THE SAGO GRAIN VESICLE

History, Aetiology

and

Histopathology

THESIS

presented for the Degree of

Doctor of Medicine

by

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PREFACE

The thesis is presented in two volumes. Volume 1 consists of the script and Volume 2 of photographic plates.

The plates to which reference is made in Volume 1 are found in Volume 2, the page numbers of which correspond to the plate numbers.

The microscopic sections utilised for the purpose of the histopathological investigation are found in slide boxes 1 and 2. They consist of serial and isolated sections.

Each slide is labelled to correspond to the biopsy and case number. The slides of serial sections are, in addition, numbered in sequence. On the average, ten serial sections are mounted on each slide, the section number being determined by counting from the labelled end.

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PURPOSE OF THESIS

Following a survey of the literature on the sago grain vesicular eruptions of the hands and feet, it was evident that although much investigation had already been carried out certain fields for further study still lay open.

Since Tilbury Fox (1873) first described such an eruption under the title "dysidrosis" numerous aetiological theories have become generally accepted. Most published findings have been deduced from the study of groups of selected cases and whereas they provide valuable information regarding causal or associated factors they present little insight into the relative frequency with which these factors operate in sago grain vesicular eruptions as a whole. Original data on this subject would appear to be provided chiefly by the valuable work of McLachlan and Brown (1934) and by that of Davidson and Birt (1943).

From the time of Fox until the present day numerous authorities have at all times believed that sago grain vesicles arise or might arise as a result of the retention of sweat in the sweat ducts, e.g. T. Fox (1873), Crocker (1878), Duhring (1881), Pusey (1917), Sicoli (1924), McCarthy (1931), Sulzberger and Baer (1948).

Those who have been opposed to the sweat retention theory have almost unanimously supported an eczematous origin, e.g. W. Williams (1891), Peck (1930), McLachlan and Brown (1934) and Percival (1947).

In view of the apparent lack of data relating to the frequency

with which various aetiological factors operate in sago grain vesicular eruptions, I considered it worth while to collect clinical data which would indicate their relative incidence and which might bring to light other aetiological factors having some bearing on further understanding of the subject.

Furthermore investigations were directed to determine the nature and origin of the lesions and their relationship, if any, to the sudoriparous apparatus because of the existing diversity of opinion in these respects.

The thesis which will now follow consists of three parts and three appendices:-

PART 1. HISTORICAL REVIEW OF THE SAGO GRAIN VESICULAR ERUPTIONS OF THE HANDS AND FEET

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PART 1

HISTORICAL REVIEW OF THE SAGO GRAIN VESICULAR ERUPTIONS OF THE HANDS AND FEET

Tilbury Fox (1873) gave the first account of a skin affection of the hands associated with palmar hyperidrosis and consisting of vesicles, not unlike boiled sago grains embedded in the skin which usually ran a distinctive and self-limiting course, but sometimes became chronic. He endeavoured to establish this condition as an entity and called it "dysidrosis", signifying "difficult sweating".

Great controversy arose regarding the priority of description when Jonathan Hutchinson (1876), in a clinical lecture, described an identical condition and called it "cheiropompholyx". The lecture was reported to have been written out in 1871, but only published for the first time in 1876. Fox, in the ensuing correspondence in the British Medical Journal and the Lancet, then claimed to have recognised the condition before 1871, having since that time repeatedly pointed it out to his students. On the other hand Hutchinson endeavoured to prove that he had recognised the disease as early as 1864, having in that year had a portrait made of a case which had only been seen for the first time by Fox in 1871 and from which the latter had gained his first impressions of the condition which he called "dysidrosis". The salient differences in both accounts lie in their respective appellations, viz. the "dysidrosis" of Fox with its dogmatic pathological implication and the "cheiro-pompholyx" of Hutchinson and its purely descriptive character. The

controversy is best summed up in the words of Thin (1877) who remarked that "to Mr Hutchinson, therefore, belongs, in my opinion, the merit as far as the published evidence goes of having first recognised that there is a distinct and previously undescribed vesicular or bullous disease chiefly attacking the hands. To Dr. Tilbury Fox belongs the merit of having, at a later date, satisfied himself independantly of the existence of the same disease and of being the first to publish an account of it which was accessible to the medical profession".

From the debate on priority of discovery arose the more substantial one on aetiology and writers on the topic arrayed themselves by the side of Fox and endeavoured to support his claim that the condition was caused "essentially by retention in the follicles of the skin, of sweat rapidly and freely secreted" or on that of Hutchinson who maintained that there was not the slightest fragment of evidence to support that the condition was a "dysidrosis".

A.R. Robinson (1877) of New York joined in the study of the subject. Biochemically he claimed to have refuted the dysidrotic theory by demonstrating that the vesicular fluid was alkaline or neutral and never acid and reacted with nitric acid, producing an albuminous coagulum in the proportions obtained in serum. He substantiated his anti-dysidrotic conclusion by pathological investigation claiming, that, though the condition had no connection with the sweat apparatus, it was a histopathological entity. In 1885

he stated that in his opinion the disease was a neurosis, having an origin similar to herpes progenitalis and not a "catarrhal inflammation" like eczema. At one time the term pompholyx had been an old name for pemphigus, but Robinson considered that it had fallen into sufficient disuse as not to create confusion when applied to a recently described sago grain vesicular disease affecting the hands and feet. He, therefore, decided to discard the prefix "cheiro" and called the disease "pompholyx" - a term which did not imply restriction to the hands.

Following Robinson's findings, Radcliffe Crocker (1877) remarked that Fox, with whom he worked in close collaboration, had pointed out, that, if sago grain vesicles were examined in the early stages when there was only sufficient fluid to make a dark circle without sensibly elevating the cuticle, the orifice of the sweat pore might be seen, with the aid of a lens, to occupy the centre of that circle. It would appear that this phenomenon which at first impression seemed a self-evident demonstration of sweat retention was the only tangible finding Fox possessed in support of his conviction and furthermore there is indication that his histological work, which will be recorded later, was undertaken in an endeavour to corroborate this pre-conceived idea. There is also a suggestion that the original exponent of the dysidrotic theory to some extent had modified his opinion, probably in the light of the biochemical findings of A.R. Robinson which prompted Crocker, Fox's chief

protagonist, to remark, "I do not believe nor do I think does Dr. Fox consider that it (sago grain vesicle) is simply a retention of sweat". Certainly Crocker had changed his mind and in 1893 he remarked that the condition was due to an inflammation in and about the sweat apparatus, but not essentially a lesion of it.

About this time investigations to some extent fell into abeyance, until Winkelreid Williams (1891) published his findings from the examination of two hundred and twenty-nine sections prepared from three specimens of sago grain vesicles removed from his own fingers. The pores and ducts in the majority of cases were at some distance from the vesicles, but in several sections, though close proximity was observed, no connection with the sweat ducts could be traced. He considered that the condition was akin to vesicular eczema and was not a "dysidrosis", the vesicular contents consisting of serum.

As a result of these findings the eczematous theory became widely accepted, despite many who were reluctant to abandon Fox's more definative explanation. Although remaining a clinical entity within this group, it had apparently been rescued, merely to be returned once more to the chaos of that classification.

Further refutation of the dysidrotic theory came from Unna (1896) who based his findings on very careful histological invest-

igations. He attributed the causation to the initial activity in the lower part of the horny layer of a micro-organism, not unlike the tubercle bacillus. This singular finding has only been corroborated by Benedek (1942 and 1946), who to this day, maintains that a causal organism can be isolated. He refers to it as the bacillus endoparasiticus of Benedek and invokes the theory of biotropism after Milian.

Despite the anti-dysidrotic conclusions of many outstanding dermatologists, we find Nesterjewsky (1906) engaged in an exhaustive histological investigation involving almost three thousand serial sections prepared from six characteristic specimens and concluding that "dysidrosis" is a disease of the sweat apparatus, effected by the occlusion of the sweat pore by plugs of detached and swollen corneus substance.

Sicoli (1924) classified certain vesicular eruptions of the hands and feet as "true dysidrosis" and "pseudo-dysidrosis" or eczema. The latter he concluded was a sequel to spongiosis, but "true dysidrosis" he considered to result from duct rupture and sweat extravasation into the epidermis.

From this period forward to the present day the term "dysidrosis" lost, to a great extent, all its original aetiological significance despite Nesterjewsky's revival of the dysidrotic theory and became merely a label of convenience by those who used it. In general the adoption of this term and others current at the time was dictated

by local usage. Thus we find that "dysidrosis" became universal in France, eczema in Germany and "cheiropompholyx" in England.

As early as 1892 Mouktar is reported as having called attention to the fact that many "dysidrosiform" eruptions were of mycotic origin, but it was only following the independant findings of Whitfield and Sabouraud that special notice was given to a mycotic aetiology.

Whitfield (1908) described three cases from which he had isolated a trichophyton fungus in scrapings and clippings from squamous and vesicular lesions and yellow, friable and longitudinally split toe-nails; and Sabouraud (1910) reported similar findings relating to the presence of the epidermophyton inguinale in intertriginous eczema of the toes.

Darier (1919) published an analysis of twenty cases of "dysidrotic" eruptions of the hands and feet seen during the Great War. He concluded that Tilbury Fox's "dysidrosis" did not exist as a distinct cutaneous disease and admitted that, although he went beyond his observed fact, he considered that these conditions should be classified as follows:-

1. Parasitic epidermophytosic dysidrosis
2. Non-parasitic dysidrosis or occupational dysidrosiform dermatitis

A year prior to the above publication of Darier, Jadassohn (1918) had described lichen-like lesions on the trunk in patients suffering from trichophytic scalp disease and Bloch (1921) had

elaborated upon this by the artificial reproduction of similar lesions by the injection of trichophytin. He consequently concluded that, with the "trichophytytes" as with other infectious diseases, the haematogenous transport into the sensitised skin of toxic or infectious material elaborated from a primary focus could provoke different dermatoses. The latter he called trichophytids. In addition to the lichenoid type he described others as erythema multiforme, scarlatiniform, erythema nodosum, pustular, papular, but no essentially vesicular lesion was mentioned.

Towards the end of the decade the subject of ringworm and "id" eruption was revived when C.M. Williams (1927) suggested that the vesicular lesions of the hands accompanying many cases of ringworm infection of the feet were due to the toxic affects of the deep seated type of the latter. "I believe that in many of the hand cases only a small area is infected and that the rest of the eruption is toxic, and, in some cases which clinically are dermatophytoses of the hands, local infection is not present at all, but the whole eruption is toxic, the source of the infection being a deep tinea of the feet" (deep on account of the fissure often present between the toes). Bloch (1929) corroborated this view and enlarged upon it by striking an analogy between this complex and kerion of the scalp associated with lichen trichophyticus as originally described by Jadassohn and later elaborated by himself.

Hitherto the "id" concept had been applied to deep fungal

infections, but, as Peck (1930) remarked, Von Graffenreid had pointed out as early as 1918 that, in spite of the apparently superficial nature of foot infections, an allergic state was reached as the trichophytin reaction was positive. Peck considered that in these cases the main criteria for the development of the "id" eruption had been fulfilled, viz. the presence of a focus of infection and a skin allergic to that infection. He recalled an investigation of Walthard, working in the same clinic as himself, who, by the injection of trichophytin, produced an aggravation and spread of vesicular lesions of the hands and feet in a girl aged thirteen, suffering from a vesicular and pustular mycosis of the feet, associated with vesicular lesions of the palms and other parts. The latter lesions were negative culturally and microscopically for fungi, and in one of his twenty-three cases, one blood culture was positive for an epidermophyton. His premises for the "id" eruption were thought to be established when a volunteer was experimentally infected between the toes with a trichophyton gypseum and developed a typical intertriginous and vesiculopustular mycotic infection. The trichophytin reaction became positive and a "dysidrotic" eruption appeared on the hands. Examination of these vesicles, unlike those of the feet, proved negative for fungus.

