treatment or its clinical or histological type.

This method saves time and trouble to all concerned and is suitable for all lesions up to one inch in diameter, except the morphoeic type or those where excision and primary suture are feasible. The post-operative discomfort is less than after radiotherapy and the cosmetic results compare favourably with those of any other method.

The Use of Indwelling Geiger Counters to Study and Manage certain Human Tumours.—B. HALE (United Bristol Hospitals).

The progress of combined research with Dr. R. C. Tudway and Mr. M. A. Bullen of the Departments of Radiotherapy and Medical Physics, United Bristol Hospitals was reported.

Phosphorus plays an important role in cell metabolism. Radiophosphorus is taken up by tumours in an amount proportional to the rate of growth. Miniature Geiger counters are inserted under anaesthetic into actively growing areas of tumour. Seven hundred and fifty microcuries of radiophosphorus is given by mouth and the concentration in the tumour is recorded continuously for prolonged periods of days or weeks if necessary. The duration depends on the information sought and the response obtained. The technique is used :

(i) To detect hormone sensitive breast cancer prior to hormone depriving surgery or hormone therapy.
(ii) To detect hormone sensitive multiple malignant melanomas.
(iii) To artificially induce a false growth pattern in tumours with drugs or radiation and then select the optimum point for treatment with radiation or cytotoxic agents.

Results to date :

(i) *Breast cancer hormone sensitivity prediction :*
100 consecutive cases 87 correct, 4 incorrect, 9 equivocal tracings.
(ii) *Multiple malignant melanomas :*
46 cases, 8 hormone sensitive, 29 not sensitive, 9 equivocal.
(iii) *Gliomas :*
17 cases. Good initial response (3–18 months clear of symptoms) 8, poor response 9.

(iv) *Response in normally radio-resistance tumours :*
Carcinoma of stomach and pancreas : 26 cases. Good local response 16, no response 10.
Connective tissue sarcomas :
18 cases. Good local response 12.

Fifty-six out of 77 tumours normally radio-resistant, showed marked response when treated using the Geiger probe technique to select the optimum time for therapy.

Light, Time and Lack of Pigment in the Aetiology of Dermal Elastosis and Skin Cancer.—Dr. S. M. MURRAY and Dr. R. D. SWEET (formerly at University College Hospital, Jamaica).

From a series of 50 post mortems on Jamaican nationals of both sexes, of varying ages, and with skin colours ranging from white to black, skin was taken from lateral buttock, back of hand and face. The basic skin colour was assessed, using buttock skin, and the degree of elastotic degeneration of the dermis was determined histologically in each specimen.

A significant correlation was found between the total amount of light reaching skin of face and back of hand (a function of age and degree of pigmentation) and elastotic degeneration. None of the buttock skin sections showed this degeneration.

The investigation confirmed that elastotic degeneration was not primarily an age induced change, but a result of exposure of skin to light, and that epidermal melanin had a protective effect.

The relationship between elastotic degeneration and pre-malginant change in the epidermis was also considered.

*The Natural History of Skin Malignancy.**—I. W. WHIMSTER (St. Thomas's Hospital Medical School, London).

Skin cancers can be divided into four groups according to the natural history of their origin.

(i) Origin from skin which is atrophic, e.g. scars of lupus, thermal burns, lichen sclerosus of genital skin.
(ii) Origin from skin which has previously undergone localized abnormal growth of developmental type to form a naevus, hamartoma or benign tumour, e.g. melanomas arising from moles.
(iii) Origin from skin which has been subjected to special exogenous carcinogenic agents, e.g. hydrocarbons, U.V.R., etc.
(iv) A small group whose natural history is unknown, e.g. Bowen's disease, erythroplasia etc.

This paper is concerned with an attempt to find an experimental approach to the first two types of carcinogenic natural history.

Atrophy.—

Examples shown : Atrophic L.V. scar and vulval lichen sclerosus, both of which had progressed to malignancy.

Problem : What is the nature and cause of atrophy?

Experiment : Atrophic and cancer-prone skin (lichen sclerosus and leukoplakia) excised from the vulva and transplanted on to the thigh subsequently became normal. Normal skin from the thigh grafted on to the vulvectomy wound subsequently developed lichen sclerosus.

Conclusion : Cancer-prone atrophy can be a reversible change imposed upon skin by extracutaneous factors emanating from the site it occupies.

Naevoid abnormality.—

Example shown : An extensive naevus sebaceus (Jadassohn) in which multiple basal-cell carcinomas arose at the age of 60.

Problem : To understand the nature and cause of cancer-prone naevoid abnormality affecting skin appendages it is necessary first to determine what initiates and controls normal appendage development.

Experiment : The model used was a toad (*Bufo marinus*) in which the dorsal skin and the ventral skin show very conspicuous differences in their appendages. When areas of dorsal and ventral skin are excised full thickness new skin forms by marginal regeneration and subsequently develops new appendages of dorsal and ventral type respectively. When an area of ventral skin has been transplanted on to the dorsum and its central part is subsequently excised an area of new skin regenerates into a dorsal site from marginal tissues which are of ventral origin. This regenerated skin develops new appendages of dorsal type.

Conclusion : The type of growth and differentiation shown by regenerating skin appendages in this animal is not determined by the quality of the marginal tissues from which regeneration has occurred but by some extracutaneous factor emanating from the site into which the new tissue regenerates.

Prospect.—

By pursuing this type of experimentation it should become possible to identify the precise nature of the following factors.

(i) Those responsible for normal skin maintenance and repair and whose failure may be the cause of atrophy.
(ii) Those which control the initiation and development of appendages and whose dysfunction may be the cause of naevoid maldevelopment.

There may even be some relationship between the two.