Although the "id" theory has remained popular to the present

day, Scholtz (1932) has been severely critical, pointing out the paucity of positive blood culture findings in all but a few cases and the conflicting reports regarding the incidence of positive or negative findings of fungus in lesions classified as "ids". In 1930 he expressed belief in the "dysidrosis" of T. Fox and maintained that fungi when present were secondary invaders which had found a favourable medium in the lesions.

The complexity of the aetiology was by this time becoming increasingly evident. O'Donovan (1930) stated that "cheiropompholyx" was a pattern reaction in individuals with a predisposition to the eruption owing to chance or heredity, this being due to a pre-destined fragility of the integument which might erupt under many factors, external and internal. He brought forward the following points which were in part investigated soon after by McLachlan and Brown (1934) - "If looked for in the same cases other skin maladies were frequently found, chronic urticaria, pruritus ani, névrodermite (lichen simplex chronicus of Vidal), a chilblain type of circulation and exophthalmic goitre might be discovered either actually present or in the patient's past history".

Lehman (1930) concluded that internal influences were important in predisposing to all vesicular lesions of the hands and feet and in the discussion conducted on his paper, Wile stated that, living in the great goitre belt of U.S.A., he commonly saw "pompholyx" in association with exophthalmic goitre. The fact that the skin

condition always recovered after operation indicated, he thought, a neurogenic origin.

Dowling (1932) suggested that "dysidrosis" complicating eczema of any type may be caused by sensitisation of the skin to tissue antolysis derived from a primary lesion.

McLachlan and Brown (1934) very carefully surveyed the subject and in the light of their own findings in one hundred and twenty-eight cases of sago grain vesicular eruptions of the hands and feet came to the following conclusions:-

1. That cheiropompholyx (sago grain vesicular eruption) is not a disease sui generis, but a form of cutaneous reaction due to a great variety of causes acting singly or together.

2. That it is frequently a contact occupational dermatitis, or an expression of a true sensitisation dermatitis.

3. That it is a cutaneous reaction of the eczematous type.

4. That in a considerable percentage of cases (17% in their cases) the hereditary factor is important that these cases belong to the asthma and hay-fever group.

5. That there is no valid evidence to support the contention that the disease is either solely due to, or connected with, sweat dysfunction or is essentially a fungus infection.

In addition they classified as acarides those sago grain lesions which arose in association with scabetic infection.

This paper was a complete synthesis of the subject to date and met with no adverse criticism. Semon (1935) could find little

to add, but he drew special attention to a 25% group in which no cause could be determined and stressed a possible metabolic cause where no external factor could be implicated.

Fox, Crocker, O'Donovan and others noted that some patients showed nervous manifestations, but until recently concentration on various theories had kept the neurogenic aspect in the background.

Becker (1932) remarked that his colleagues and he were unable to distinguish a "dysidrosis", in which a fungus could be isolated, from one in which none could be demonstrated. He remarked, that the recent tendency to attribute most cases to fungous infection had diverted attention from neurogenic "dysidrosis". The many low readings of the basal metabolic rate in patients suffering from disease where there was often a neurogenic background, e.g. generalised and local pruritus, neuro-dermatitis, dysidrosis, etc., led him to believe that there was a "deficiency of energy" which caused irritability, thereby producing still further demands for "energy". His case of dysidrosis had a B.M.R. of minus 24% which appears to be at variance with Wile's suggestion (1930) that non-mycotic types may have some association with hyperthyroidism.

From this period onwards those who have investigated or made special pronouncements on the subject have added little which is new. Their findings have only served to elaborate aspects of the condition previously described. Thus we find Gougerot (1936) emphasising the allergic diathesis in connection with "dysidrotic"

eruptions. He described a young woman who consulted him with her child aged eleven months, the former suffering from a "dysidrotic" eruption of the hands and feet and the latter from infantile eczema. On interrogation, he discovered that the mother had suffered from eczema and urticaria at the onset of puberty. She was now twenty-four, the "dysidrosis" having appeared a few days after parturition some eleven months previously. And again we find him expounding old theories, viz. that the dermatosis is:-

1. An eruption caused by direct mycotic infection.
2. An eczema with or without superimposed mycotic infection.
3. An eczema caused by or secondarily infected with cocci.

The contact theory had been advanced as causative in the production of vesicular lesions of the hands and feet by Sequeira (1917) when he implicated hexa-nitro-diphenyl-amine of aerial bombs, and by Darier (1919) who was of the opinion that, if "dysidrotic" lesions were not due to direct mycotic infection, they could be labelled as "occupational dysidrosiform dermatitis". Brain (1926) implicated iodine as a causative agent and Levy (1938) attributed "dysidrotic" eruptions in two cases to hair dyes. An occupational type was dealt with by Blaisdell and Schwartz (1945) who referred to it as dermatitis margaritata recurrens because of the pearly nature of the lesions and to distinguish it from cheiropompholyx which they considered to be an idiopathic disease.

Cases due to the ingestion or injection of drugs and more recently to antibiotic therapy have been mentioned. Thus Wise (1930) described two cases where ingestion of oranges resulted in the appearance of "cheiropompholyx" and McLachlan and Brown (1934) attributed one case to a pill made from rhus toxicodendron. In the same year Muende recorded a case caused by the ingestion of synthetic salicylic acid. Again Carpenter and Summit (1936) implicated ephedrine used in nasal applications, whilst Graves, Carpenter and Unangst (1944) referred to intramuscular penicillin as a causal agent.

A case attributed to sepsis had been described by Shillitoe (1904), the patient having scraped an area on the dorsal aspect of the right hand, the affected part remaining septic and not healing and becoming associated after ten weeks with bilateral "cheiropompholyx". Lehman (1930) recorded a case where on two occasions the removal of a bad tooth was followed by a "dyshidrotic eruption" on the palms and fingers. He was, however, uncertain whether or not to ascribe the cause to toxaemia from the tooth or to procaine hydrochloride. He attributed another to the local application of iodine to an interdigital cellulitis of the foot.

Further elaboration of existing neurogenic theories followed developments in the field of psychosomatic medicine. A group was dealt with by McKenna (1944) who referred to it as one which appeared to be idiopathic and chronic and had eluded classification,

the skin manifestation appearing as a vesicular eruption of the hands and/or feet, often associated with hyperidrosis, tremors of the fingers and nervousness. Based on his service experience, he placed this form in the psychosomatic group and remarked that it was little appreciated that a chronic dysidrosis was often the result of a chronic state of anxiety. Support for this classification was offered by Wittkower (1948) who stated that many "pompholyx" cases display a typical hysterical or obsessional character.

It is apparent from this review that since the time of Fox (1873) the histological study of the vesicle has excited much diversity of opinion. One school of thought maintains that its genesis is that of spongiosis and sequelae; and if the lesion is not that of vesicular eczema it is closely akin to it in character. The other is the "dysidrotic" school which regards the vesicle as being due to sweat retention in the duct at the level of the rete Malpighii. Others again deny a sudoriparous origin, but have not committed themselves to positive pronouncements.

In their most recent text-book Ormsby and Montgomery (1948) still retain the term "dysidrosis" and leave the reader to his own interpretation regarding whether or not to attribute the disease to sweat retention. Again in the same year Sulzberger and Baer indicate several lines of investigation which might be followed in order to establish that the mechanism of vesicle formation is one of sweat duct occlusion.

It can thus be inferred that although the "dysidrotic" theory is not universally held many authorities past and present have accepted or accept its feasibility. Because of this prevailing diversity of opinion, it was considered worth while to undertake further histopathological investigations.

Regarding the aetiology of sago grain eruption of the hands and feet, the combined work of McLachlan and Brown (1934) would appear to have been the most comprehensive. They confirmed the existence of many of the aetiological factors determined by previous workers. In addition they published figures to indicate the relative frequency in which these factors operate in sago grain vesicular eruptions as a whole. Such figures seem to have been published only by very few others, i.e. Lehman (1930), Davidson and Birt (1943). On account, therefore, of the lack of comment on the relative incidence of such factors, it was considered justifiable to undertake further aetiological investigations which might reaffirm or refute this incidence and which might bring to light other factors hitherto unrecognised.

PART 2

INVESTIGATION

From an investigation of the literature it appears that the terms dysidrosis, pompholyx and cheiropompholyx have been applied to embrace conditions of the hands and feet manifesting themselves by the presence of vesicles resembling boiled sago grains irrespective of other skin lesions which also might be present on these or other parts. Thus Tilbury Fox, in his first description of "dysidrosis", stated "the eruption about the hand or hands may be complicated by a rash more or less general over the body". He further described some of these eruptions as resembling other conditions thought to be due to sweat retention, viz. lichen tropicus and miliaria. On one occasion Crocker mentioned that eczema might also be found affecting other parts of the body. Again Shillitoe described a case of "pompholyx" arising in association with what would appear to have been a post-traumatic infective dermatitis of the hands. McLachlan and Brown (1934) have expressed doubt regarding whether or not to restrict the term "cheiropompholyx" to a distinctive eruption of the hands found in association with hyperidrosis or to any vesicular condition of a definite type on these parts. They pointed out, however, that hyperidrosis was by no means an invariable accompaniment of such dermatoses and, as a result, included in their cheiropompholyx series all cases which presented an eruption of vesicles of the sago grain type on the hands and feet. The tendency in America

on the other hand is to use the terms cheiropompholyx or dysidrosis in a more restricted clinical sense. Thus Davidson and Birt (1943) apply the term"cheiropompholyx"only to cases in which an external cause cannot be found. Again Andrews (1946) states that the term pompholyx is at present limited to deep seated vesicular eruptions of the extremities where the cause is not due to fungus or chemical, a view which is in accord with that of Ormsby and Montgomery (1948). The different interpretation placed on terminology is remarked by Wise and Wolf (1936) who state that in the United States pompholyx implies a non fungous origin and in England the term covers palmar and plantar vesicular eruptions in general with qualifying adjectives, e.g. toxic, fungous, parasitic, non-parasitic.

It is apparent, therefore, that the terms,"dysidrosis","cheiropompholyx"when undefined leave one in doubt as to what is really meant. Because of this, I have avoided the use of these terms as applied to my own series of cases to which the expression deep seated sago grain vesicular eruptions of the hands and feet has been given. The terms,"dysidrosis," etc. have only been used when dealing with the work of others, but in these cases the applications are entirely contextual. Furthermore as in McLachlan and Brown's series, cases were chosen irrespective of any other concomitant cutaneous anomaly. In every other way they were entirely unselected, the records and investigations being made as patients appeared in the wards or at the out-patient department with a view to studying the aetiology and histopathology of the sago grain vesicles.

PART 2(a)

AETIOLOGICAL INVESTIGATION OF THE SAGO GRAIN VESICULAR ERUPTIONS OF THE HANDS AND FEET

The foregoing survey of the literature indicates that sago grain vesicular eruptions of the extremities may be placed in the following aetiological groups:-

1. Epidermophytid (Peck(1930) and others)
2. Occupational dermatitis (Darier (1919), Blaisdell & Schwartz (1943))
3. Dermatitis venenata (Sequeira (1919), Brain (1926), Levy (1938) and others)
4. Neurogenic (Wile (1930), Becker (1932))
5. Psychosomatic (McKenna (1944), Wittkower (1948))
6. Allergic (McLachlan and Brown (1934))
7. Endogenous (Lehman (1930), Semon (1935))
8. Focal Sepsis (Lehman (1930), McLachlan and Brown (1934))
9. Drug idiosyncrasy (McLachlan and Brown (1934), Muende (1934), Carpenter and Summit (1936), Graves, Carpenter and Unangst (1944)
10. Food idiosyncrasy (Wise (1930)
11. Sensitisation dermatitis (Shillitoe (1904), McLachlan and Brown (1934), Davidson and Birt (1943)
12. Acaride (McLachlan and Brown (1934)
13. Idiopathic (McLachlan and Brown (1934), Davidson and Birt (1943) and others)

Although the collective work of many authorities has established and confirmed the existence of these groups, few have endeavoured to determine the relative frequency with which they operate. Lehman (1930), McLachlan and Brown (1934), Davidson and Birt (1943) appear to be the chief workers to produce such data.

As the investigations of McLachlan and Brown (1934) were

conducted here in Glasgow particular attention was given to their findings.

The cases from which data was obtained were examined in Glasgow at the Western Infirmary, Southern General Hospital, Dispensary of the Royal Hospital for Sick Children and a few at Stobhill Hospital.

My findings were determined from case histories, personal and family, from clinical examination and mycological studies.

As is the case in the histological section of this thesis, a short resumé of the pertinent data of others will be given prior to the presentation of my personal findings.

INCIDENCE OF AETIOLOGICAL FACTORS

Lehman (1930) classified one hundred and thirty-one cases and gave the relative incidence of aetiological groups as follows:-

Table 1

Diagnosis	No. of Cases	Percentage
Dermatophytosis	86	65.6
Dermatitis Venenata	25	19.1
Pompholyx	20	15.3

McLachlan and Brown (1934) published the following findings in one hundred and twenty-eight cases:-

Table 2

Cause or Associated Factors	No. of Cases	Percentage
Allergic family and personal history (eczema, asthma, etc.)	17	13.3
Focal sepsis, internal or external	25	19.6
Pregnancy, menstruation, endocrine disturbance and neurosis	21	16.4
Occupation and acute sensitisation	20	15.6
Fungus	4	3.1
Definite gastric trouble at each attack	3	2.3
Drugs	1	0.78
No definite cause	37	28.9

Davidson and Birt (1943) in a study of two hundred cases concluded that the relative incidence of aetological factors was as follows:-

Table 3

Diagnosis	Percentage
Infectious eczematoid dermatitis	3.5
Dermatophytid	7.0
Cheiropompholyx	12.0
Dermatitis venenata	76.5

Having tabulated these figures of previous workers, my personal findings will now be presented.

EXOGENOUS AETIOLOGY

Cases were considered as having an exogenous aetiology if the probable causal factor was of exogenous origin.

Discrete Sensitisation Dermatitis Group

This term was applied to conditions which appeared as discrete

papular or papulo-vesicular eruptions of a widespread or localised nature and which usually followed antecedent contact with substances to which the skin seemed sensitive or resulted from pre-existing epidermal damage in the form of skin trauma or skin infection.

The sensitisation eruptions usually occured around these primary lesions after the latter had persisted for a varying period. When the eruptions affected the extremities they almost invariably did so as sago grain vesicles (vide Plate 1).

That the sago grain vesicles present in association with these sensitisation eruptions were of an origin similar to the papules or papulo-vesicles of other parts was apparent in certain instances. In these cases the discrete sensitisation lesions, when traced across the wrists in the direction of the hands, were seen to manifest every transition from the papule or papulo-vesicle of the forearm to the sago grain vesicle of the hand. Plate 2 demonstrates this transition on the anterior aspect of the wrist in a case in which a concomitant sago grain vesicular eruption was associated with a widespread discrete sensitisation dermatitis.

Included in this group were some cases which, though not having a discrete papular or papulo-vesicular eruption of other parts, presented sago grain vesicles of the hands which seemed to arise as local sensitisation eruptions.

The antecedent lesions in these cases were again abrasions, fissures or infective dermatitis of the extremities, e.g. Cases 29,

57, 76 and 80.

Some cases were also included where vesiculation appeared to be due to sensitisation of a recurring type, e.g. the eruption in Case 82 was considered to be a locally recurring sensitisation condition resulting from burns of the hands sustained two years previously.

The cases falling within the discrete sensitisation dermatitis group are analysed in Tables 4 and 5.

Table 4

Discrete Sensitisation Dermatitis (Infective Origin)

Case No.	Type of Initial Epidermal Damage	No. of Cases
2, 4, 29, 48, 52, 80, 88	Infective fissure of finger or hand	7
14, 17, 35, 76	Cut, laceration, abrasion	4
15, 82, 85, 99	Burn of skin or scald	4
70, 78	? Circulatory (Varicose Veins)	2
18, 49	Friction on skin	2
1, 12, 23, 46, 56, 57	Infective Dermatitis (arising de novo)	6

Total number of cases due to discrete sensitisation dermatitis of infective origin = 25

Table 5

Discrete Sensitisation Dermatitis (Contact Origin)

Case No.	Contact Agent	Nature of Primary Lesion
9	Watch strap	Dermatitis venenata (wrists)
38	Penicillin cream	Erythema Multiforme (dorsum of foot)
40	Copper Oleate ointment	Nummular vesicular eczema (right wrist)
67	Sulphonamide powder	Laceration (right calf)
72	Penicillin cream	Traumatic dermatitis (left elbow)
77	Penicillin cream	Burn scar (right calf)
79	Adhesive plaster	Laceration (left thumb)
95	Elastoplast	Laceration (right thumb)

Total number of cases due to discrete sensitisation dermatitis of contact origin = 8

Total number of cases due to discrete sensitisation dermatitis = 33

Dermatitis Venenata Group

A substantial number of cases appeared to be the expression of a true contact dermatitis. More than 50% of this group was attributed to skin cleansing agents, chiefly alkali in type. Concomitant evidence of fat solvent skin irritation of the hands was frequently present.

In the majority of cases the noxious substance only affected the hands, but in Cases 11 and 31 the hand condition was part of a widespread dermatitis venenata.

Plates 3, 4 and 5 demonstrate some cases falling into the dermatitis venenata group.

Table 6

Dermatitis Venenata Group

Case No.	Contact Agent	No. of Cases
6, 44, 65, 83, 89	Soap and Water	5
7, 13, 87	Fat Solvents (caustic soda, sodium carbonate)	3
45	Cutting oil	1
94	Dettol	1
86	Arpidol (trade name)	1
31	Primula obconica	1
11	Probably plant	1
24	"Inecto" hair dye	1

Total number of cases attributed to dermatitis venenata = 14

Scabetic Group

Cases were placed in this group when scabetic infection appeared to be the factor conditioning the onset of the eruption.

In Case 34 sago grain vesicles had appeared on the fingers and palms as a recurrent eruption following the treatment of scabies with sulphur ointment. Cases 42 and 90 had sago grain vesicles on the hands and feet in association with, but apart from, typically scabetic lesions.

Table 7

Scabetic Group

Case No.	No. of Cases
34, 42, 90	3

Total number of cases attributable to scabies = 3

Fungous Group

Mycological studies were undertaken accepting the popular belief that the hyphomycetes affecting the feet are the aetiological agents of associated deep seated vesicular eruptions of the extremities (Peck (1930) et al.).

The cases selected were those in which no other external cause was apparent. Not all suffered from an interdigital intertrigo of the feet.

The tissues chosen for study were vesicles and scales from the feet and from between the toes. Where the possibility of mycotic infection of the nails arose the latter were also examined.

The specimens were studied directly microscopically, after clearing in 20% liquor potassae, and in each case tissues were placed on three slopes consisting of Sabouraud's medium (please see Appendix 2).

Plate 7A represents a colony grown as a medium control from scales removed from a typical tinea circinata lesion. Plates 7B to7H are photographs of cultures grown from specimens in the cases indicated.

Table 8 indicates the cases and tissues from which ringworm fungus was isolated.

Table 8

Fungus positive Cases

Case No.	Lesion from which fungus was isolated	No. of cases
32, 47, 58, 63, 73, 74	Scale from interdigital intertrigo of the feet	6
51, 68, 96	Vesicle of toe	3
75	Toenail	1

Total number of cases attributable to fungous infection of the feet = 10

(It is pointed out that this percentage figure is almost doubled if cases having other concomitant lesions are excluded, e.g. discrete sensitisation eruptions)

ENDOGENOUS AETIOLOGY

Cases were considered to be of endogenous origin when eruptions could not be attributed to an extraneous cause.

Allergic Group

Those classified under this heading were selected according to the criteria of McLachlan and Brown (1934), viz. the existence of a personal or family history of eczema, asthma or hayfever. Migraine hemicrania was considered as an allergic condition in the present series. Furthermore other cases were included which manifested concomitant conditions of probable allergic origin, e.g. papular urticaria.

Table 9

Personal or Family History of Allergic Conditions

Case No.	Allergic Condition in Personal or Family History
25	Sister, paternal grandmother and aunt suffered from asthma and hayfever
26	Personal history of seasonal hayfever
27	Sister suffered from frequent asthmatic attacks
33	Sister suffered from frequent asthmatic attacks
39	Sister had suffered from chronic eczema from infancy
50	Personal history of urticaria
54	Mother suffered from Migraine hemicrania
69	Personal history of urticaria. Brother suffered from asthma
91	Personal history of urticaria after fish. Sister suffered from chronic eczema and Migraine hemicrania
98	Maternal grandmother suffered from localised lichenified dermatitis and maternal aunt from recurrent dermatitis of the hands
100	Personal history of chronic dermatitis of the face from age seventeen to twenty-four

Number of cases without apparent external cause, but having a personal or family history of allergic conditions = 11

Table 10

Concomitant Allergic States

Case No.	Concomitant Allergic State	No. of Cases
8, 16	Flexural eczema	2
3	Papular urticaria	1
28	Erythema multiforme	1

Number of cases without apparent external cause, but associated with concomitant conditions of probable allergic origin = 4

Total number of cases placed in allergic group = 15

Neurogenic Group

A number of cases presented minor nervous manifestations, such as slight tremors of the fingers. Only those, however, in which a nervous state was marked or appeared to be associated with the eruption were included in this group. The following case exemplifies the type included:-

Case 20 (Male, age 28) He was a doctor who had developed a sago grain vesicular eruption of the hands following his being confronted with a case of severe post-partum haemorrhage which had almost resulted in the woman's death. He admitted that he had been greatly frightened by this event. From then on the eruption recurred every time he attended a confinement. Gloves and antiseptics were excluded as possible causes and no other internal or external factor could be implicated.

Table 11

Neurogenic States

Case No.	Neurogenic States
37	Thyrotoxicosis
20, 30, 55, 60, 62, 71	Neurosis
36	Exhaustion (overwork)

Total number of cases associated with having neurogenic disturbances = 8

Idiopathic Group

Certain cases could not be classified on a causal basis or

placed in a group having a common associated factor. They were thus included in the idiopathic group. The majority, however, possessed a factor to which some possible aetiological significance could be ascribed. This group was, therefore, sub-divided into Group 1 consisting of those cases in which possible aetiological factors were present and Group 2 of those to which no possible factor could be ascribed.

As will be seen in Table 12, the following factors were included:-

1. Antecedent history of ringworm infection.

2. Tonsillectomy which appeared to cause an acute exacerbation in a chronic case.

3. Chilblains O'Donovan (1930) mentioned that a chilblain circulation may be present in patients suffering from "cheiropompholyx". In the present series five cases altogether gave a history of chilblains or actually suffered from a chilblain type of circulation. Three (Cases No. 19, 39 and 98) were placed in other groups on account of more prominent factors, but the remaining two were classified in the idiopathic group 1. Thus Case 98 developed sago grain vesiculation of the hands in cold weather often with concomitant chilblains. Case 93 was actually under treatment for chilblains with high potency calciferol when a sago grain vesicular eruption of the hands developed.

4. Non-mycotic interdigital intertrigo This type of lesion was classified as a possible aetiological factor because it was difficult on a clinical basis to differentiate the squamous stage of sago grain vesicles between the toes, from an intertrigo of mycotic origin. Although many of these intertrigos were probably due to non fungous causes, it was considered possible that, despite mycologically negative findings, a certain number may have been

essentially mycotic in origin, the infection having been destroyed by local medicaments prior to examination.

Table 12

Idiopathic Group 1

Case No.	Possible Associated Aetological Factors	No. of Cases
22, 84	Antecedent ringworm infection Beard and Scalp - Case 22 Feet - Case 84	2
21	Septic tonsils	1
19, 59, 93	Chilblain or chilblain circulation	3
10, 41, 43, 61, 66, 92, 97	Interdigital intertrigo of the feet (Fungus -negative)	7

Number of cases without apparent external cause, but in which possible associated factors were present = 13

Idiopathic Group 2

This group consisted of all cases to which no cause could be ascribed and in which no apparent associated factor appeared to operate.

Table 13

Idiopathic Group 2

Case No.	No. of Cases
5, 53, 64, 81	4

Number of cases to which no causal or associated factor could be ascribed = 4

Total number of cases in the idiopathic group = 17

The lesions in these cases differed in no way from those which resulted from some extraneous cause. Thus Plate 6 demonstrates a sago grain eruption arising without cause or associated factor. This eruption differs in no way from that shown in Plate 1 which was part of a widespread discrete sensitisation dermatitis.

Summary of Findings

Number of cases due to or associated with

1.	Discrete sensitisation dermatitis		
	(a) Infective origin		25%
	(b) Dermatitis venenata origin		8%
	Total due to discrete sensitisation dermatitis		33%
2.	Dermatitis venenata		14%
3.	Scabies		3%
4.	Fungous infection		10%
5.	Allergic factors		15%
6.	Neurogenic factors		8%
7.	Idiopathic		
	Group 1	13%	
	Group 2	4%	
	Total to which no cause could be ascribed and in which no common associated factor seemed to operate		17%
Total			100%

COMPARISON OF FINDINGS WITH THOSE OF LEHMAN AND DAVIDSON AND BIRT

Lehman (1930) and Davidson and Birt (1943) classified their cases in the following groups:-

(a) Dermatophytosis, Epidermophytid,, (fungous).
(b) Dermatitis venenata.
(c) Pompholyx, Cheiropompholyx (idiopathic).

In addition an infectious eczematoid group was included by Davidson and Birt in which vesicles of the hands were produced as a local manifestation of infectious eczematoid dermatitis or as "bacterids" from such dermatitis of other parts of the body. In order, therefore, to compare findings with these workers, it was necessary to eliminate the discrete sensitisation dermatitis and the scabetic groups from my series and the very small infectious eczematoid dermatitis group from that of Davidson and Birt.

For the following comparison, therefore, the figures shown in each case are the percentage of the total cases represented by the fungous, dermatitis venenata and idiopathic groups:-

Table 14

Incidence of Groups compared

Group	Lehman (1930) United States	Davidson & Birt (1943) Canada	Personal
Fungous (Dermatophytosis, Epidermophytid)	65.6%	7.3%	15.6%
Dermatitis venenata	19.1%	80.1%	21.9%
Idiopathic (Pompholyx, Cheiropompholyx)	15.3%	12.6%	62.5%

Fungous Group

The figures suggest that the incidence of foot mycosis found in association with vesicular eruption of the extremities might be

much greater in the United States than in other countries. Whereas my figure is only a quarter of Lehman's, it is twice that found in Canada by Davidson and Birt.

The relatively low incidence of the latter workers might, to some extent, be due to an admitted lack of mycological investigation. My personal investigation indicated that, whereas in some cases the finding of a ringworm fungus could be anticipated, this was not invariably the case. Thus Case 74 had all the appearance of an eczematoid tinea of the feet and ringworm fungus was readily found. Case 41, which again suggested ringworm infection clinically, proved negative on investigation. Case 51 did not suggest mycotic infection clinically, but on culture a ringworm fungus was grown from a vesicle of the toe.

It is inferred, therefore, that the incidence of ringworm infection as a cause of sago grain vesiculation of the hands and feet is probably dependent upon geographical factors. Furthermore in order to be certain of the presence of ringworm infection, it is necessary to carry out mycological investigations as clinical appearances are often misleading.

Dermatitis Venenata Group

My observations in relation to the frequency of operation of contact agents agree closely with those of Lehman, but differ widely from those of Davidson and Birt series, a discrepancy which is difficult to explain (vide Table 14).

Pompholyx, Cheiropompholyx

Lehman and Davidson and Birt classified under these headings all cases to which an external cause could not be attributed. They correspond to the group in the present series which has been designated idiopathic, together with what I have called neurogenic.

A glance at Table 14 indicates that the figures of Lehman and Davidson and Birt correspond closely as far as this group is concerned. My findings would appear to show a much greater incidence. This would seem to depend largely, however, on the great number of fungous cases in the Lehman series and on the high incidence of dermatitis venenata in Davidson and Birt's cases.

Comment

The comparison, therefore, indicates a similarity with Lehman regarding the frequency with which dermatitis venenata may be a cause of sago grain vesicular eruptions.

A wide discrepancy regarding the incidence of ringworm infection as a probable cause has been observed. It is suggested that these differences may be due to geographical factors and to the lack of mycological investigations of some workers.

The low incidence of idiopathic cases in Lehman's and Davidson and Birt's series is largely in proportion to the high incidence of fungous and dermatitis venenata types respectively amongst their cases.

INCIDENCE OF AETIOLOGICAL FACTORS COMPARED WITH THOSE OF MCLACHLAN AND BROWN

The next stage in the comparison deals with the findings of McLachlan and Brown (1934). Their lines of investigation as far as the aetiology was concerned were parallel to my own. They selected only those cases which presented a sago grain vesicular eruption of the hands and feet. In this respect the material used was more definitely specified than that of Lehman and Davidson and Birt. Furthermore they brought to light an allergic group to which I have given special attention.

Allergic Group

This corresponds to what the above workers called the eczema, asthma, hayfever group and consists of those cases arising in the absence of an obvious cause, but in which there is a personal or family history of disease of supposedly allergic origin.

15% of my cases fall within this group and would seem to correspond closely with the incidence of such cases in the McLachlan and Brown series where it represented 13.3%.

Focal Sepsis (internal or external)

The above workers place 19.6% of their cases under this heading. In a certain number of my cases sepsis was obviously a factor, but where this operated externally it most frequently did so through the intermediary phases of infective dermatitis and subsequent discrete sensitisation dermatitis which, when affecting the hands,

appeared in the form of sago grain vesicles.

Many cases, therefore, which in my series might have been classified as being due to external focal sepsis, fell within the discrete sensitisation group. A few, however, appeared to be associated with other types of focal sepsis which were considered to be precipitating factors rather than actual causes. Thus Case 21 at the age of twelve developed a chronic sago grain vesicular eruption which coincided with her first menstrual period. At the age of sixteen her tonsils were noticed to be chronically inflamed. During a quiescent phase of her skin eruption, tonsillectomy was performed and resulted in an immediate exacerbation of vesicles on the hands. This case was placed in idiopathic group 1 because sepsis was only a possible associated factor.

Case 25 at the age of nine developed a sago grain vesicular eruption of the hands following mastoidectomy. Since then annual recurrences had developed in warm weather. Because her sister, paternal aunt and paternal grandmother suffered from recurrent bronchial asthma, this case was placed in the allergic group, the mastoidectomy being considered as a precipitating factor.

Pregnancy, Menstruation, Endocrine, Neurosis

McLachlan and Brown placed 16.4% of their cases in this category, but did not indicate the relative incidence of the included factors. In my series pregnancy and menstruation, though sometimes coinciding with attacks (e.g. Cases 21 and 33), were

considered to be indefinite associated factors. Thus Case 33 developed the condition during the puerperium period, but on account of a previous history of dermatitis and asthma in a sister the case was placed in the allergic group.

Apart from the indefinite operation of endocrinal factors indicated by these examples, no case could be attributed to endocrinal imbalance. An endocrinal origin in certain cases, as suggested by McLachlan and Brown, in some measure lent support to the contention of Wile (1930) that many cases might be due to hyperthyroidism and of Lehman who considered that any finger tremor present was similar to that associated with this disturbance.

The findings in the present series are apposed to this view as it was found that the pulse rates in most cases were notably within normal limits even in cases where the presence of finger tremors or the nervous temperament of the patient suggested that the rate might be increased (e.g. Cases 32, 51 and 64).

The basal metabolic rate was estimated in three cases only. In Case 37 the increase was consistent with the degree of thyrotoxicosis present and in the other two (one of whom was nervous) it was slightly less than normal.

These findings, therefore, provide no evidence to suggest that the eruptions are in any way associated with hyperthyroidism. They are consistent with the view of Becker that "dyshidrotic" eruptions might be associated with a depression of metabolism.

The following table illustrates the consistency of normal pulse rates and indicates the basal metabolic rate in the cases in which it was estimated:-

Table 15

Case No.	Aetiological Group	Pulse Rate	Basal Metabolic Rate
5	Idiopathic	74	-
32	Fungous	70	-
33	Allergic	74	-
37	Neurogenic	160	+70%
41	Idiopathic	68	-5%
47	Fungous	68	-
51	Fungous	68	-10%
58	Fungous	76	-
64	Idiopathic	74	-
73	Fungous	88	-
74	Fungous	100	-
98	Allergic	68	-
99	Discrete sensitisation dermatitis	80	-
100	Allergic	66	-

Comment

As McLachlan and Brown embraced different conditions in their combined group (pregnancy, menstruation, endocrine, neurosis) and published no figures to show the individual incidence of conditions included, comparative studies in these respects are impossible.

Although a few indefinite associations with endocrinal phenomena were noted, no case could be attributed to actual endocrinal imbalance.

Occupation and Acute Sensitisation

The last named workers again give no indication as to the

relative incidence of operation of each condition, but the total figure of 15.6% is widely at variance with my own combined total in which the fraction representing discrete sensitisation dermatitis and dermatitis venenata is 47%.

It is probable that the difference can be explained on the following basis:-

(a) The above workers state that much of their data was collected from records or cases which had been actually indexed as cheiropompholyx. By using this method it is probable that many cases of sago grain vesicular eruption classified on a causal basis were omitted. Discrete sensitisation dermatitis, dermatitis venenata and epidermophytosis manifest as sago grain vesicles on the hands in all probability would not have been indexed as cheiropompholx.

(b) Some cases in which the original sepsis was in the skin may have been included in their focal sepsis group and not under occupation and acute sensitisation.

Fungus

The number of cases in the present series associated with ringworm infection is two and a half times that of McLachlan and Brown. It is difficult to explain the difference, but the following factors might account for it:-

(a) The increase of almost epidemic character of fungous infection since the war.

(b) A seasonal variation as mentioned by Darier (1919) and Lehman (1930) which might explain why different workers in the same area can have totally different findings.

Definite Gastric Trouble

2.3% of the McLachlan and Brown series fell into this group. In the present series patients were questioned concerning past and present gastric symptoms.

Case 10 gave a history of dyspepsia and perforating peptic ulcer. Because of a concomitant recurrent and associated intertrigo of the toes, this case was placed in the idiopathic group 1.

Case 19 developed an acute sago grain vesicular eruption of the hands and feet preceded by nausea and epigastric discomfort. As her dyspepsia was only a possible associated aetiological factor and a chilblain circulation was marked, her condition was placed in idiopathic group 1. Similarly Case 68 for a month had experienced attacks of nausea and vomiting corresponding to the onset and exacerbations of a vesicular eruption of the hands and feet. Because of the positive finding of a ringworm fungus in a vesicle of the toe, the case was placed in the fungous group. Case 60 gave a history of duodenal ulcer, but on account of his exceedingly nervous disposition and the absence of an extraneous cause he was placed in the neurogenic group.

Drugs

Reports of drug ingestion as being causative are rare (e.g. Muende (1934)). McLachlan and Brown had one case in one hundred and twenty-eight (0.78%). In the present series no such case was

found.

No definite Cause

17% of cases came within this category, although the majority had some factor which was considered to be of some aetiological significance. On the other hand McLachlan and Brown included 28.9% under this heading.

The difference, to some extent, can be explained by my relatively high incidence of ringworm infection, cases due to soap and water, and grease solvents, and in all probability to a higher incidence of discrete sensitisation dermatitis cases.

Comment

The foregoing comparison demonstrates the existence of all the aetiological factors implicated by McLachlan and Brown with the exception of ingested drugs.

The proportion of my cases falling within the allergic or asthma, eczema and hayfever group corresponds with that of McLachlan and Brown.

The largest single group in the present series is the discrete sensitisation group. When added to the dermatitis venenata group, the total is 47% of cases. The relatively high incidence represented by this combined group, together with that of ringworm infection, is probably the cause of variation from the figures of McLachlan and Brown.

That the combined discrete sensitisation dermatitis and derma-

titis venenata group is large in comparison with that of these workers is suggested to be due to the possibility that McLachlan and Brown did not include some cases due to discrete sensitisation by selecting cases actually indexed as "cheiropompholyx". Furthermore some of their cases due to discrete sentisisation dermatitis may have been included in their focal sepsis group (external).

AGE AND SEX INCIDENCE

The following table shows the sex incidence of sago grain vesicular eruption in the various decades:-

Table 16

Age	Male	Female	% of Total
0 - 10 years	9%	5%	14%
11 - 20 years	6%	7%	13%
21 - 30 years	10%	9%	19%
31 - 40 years	18%	10%	28%
41 - 50 years	8%	4%	12%
51 - 60 years	6%	5%	11%
61 - 70 years	3%	0%	3%
Total	60%	40%	100%

The following table shows the cases in the different aetiological groups occurring in the various decades:-

Table 17

M = Male, F = Female, Number = Case Number

Age Group	Discrete Sensitisation Dermatitis	Dermatitis Venenata	Scabetic	Fungous	Neurogenic	Allergic	Idiopathic
0-10	M35,F48, M76,M77	-	M42,M90	F75,M96	F30	M3,M28, F98,F54,M50,	-
11-20	M82	M6	F34	M47,F51	F36	F25,F8	M5,F21, M41,F66, M97
21-30	F1,F4, M29,F88	F89,F94	-	M68	M20	M16,M27, F33	F19,M53, M61,M64, F81,M84, M92,F93
31-40	M2,M9, F12,M14, M15,M17, M18,F23, M46,M72, M80,F95, M99	F31,F83	-	M58,F73, M74	M55,M60, M62,M71	F26,F69	M10,M22, F43,F59
41-50	M38,M52, M70,F79	M7,M13, M44,M45	-	F32,F63	F37	M91	-
51-60	F40,M49, M57,M67	M11,F24, M65,F86, F87	-	-	-	F39, M100	-
61-70	M56,M78, M85	-	-	-	-	-	-
Over 70	-	-	-	-	-	-	-

The following tables show the sex incidence of aetiological groups occurring in the various decades:-

Table 18

Discrete Sensitisation Dermatitis

Age Group	0-10	11-20	21-30	31-40	41-50	51-60	61-70
No. of Males	3	1	1	10	3	3	3
No. of Females	1	0	3	3	1	1	0
Total	4	1	4	13	4	4	3

Total number of male cases = 24
Total number of female cases = 9
Total number of cases in discrete sensitisation dermatitis group = 33

Table 19

Dermatitis Venenata

Age Group	0-10	11-20	21-30	31-40	41-50	51-60	61-70
No. of Males	0	1	0	0	4	2	0
No. of Females	0	0	2	2	0	3	0
Total	0	1	2	2	4	5	0

Total number of male cases = 7
Total number of female cases = 7
Total number of cases in dermatitis venenata group = 14

Table 20

Scabetic

Age Group	0-10	11-20	21-30	31-40	41-50	51-60	61-70
No. of Males	2	0	-	-	-	-	-
No. of Females	0	1	-	-	-	-	-
Total	2	1	-	-	-	-	-

Total number of male cases = 2
Total number of female cases = 1
Total number of cases in the scabetic group = 3

Table 21

Fungous

Age Group	0-10	11-20	21-30	31-40	41-50	51-60	61-70
No. of Males	1	1	1	2	-	-	-
No. of Females	1	1	0	1	2	-	-
Total	2	2	1	3	2	-	-

Total number of male cases = 5
Total number of female cases = 5
Total number of cases in fungous group = 10

Table 22

Neurogenic

Age Group	0-10	11-20	21-30	31-40	41-50	51-60	61-70
No. of Males	0	0	1	4	0	-	-
No. of Females	1	1	0	0	1	-	-
Total	1	1	1	4	1	-	-

Total number of male cases = 5
Total number of female cases = 3
Total number of cases in neurogenic group = 8

Table 23

Allergic

Age Group	0-10	11-20	21-30	31-40	41-50	51-60	61-70
No. of Males	3	0	2	0	1	1	-
No. of Females	2	2	1	2	0	1	-
Total	5	2	3	2	1	2	-

Total number of male cases = 7
Total number of female cases = 8
Total number of cases in allergic group = 15

Table 24

Idiopathic

Age Group	0-10	11-20	21-30	31-40	41-50	51-60	61-70
No. of Males	-	3	5	2	-	-	-
No. of Females	-	2	3	2	-	-	-
Total	-	5	8	4	-	-	-

Total number of male cases = 10
Total number of female cases = 7
Total number of cases in idiopathic group = 17

Total number of male cases of sago grain vesicular eruptions of the hands and feet = 60
Total number of female cases of sago grain vesicular eruptions of the hands and feet = 40
Total number of cases in series = 100

A survey of the preceding tables indicates that in a series of a hundred cases sixty were male and forty female. With the exception of the 11-20 age group where sex incidence is almost equal, a preponderance of male over female was noted in all age groups. That this preponderance is consistent throughout seems to indicate that the increased liability depends possibly on some innate factor in the male.

With the exception of the scabetic group which is too small to provide reliable statistical data, it was noted that the age incidence in groups seemed to differ according as aetiological factors were extraneous or entirely endogenous. Where factors were extraneous it was noted generally that most age groups were affected and that the incidence of the aetiological group was greatest during the most active years of life. Thus cases in the discrete sensitisation

dermatitis group occurred fairly uniformly throughout life reaching a sharp peak in the fourth decade.

A similar, but less marked, tendency is noticed in the fungous group. The hazard of infection is presumably ever present being greatest in the fourth decade when the activity of the individual is probably greatest.

A similar trend is shown by the neurogenic group. Although classified as endogenous, it is probable that in most cases the original mental trauma was of extraneous origin. Here again during the most active phase of life the sharpest peak occurs.

Cases of the allergic and idiopathic group which are largely endogenous would appear to reach the peak period earlier in life. Tables 23 and 24 indicate that more than 75% of cases in these groups occur before the age of thirty.

The dermatitis venenata group, like others of the exogenous class, affects most ages. No cases were found in the first decade and a high incidence between the age of thirty and forty was not noted. On the other hand an upward trend of case incidence occurred between the fourth and the sixth decade inclusive. Reference to Table 6 (page 26) indicates that by far the most common causative agents of this group are ordinary domestic hazards such as soap and water, antiseptics and plants. Industrial chemical factors would appear to play a relatively minor role (cf. Davidson and Birt (1945)).

This probably largely explains the continuing upward trend after the middle decades of life.

COMPLEXITY OF AETIOLOGICAL FACTORS

The Complex Aetiological Group

It will now be shown that many of the cases already classified, in addition, possessed other criteria which might warrant their inclusion within more than one group.

The type of cases may be exemplified as follows:-

Case 74 Whilst serving in the Navy he had developed a vesicular eruption of the hands and feet a few weeks after being shipwrecked. His condition healed quickly with hospital treatment. Subsequently he had to be evacuated ashore on account of recurrences on every occasion that naval operations were liable to bring him into contact with the enemy. After about a year of relapse and intermission, he was finally discharged from the Service.

This case might have been placed in the neurogenic group, but for the fact that on examination he was found to be suffering from tinea pedis in association with the vesicular eruption of the hands. Owing, therefore, to positive cultural findings, this case was placed in the fungous group.

Case 23 A year prior to examination she had developed a widespread dermatitis commencing around hacks on the backs of the hands. The condition, after some months, had cleared apart from a

small localised area in the left cubital fossa. A few weeks before consultation the dermatitis had again recurred as a weeping infective dermatitis of the dorsa of the feet soon followed by the appearance of sago grain vesicles on the hands. This case was placed in the discrete sensitisation dermatitis group because it appeared that the sago grain vesicles of the hands were a sensitisation secondary to antecedent infective dermatitis. On the other hand in the absence of such a primary cause, this case could have been placed in the allergic group as her father suffered from bronchial asthma and she herself from chronic lichenification of the cubital fossae. She always developed urticaria following the ingestion of strawberries.

Case 30 (age seven) She had suffered from a recurring sago grain vesicular eruption of the hands and feet for about a year. The onset followed scalding of the right foot with hot water, but only after the second degree burn had healed without complication. It was difficult to decide whether the eruption had resulted from the thermal trauma or was associated with a nervous state resulting from the burn. The nervous disturbance consisted of an abnormal terror of heat of every description, the fire, warm washing water, etc., and as a result presented a great problem of child management.

These cases are examples falling within what I have called the complex aetiological group because they possess factors which were sufficient to place them in more than one aetiological group.

The following Table 25 indicates the cases falling within this group and shows the respective multiple aetiological factors present in each case:-

Table 25

Complex Aetiological Group

Case No.	Group in which classified	Factors which could place case in other group			
		Discrete Sensitisation Dermatitis	Dermatitis Venenata	Allergic	Neurogenic
4	Discrete sensitisation dermatitis	-	-	+	-
23	Discrete sensitisation dermatitis	-	-	+	-
25	Allergic	-	-	-	+
26	Allergic	-	+	-	-
30	Neurogenic	+	-	-	-
40	Discrete sensitisation dermatitis	-	-	+	-
47	Fungous	-	-	-	+
48	Discrete sensitisation dermatitis	-	-	+	-
52	Discrete sensitisation dermatitis	-	-	+	-
68	Fungous	-	-	+	-
70	Discrete sensitisation dermatitis	-	-	+	-
74	Fungous	-	-	-	+
77	Discrete sensitisation dermatitis	-	-	+	-
91	Allergic	+	-	-	-

+ represents presence of factor

Number of cases having complex aetiological factors = 14

It has, therefore, been shown that in addition to those generally accepted, a 14% group exists which can be named the complex aetiological group because the cases included possess factors which could place them in more than one group.

Precipitating Factors

In the present series further to findings already presented other aetiological factors were brought to light which would seem to have been disregarded hitherto. They have been termed precipitating factors as they appeared to condition the onset of the eruption.

These factors seemed to operate in all groups and in their absence the eruption might not have arisen despite the existence of factors which are generally considered to be causal or intimately associated with the production of eruptions.

48% of cases were found to arise as the result of such factors which are classified as follows:-

1. Warm Weather.
2. Medicaments applied locally to skin lesions causing discrete sensitisation dermatitis.
3. Miscellaneous factors which included surgical operations, exposure of the hands to sunlight, local heat and cold weather.

The following tables enumerate cases and their corresponding precipitating factors:-

Table 26

Warm Weather as a Precipitating Factor

Group	Case No.	No. of Cases
Discrete sensitisation	9,57,82	3
Dermatitis venenata	6,13,89	3
Fungous	32, 47, 63, 68, 73, 96	6
Scabetic	34	1
Allergic	25*, 26, 28, 50, 54, 69*, 100	7
Neurogenic	37 (Thyrotoxicosis), 71	2
Idiopathic	5, 10, 41, 59, 61, 64, 92	7

* indicates multiple precipitating factors

Total number of cases precipitated by warm weather = 29

Table 27

Medicaments applied to skin lesions acting as precipitating factors by causing discrete sensitisation dermatitis

Case No.	Lesion	Local Precipitating Cause
2	Infective fissure	Local penicillin cream
17	Infective dermatitis	Siccolam ointment
38	Erythema multiforme	Penicillin cream
40	Nummular eczema	Copper oleate ointment
46	Infective dermatitis	Sulphonamide powder
52	Infective dermatitis	Penicillin cream
56	Infective dermatitis	Penicillin cream
67	Laceration	Sulphonamide powder
72	Traumatic dermatitis	Penicillin cream
77	Burn scar	Penicillin cream
78	Infective dermatitis	Sulphonamide powder
80	Infective fissures	Unknown ointment
85	Scald	Unknown ointment

Number of cases in which medicaments applied to the skin acted as precipitating causes of discrete sensitisation dermatitis manifesting itself as a sago grain vesicular eruption of the extremities = 13

Table 28

Miscellaneous Precipitating Factors

Group	Case No.	Precipitating Factor
Idiopathic	21	Tonsillectomy
Allergic	25 *	Mastoidectomy
Allergic	39	Sunlight on hands
Allergic	69 *	Local heat to extremities
Allergic	91	Abrasion of sole
Allergic	98	Cold weather

* indicates cases having multiple precipitating factors

Number of cases precipitated by miscellaneous factors = 6

The total number of cases, therefore, in the present series of a hundred cases having precipitating factors is given as follows:-

Number of cases precipitated by warm weather = 29
Number of cases precipitated by medicaments applied to the skin = 13
Number of cases precipitated by miscellaneous factors = 6
Total number of cases having precipitating factors = 48

Table 29

Number of cases in each group having precipitating factors

	Discrete Sensitisation dermatitis	Dermatitis Venenata	Scabetic	Fungous	Allergic	Neurogenic	Idiopathic
No. of cases	16	3	1	6	12	2	8
% of group	48.5	21.4	33.3	60	80	25	47.1

Table 29 indicates that in each aetiological group a substantial proportion of cases possessed precipitating factors which seemed to condition the onset of the eruptions, despite the existence of factors which are generally considered to be causal or closely associated with the causation of sago grain vesicles. It is apparent in these cases, therefore, that factors producing the eruptions do not act singly.

When the number of these cases is combined with that within the complex aetiological group (Table 25), the total is considerable.

The following calculation, which is necessary because of the multiple inclusion of cases in various tables, determines this figure as follows:-

Table 30

To show multiple inclusion of cases in Tables 25, 26, 27, 28

Case No.	Complex Aetiology Group	Precipitating Factors			
	Table 25	Table 26 Warm Weather	Table 27 Medicaments applied to skin lesions	Table 28 Miscellaneous	No. of times case is repeated in tables
25	+	+	-	+	2
26	+	+	-	-	1
40	+	-	+	-	1
47	+	+	-	-	1
52	+	-	+	-	1
69	-	+	-	+	1
77	+	-	+	-	1
91	+	-	-	+	1

Total number of repetitions in Tables 25, 26, 27, 28 = 9

Therefore total number of cases in which aetiology is complex, equals total in Tables (25, 26, 27, 28) minus number of times cases are repeated in tables which is 62 minus 9, equals 53.

Comment

It has been indicated, therefore, that in 53% of cases of sago grain vesicular eruptions of the hands and feet, there is evidence to indicate that the causation is not a single factor, but the complex interplay of more than one causal, associated, or group of factors.

Conclusions 1-14 refer to the aetiological investigation.

Please see Part 3, pages 114 - 117.

P A R T 2(b)

HISTOPATHOLOGICAL INVESTIGATION OF THE SAGO GRAIN VESICULAR ERUPTIONS OF THE HANDS AND FEET

For details of the methods and technique employed please see appendix No. 2

A short summary of the histological opinions and conclusions of the main authorities on the subject will now be given and a fuller account of their work where relevant will be presented.

T. Fox, Radcliffe Crocker, W. Williams, A.R. Robinson, Unna, Sutton, Sicoli, Peck and others have published accounts of special investigation into the histological nature of the lesions under consideration. At various times other eminent dermatologists have expressed opinions which shall be considered, although on many occasions they have not supported them by published histological evidence.

Sudoriparous Origin

That the primary lesion existed in the sweat apparatus was held by T. Fox (1873), Crocker (1878), Duhring (1881) (one type), Nesterjewsky (1906), Pusey (1917), Sicoli (1924) (dysidrosis), McCarthy (1931) (one type). Peck (1930), the chief proponent of the "id" concept (page 10), could not deny that some cases may be due to essential sweat retention (true dysidrosis).

Non-sudoriparous Origin

The conclusion that the lesions were not due to sweat retention (dysidrosis) was submitted by R.L. Sutton (1913),

Bacillary Origin

That lesions were the sequel to the initial activity of micro-organisms was advocated by Unna (1896) and more recently by Tibor Benedek (1942 and 1946).

Eczematous Origin

This is in accordance with the view of W. Williams (1891), Sicoli (1924) (pseudodysidrosis), Peck (1930) (most cases), McLachlan and Brown (1934), McLeod and Muende (1940), Sequeira (1947), Percival (1947) and others.

It is on the basis of the points mentioned in the above summary that the following scheme of investigation was undertaken:-

SCHEME OF HISTOLOGICAL INVESTIGATION

1. The correlation of clinical similarity of lesions with identical histology.

2. Relation of the sago grain vesicle of the hands to the intra-epidermal course of the sweat ducts.

3. The resistance of the intra-epidermal portion of the sweat ducts to changes found in the prickle cells in association with sago grain vesicles of the hands.

4. The normal histology of the intra-epidermal portion of the sweat duct and its relationship to an apparent resistance to disintegrative changes occurring in the prickle cells in association with sago grain vesicles of the hands.

5. The structure of the sago grain vesicle, its process and mechanism of formation.

6. The histological comparison between the sago grain vesicle and the vesicle of discrete sensitisation dermatitis.

7. The sub-corneal fluid filled recess of Unna.

8. Degrees of morbid change corresponding to cell morphology.

The following Tables 31 and 32 analyse the material utilised for the purpose of the histopathological investigation:-

Table 31

Biopsies of sago grain vesicles

Biopsy No.	Case No.	Condition with which sago grain vesicles were associated	Area from which tissue was excised	No. of serial sections examined	No. of isolated sections examined
1	2	Discrete sensitisation dermatitis	Dorsum of foot	0	1
2	14	Discrete sensitisation dermatitis	Palm	131	9
3	15	Discrete sensitisation dermatitis	Palm	140	8
4	16	Chronic flexural eczema	Palm	39	20
5	17	Discrete sensitisation dermatitis	Palm	11	7
6	18	Discrete sensitisation dermatitis	Palm	298	15
7	19	Palmar hyperidrosis	Palm	150	1
8	57	Discrete sensitisation dermatitis	Dorsum of hand	68	4
9	72	Discrete sensitisation dermatitis	Thenar eminence	179	0

Total number of serial sections of sago grain vesicles of hand and feet examined = 1016
Total number of isolated sections of sago grain vesicles of hand and feet examined = 65
Total number of serial and isolated sections of sago grain vesicles of hand and feet examined = 1081

Table 32

Biopsies of eczematous eruptions

Biopsy No.	Case No.	Condition with which sago grain vesicles were associated	Area from which tissue was excised	Lesion examined	No. of serial sections examined	No. of isolated sections examined
10	73	Sago grain vesiculation of extremities, discrete sensitisation dermatitis, tinea pedis	Anterior aspect of forearm	Area of discrete sensitisation dermatitis	212	4
11	101	Nummular vesicular eczema	Forearm	Area of moist eczema	14	2
12	101	Area of moist eczema	Leg	Area of nummular vesicular eczema	23	0

Total number of serial sections of eczematous conditions examined = 249
Total number of isolated sections of eczematous conditions examined = 6
Total number of serial and isolated sections of eczematous conditions examined = 255

Total number of sections examined for purpose of histological investigation =1336

THE CORRELATION OF CLINICAL SIMILARITY WITH IDENTICAL HISTOLOGY

McLachlan and Brown (1934) have drawn attention to the apparent identity of lesions and compare microphotographs of vesicles having scabetic, idiopathic and occupational origins and two found in association with eczema of other parts. Their photographs would appear to differ in no way from the vesicular eruptions as reproduced by Peck (1930) which were considered to be of fungal origin. This apparent identity is supported by examination of many lesions in the present series where no essential difference was ever determined as exemplified from the study of the following microphotographs.

Plate 19 represents a section through a sago grain vesicle of the hand, the lesions having arisen in the absence of an apparent cause, the only other associated abnormality being palmar hyperidrosis.

Plate 23 reproduces an apparently clinically identical lesion arising in association with a widespread sensitisation skin eruption of the papulo-vesicular type which followed the development of an infective dermatitis.

The appearance in both cases are those of rounded multilocular fluid filled spaces containing the rudiments of degenerated prickle cells and confined to the prickle cell layer, the corium in both cases showing minimal non-specific change.

Plate 15 demonstrates a further lesion which was unassociated

with apparent cause, the only other conspicuous abnormality being palmar hyperidrosis.

Plate 30 shows a lesion which arose in conjunction with a generalised sensitisation eruption of the papulo-vesicular type following upon history of skin trauma.

Comparison between these two latter specimens can bring to light no essential difference though Plate 30 demonstrates more marked changes in the corium which consist of slight vascular dilatation and round cell cuffing of blood vessels.

Similar comparisons were made between numerous other specimens and no essential differences were ever apparent. Slight differences, when they did arise, were confined to the corium, but were never constant even in cases of apparently similar aetiological origin (contrast Plates 12 and 21).

Comment

The histological identity of sago grain vesicles, irrespective of apparent aetiological origin, has been confirmed. It will further be shown that, in addition to histological identity, lesions differing aetiologically have a constant relationship to the intra-epidermal course of the sweat ducts.

RELATION OF THE SAGO GRAIN VESICLES OF THE HANDS TO THE INTRA-EPIDERMAL COURSE OF THE SWEAT DUCTS

T. Fox and Radcliffe Crocker (1877), after examining seventy

to eighty specimens, concluded that sago grain vesicles of the hands were due to sweat retention in the sweat ducts at the level of the rete Malpighii in the light of the following findings:-

1. All but two of the vesicles examined were in relation to papillae.

2. Distention of sweat ducts could be seen in the upper parts. Globular dilatations were sometimes observed at the central point of the vesicular summits.

3. "The central axis of the vesicles were opposite to the continuation in the rete answering to the normal spot where the sweat coil entered this layer from above".

Again Fox (1878) demonstrated from a drawing of a specimen the continuity of the sweat duct with a small vesicle.

Nesterjewsky (1906), after studying 2,864 sections from six typical lesions, concluded that changes present resulted from a retention of sweat in the duct at mid rete level. As a result, distention occurred and subsequent rupture caused sweat extravasation amongst the prickle cells producing necrosis of the latter. The blockage of the ducts was, in his opinion, the result of plugging by masses of detached and swollen horny substance.

Sicoli (1924) classified the eruption as 'pseudo-dysidrosis' and true 'dysidrosis.' His findings regarding the latter type supported those of Nesterjewsky. In his publication he produced a photograph showing a sweat duct in apparent continuity with an early vesicle.

Peck (1930), though finding nothing to indicate that the essential cause of the sago grain lesion was a sweat retention, was hesitant to refute the existence of true dysidrosis in some cases where the cause was unknown and conceded that a few cases of vesicular eruption of the hands may have an origin in the sweat apparatus.

Other authors of eminence who have not published special histological findings have expressed opinions as follows:-

Duhring (1881) believed that two diseases existed, viz. one due to a disordered sweat apparatus and another to a different cause which he did not specify.

Pusey (1917) maintained that the sago grain eruption of the hand was analagous to the lesion of miliaria, a condition which Pollitzer (1893) and others on histological grounds attributed to sweat duct occlusion.

McCarthy (1931) thought that only some sago grain vesicles resulted from sweat retention.

Blaisdell and Schwartz (1945) stated that they were carrying out histopathological studies of the sweat ducts in relation to such vesicles arising as a complication of previous chronic irritation of the skin originating in industrial or private life.

Sulzberger and Baer (1948) indicate that their views support the dysidrotic theory. They suggest several lines of investigation which might be adopted regarding the mechanisms which possibly

operate to produce sweat duct occlusion in conditions which they classify as "dysidrotic eczema".

Authorities, who do not necessarily classify the lesion as one of the sweat apparatus, have, at times, indicated some relation to sweat ducts without further comment as is evident from the following findings mentioned in the literature:-

A.R. Robinson (1885) referred to a section where the sweat duct was the principal structure between two vesicles apparently delaying their union.

Radcliffe Crocker (1893), who at this period maintained that the lesions were intimately related to the sweat apparatus, remarked that occasionally a duct could be traced between vesicles.

Unna (1896) pointed out that the vesicles often lay quite close to the sweat pores which were pressed aside and diminished in size forming wide loops around the former.

R.L. Sutton (1913) admitted that sweat ducts might be implicated accidentally.

Apart from the above four references, it seems strange that continuity or close relationship between ducts and vesicles has not been more commonly demonstrated as, according to McLeod and Muende (1940), about 3,000 sweat ducts are present per square inch on the palms of the hands. If a vesicle be the size of a pin's head (approximately 1/16th of an inch) and it is assumed that the ducts are evenly scattered over the skin, it would mean that such

a small vesicle would be in close proximity to four sweat ducts as the distance between the latter by calculation would be approximately 1/55th of an inch. The mathematical possibility, therefore, of a small vesicle accidentally cutting across the path of several ducts is probably very great. Having this possibility in view, it is surprising that those who have refuted the dysidrotic theory have not considered more often the problem of determining whether or not the existence of a vesicle cutting across the path of a sweat duct is due to duct distention, or rupture or to accidental disruption by implication within the vesicle. In view of this noticeable lack of comment on continuity between duct and vesicle, investigation was undertaken with reference to ducts in the neighbourhood of vesicles.

Only small lesions were studied as it appeared that disruption of ducts found in association with large vesicles could be attributed to stretching resulting from the vesicle expansion.

Serial Section of a Small Vesicle in relation to a Sweat Duct

Plate 8 shows the first section of serials taken through a small vesicle which is indicated by the arrowhead.

Note: The section prior to this one (Biopsy 9 Case 72 Slide 4 Section 10) passed beyond the periphery of the vesicle, no part of the latter or any sweat duct being seen.

Plate 9 The vesicle is now seen at a slightly deeper level but still having no relationship to the sweat apparatus.

Plate 10 indicates the portion of the intra-rete course of a sweat duct, but it would appear to be entirely unconnected with the vesicle.

Plate 11 This photograph shows the greater course of the duct in the rete and, although close to the vesicle, no communication is seen.

Plate 12 The vesicle has now passed out of the plane of section. At the same level as in the previous section, part of the sweat duct is visible, but a further high power photograph (Plate 13) demonstrates that its structure is intact and consequently it could not have been in continuity with the vesicle.

Plate 13 As already indicated, this plate is a high power reproduction of the previous section to show that the duct is intact at the level of the vesicle, suggesting that the two are not in communication. Normal cohesion of cells around the duct at this level would appear to exist and no abnormal fluid spaces can be seen between them.

Note: The arrowhead indicates the point where the duct is cut across and becomes continuous with the portion shown on Plate 11.

Comment

A complete series of sections passing through a small vesicle at every level indicates that no connection exists between it and the intra-epidermal portion of a sweat duct in close proximity.

Serial section examination demonstrates that no other duct was in any way connected with this vesicle. No evidence exists to suggest that fluid has been extravasated from the duct at any part of its course throughout the epidermis.

Further Sections through Vesicles in relation to Sweat Ducts

The microscopic sections, to which reference will now be made, will serve to indicate in other specimens the same apparent lack of direct connection between the intra-epidermal portion of the sweat duct and vesicles, including lesions which have arisen under apparently different aetiological circumstances.

Plate 14 A complete series of microscopic sections through the vesicle shown can be examined from biopsy 9 case 72 slide 6 section 2 to slide 7 section 1. The microphotograph shows the only sweat duct found in relation to the vesicle. At all levels no connection was demonstrated. The duct and its surrounding prickle cells are apparently normal whereas adjacent prickle cells show signs of degeneration.

Plate 15 Serial sections of the vesicles shown demonstrate that, although close proximity between vesicle and duct exists, any communication would appear to be absent. The portion of the duct shown is actually passing between the walls of two vesicles. The relatively pale cells to the right of the portion of the duct, indicated (x), represent the wall of a vesicle cut in a tangential plane. At the point marked by the arrowhead the duct is cut

transversally in the mid prickle cell zone. A darkened line of relatively compact cells is seen to follow its main course suggesting that, of all the cells in a portion of the rete showing degenerative changes, they are apparently least affected. The portion of the sweat gland glomerulus would appear to be normal, no cellular infiltration being present.

Plate 35 demonstrates a vesicle in an apparently early stage of development. Examination of all serial sections through it failed to demonstrate the presence of a sweat duct.

Plates 8 (lesion marked by arrowhead) - 15 & 35 represent sections from cases of sago grain vesicular eruption of the hand arising under apparently different aetiological circumstances, Plate 15 demonstrating a lesion arising without apparent cause, the only other conspicuous abnormality being palmar hyperidrosis and the others representing lesions which have occurred in association with generalised papulo-vesicular sensitisation eruptions. In all cases the vesicles would appear to be independent of sweat ducts. There is a suggestion that the rete in relation to a sweat duct in one specimen (Plate 15) shows less degeneration than surrounding cells as indicated by its more deeply staining character.

Comment

At this point it has so far been demonstrated from specimens that no connection would appear to exist between vesicles of the sago grain type affecting the hands and the intra-epidermal portion

of the sweat duct even where lesions appeared to be idiopathic and associated with palmar hyperidrosis. No evidence could be detected to suggest that sweat had been extravasated from related ducts as their structural lining was seen to be normal and intact and no abnormal fluid spaces were seen between the prickle cells immediately surrounding them.

THE RESISTANCE OF THE INTRA-EPIDERMAL PORTION OF THE SWEAT DUCTS TO CHANGES FOUND IN THE PRICKLE CELLS IN ASSOCIATION WITH SAGO GRAIN VESICLES OF THE HANDS

The apparent fact that continuity of vesicles and ducts does not exist despite the marked mathematical possibility of lesions cutting across their paths would appear to suggest that the ducts and their surrounding prickle cells offer some resistance to the processes associated with vesicle development. This section is an endeavour, by means of microphotographs, to demonstrate that such a resistance is offered by the intra-epidermal portion of the sweat duct to these morbid changes affecting the adjacent rete.

Plate 14 demonstrates a sweat duct passing between the walls of two vesicles, the cavity of the one on the right being plainly shown. To the left of the duct the pale cells of a vesicular wall are visible, the plane of section having passed tangentially to it and missing its cavity. The sweat duct and its surrounding prickle cells appear normal and the adjacent cells show a varying degree of degeneration.

Plate 15 shows a similar, but less marked, example of a sweat duct and its surrounding prickle cells (relatively dense area) passing unaffected between the walls of two vesicles, the cavity of the one on the right not being shown as again the section passes tangentially to its wall, the cells of which would appear to be in a state of degeneration.

Plate 16 Serial sections demonstrated that the sweat duct shown passed through the cavity of the vesicle, the portions of the latter on either side of it being really part of the same cavity. The specimen serves to demonstrate an apparent resistance of the intra-rete portion of the sweat duct to the process which operates in vesicle formation.

Plate 17 The only sweat duct seen in the vicinity of these vesicles passes between them. The section subsequent to this one (Biopsy 7 Case 19 Slide 2 Section 3) demonstrated a small vesicle apparently in the line of the duct, but serial sections followed back from the present one demonstrate that the duct lies entirely on a different plane. This sweat duct and its regional prickle cells were seen to be threaded, apparently unaffected, through an area almost completely excavated by vesicles.

Plate 18 A sweat duct is seen passing within the partition of a multilocular vesicle, the breadth of the partition being barely sufficient to accommodate the duct. Serial section examination indicates that in its entire course it remains extra-vesicular

Plate 19 A similar arrangement is demonstrated in this photograph. Two sweat ducts are shown. The one on the right can be seen throughout its course passing within the partition of prickle cells. The duct on the left, though less obviously doing so in this photograph, is seen to pass through the partition in its entire course in the subsequent two serial sections. The partitions are again no greater in breadth than that of the ducts.

Plate 20 The resistance of the sweat duct and its surrounding prickle cells is further demonstrated. The duct passes between two vesicles; the cavity of that on the right is not shown for again the plane of section has passed tangentially to its wall. The sweat duct throughout its course appears normal, the only prickle cells not involved in the whole area being those surrounding this structure and which pass through the affected area as a dense core of apparently normal prickle cells.

Plate 21 Three sweat ducts are seen in relation to this vesicle, two passing within the wall and another in the partition dividing the loculi. The middle duct passes along the thin floor separating the vesicle from the corium.

Plate 22 The sweat duct shown, when traced serially, was seen to pass between the vesicle at all stages of its intra-epidermal course, the duct and its surrounding prickle cells forming a dense core in the midst of an isthmus of prickle cells showing early degeneration.

The vesicles demonstrated in the following two specimens were

intravitally injected with 0.5% aqueous trypan blue.

Plate 23 The arrowheads indicate a sweat duct passing between two vesicles. Only another example of the dye passing into a duct was seen in all the serial sections prepared from this tissue. Nothing existed to suggest that the dye gained access to the duct other than by direct diffusion through the tissues and also to some extent on account of an affinity of the intra-epidermal portion of the ducts for the dye.

Plate 24 This section, following intravital injection of trypan blue, demonstrates a duct passing through the cavity of a vesicle, all its surrounding prickle cells having been involved in the reaction, leaving the sweat duct to withstand the pathological process.

Plate 25 This is a high power photograph of a multilocular vesicle cut in transverse section. A sweat duct, indicated by the arrowhead, is seen cut transversely in one of the dividing partitions. The bulging of the part corresponding to the sweat duct probably indicates resistance to the pathological process and perhaps also a relative rigidity of the sweat duct structure.

Comment

The study of the foregoing specimens in this section demonstrates an apparent resistance of the intra-epidermal portion of the sweat ducts to the morbid process involved in the formation of sago grain

vesicles.

THE NORMAL HISTOLOGY OF THE INTRA-EPIDERMAL PORTION OF THE SWEAT DUCT AND ITS RELATIONSHIP TO AN APPARENT RESISTANCE TO DISINTEGRATIVE CHANGES OCCURRING IN THE PRICKLE CELLS IN ASSOCIATION WITH SAGO GRAIN VESICLES OF THE HANDS

At this stage the morbid process involved in sago grain vesicle formation has not yet been discussed, but it is evident from examination of any lesion so far demonstrated that degeneration of foci of prickle cells has occurred. It has again been observed in the preceding sections dealing with the relationship of vesicles to ducts that this degeneration, whatever be its cause, fails, originally at least, to disturb the cohesion of the sweat ducts. This apparently singular resistance of the latter structures was the subject of further investigation to determine whether or not any essential character of the normal structure of these ducts and surrounding cells rendered them different from the prickle cells implicated in the process of vesiculation.

Way and Memmesheimer (1936), referring to the intra-epidermal portion of the sweat duct, stated that the cells forming its wall are concentrically arranged in two or three layers, are flat and contain eleiden granules.

Pinkus (1939) presented evidence which, he considered, indicated that in their intra-epidermal course the sweat ducts were lined by their own particular epithelium. He maintained that such a duct lining was suggested microscopically and that its component cells

differed from the surrounding prickle cells in that they possessed no tono-fibrils. The main argument in support of his contention, however, was based on the histological findings in some diseases where the pathological process seemed to be essentially confined to the prickle cells. In these conditions the component cells of the corresponding portion of the sweat duct seemed to escape the morbid changes of the surrounding prickle cells. His evidence in this connection may be summarised as follows:-

1. In pigmentary diseases melanin is found in the prickle cells, but not in the lining cells of the sweat ducts.

2. The cells surrounding the sweat ducts would appear to escape the anaplasia of the prickle cells in senile keratosis and Bowen's disease.

3. In generalised exfoliative dermatitis the ostia of sweat ducts appeared to form normal keratin.

4. In some vesicular conditions, e.g. acute vesicular eczema, the prickle cells around a duct may disappear leaving the latter structure intact.

MacLeod and Muende (1940) stated that the intra-epidermal portion of the sweat duct "is represented simply by a spiral cleft between the prickle cells of an interpapillary process. Towards the surface the transitional layers acquire a thin lining of the stratum granulosum which dips down to form a funnel for the duct".

O'Brien (1947) produced a microphotograph of a sweat duct in its intra-epidermal course. He indicated a layer of stratum granulosum around one of its uppermost loops, but commented no

further upon this feature.

Maximow and Bloom (1948), referring to the same portion of the sweat duct, state that in the epidermis the duct is devoid of a wall of its own and is simply an intercellular channel surrounded by concentrically arranged epidermal cells.

Ormsby and Montgomery (1948) do not commit themselves regarding the structural lining of the intra-epidermal portion of these ducts and merely refer to Pinkus who emphasised that they possessed an epithelium of their own and to others who regard it as a channel without walls.

It is evident from the foregoing notes that as yet no fixed opinion exists regarding the structure of the sweat duct as it passes through the epidermis. Some maintain that it is represented by clefts without walls in the prickle cell layer and others that a special lining epithelium exists whilst there are those who have made some allusion to a layer of surrounding stratum granulosum cells in its intra-epidermal course.

With the above conflicting hypotheses in view, some ducts were carefully examined by serial sections, the findings being demonstrated as follows:-

Plate 26 The intra-epidermal course of a normal sweat duct is demonstrated. As it passes through the stratum granulosum in a downward direction, it seems to become enveloped in this layer and, subsequently at all levels shown in the section, granulosum

cells are seen to constitute its wall though the granular appearance diminishes the deeper it passes into the rete.

Plate 27 Again a normal duct is seen under high power and, as in the previous section, its wall appears to consist of stratum granulosum. The granular appearance lessens in intensity the deeper the level in the rete, though it is still present at a very deep level, viz. in one of the rete pegs. The prickle cells immediately adjacent to its walls are compact and somewhat spindle shape.

Plate 28 The apparent stratum granulosum structure of the sweat duct wall is again demonstrated. Though once more less marked the deeper their level, granulosum type cells are still present at the level of the rete pegs. The prickle cells adjacent to the walls on section are of a spindle shape whereas those of the normal prickle cells can be seen to be polyhedral.

Plate 29 As was the case with some sweat ducts, a transition from basophilic to eosinophilic staining was noted in the granules of the cells of their limiting walls, in the deeper layers of the rete. The red ink marks demonstrate roughly the position of such granules as seen microscopically.

Comment

From a survey of the preceding specimens it would appear that in the greater part of their intra-epidermal course the walls of the sweat ducts are composed of stratum granulosum. These cells,

unlike normal prickle cells, apparently possess no tono-fibrils and in this respect are similar to the granulosum cells immediately adjacent to the stratum lucidum. The prickle cells surrounding them are somewhat flattened and would appear to be more compact than other prickle cells (vide Plates 28 and 29). Their appearance and relationship to stratum granulosum cells of the ducts would suggest morphological similarity to the few layers of cells which in the epidermis underlie the normal stratum granulosum proper.

In many cases granules in the cells lining the sweat duct can be traced to the deepest loop in the rete, but in all cases the number of granules per cell would appear to diminish with the depth in the rete. In some cases a transition in the staining reaction of these granules was noted; in the upper parts they took up the basic stain and in the lower they seemed to have affinity for the eosinophilic stain.

The presence of granules within the cells forming the walls of the intra-epidermal portion of the sweat ducts indicates that these cells differ from the surrounding prickle cells and that they probably correspond morphologically to those of the stratum granulosum. It is probable, therefore, that the relative resistance of the sweat ducts to the morbid changes affecting the prickle cells proper depends on this histological difference.

THE STRUCTURE OF THE SAGO GRAIN VESICLE, ITS PROCESS AND MECHANISM OF FORMATION

From a survey of the literature detailed accounts of the structure of the vesicle would seem to be lacking, apparently because of concentration of study on the relationship which might exist between sweat duct and lesion. Even those whose conclusions are at variance with a sudoriparous origin often lack detail in their descriptions of the average lesion.

A.R. Robinson (1877) maintained that the process of vesiculation consisted of an escape of serum and white blood cells from the vessels of the papillae, which, forcing its way through the rete, pressed its cells aside and so collected in the form of vesicles. Apart from considerable round cell infiltration in its upper part, the corium was otherwise normal.

W. Williams (1891) concluded from examination of two hundred and twenty-nine sections prepared from three tissue specimens of his own skin that the condition was akin to eczema and resulted from an infiltration of "lymph and leucocytes" into the rete causing a subsequent swelling of the prickle cells and their later separation in clumps which formed reticulated areas within vesicles.

Unna (1896) described the sago grain lesions in more detail, but was of opinion that the essential site of origin was the area adjacent to the lower limit of the stratum corneum from where the vesicles extended to implicate the prickle cell layer. He was

strongly of opinion that the morbid process was caused essentially by the activity of micro-organisms not unlike the tubercle bacillus. He described changes in the corium consisting of flattening of the papillary bodies and slight vascular dilatation associated with some lymphocytic infiltration.

Sutton (1913) examined 2038 serial sections from nine specimens and concluded that changes in the epidermis were almost entirely in the prickle cell layer, those in the corium consisting only of slight perivascular infiltration.

Sicoli (1924), after careful investigation, concluded that in the case of lesions which did not arise in association with the sweat apparatus their origin was identical with that of eczema and resulted from spongiosis.

Peck (1930) maintained that in the majority of cases the sago grain vesicles arose originally as multiple foci of hydropic swelling of prickle cells with associated intercellular oedema. Polymorphonuclear leucocytes invaded the cutis at an early stage and in the corium the blood vessels were dilated and often showed perivascular infiltration of polymorphonuclear leucocytes and lymphocytes.

McCarthy (1931), whose opinion was similar to that of Sicoli (1924), considered that in some cases lesions were not due to essential disorder of the sweat apparatus, but were essentially identical to eczema vesicles. They lay under the horny layer and might occupy the entire thickness of the rete. The vesicular

contents consisted of fibrinous exudate and polymorphonuclear leucocytes, the cells of the walls showing degenerative changes attributable to pressure atrophy. In the corium the papillae were dilated and the lymphatics were surrounded with moderate cellular infiltration consisting mainly of polymorphonuclear leucocytes with associated oedema. Fungi could sometimes be demonstrated in vesicular roofs.

MacLachlan and Brown (1934) concluded that the changes producing vesicles of the sago grain type on the hands were the same as those causing the eczematous reaction and that the vesicles arose in association with areas of spongiosis.

Percival (1947) regarded the "pompholyx" vesicle as being identical with that of eczema as evoked by chemical irritation, but on account of the thickness of the horny layer of the hand, the development of structurally intact vesicles was ensured.

From the above summary of the findings of those who have attributed an origin other than sudoriparous to lesions of the sago grain type affecting the hands, it seems that a substantial bulk of opinion regards the eruption to be of the "eczematous type" affecting mainly the prickle cell layer. On the other hand Unna regarded the lesion as being the sequel to the activity of micro-organisms just deep to the stratum corneum and Sutton, though refuting the dysidrotic theory, did not commit himself as to its identity. It would appear further that a certain paucity of

descriptive detail exists in the literature regarding its structure and the sequence of events leading to its formation.

Having regard for these apparent deficiencies in the literature, the following sections of the thesis were undertaken to determine:-

(a) The histological structure of the vesicle.

(b) The process and mechanism of vesiculation.

(c) The connection, if any, between the vesicle and the eczematous reaction by histological comparison between the sago grain vesicle and the vesicle of discrete sensitisation dermatitis.

THE STRUCTURE OF THE SAGO GRAIN VESICLE

Plate 70 This specimen was chosen because it represents a characteristic vesicle. Serial section, as with all vesicles examined, demonstrates its essential confinement to the prickle cell layer, except at the summit of its roof where communication is established through a cleavage with a little fluid filled recess lying under the stratum corneum. The vesicle consists of a rounded cavity containing fluid and numerous prickle cell rudiments. The walls are of rounded contour and constituted by several layers of apparently elongated prickle cells, their long axes being arranged longitudinally. Maximum apparent elongation would appear to be present in the cells of the lateral walls. In the floor, though less evident, it would appear to be fairly marked. In the few layers of prickle cells forming the vesicular roof in this section apparent elongation would seem to be only slightly more marked than is the case normally with cells in that part of the rete. Spaces

apparently greater than those between normal prickle cells can be seen between those constituting the lateral walls. Regarding the apparent cleavage in the vesicular roof, fuller reference will be made in a subsequent section, but at this stage it will be recorded that most lesions, no matter how small, studied in serial section, communicated at their summits with little fluid filled recess underlying the stratum corneum. As is characteristic of most vesicles, bulging would appear to be greater in the direction of the corium than towards the surface due to flattening of the papillary bodies.

The vesicular content consists of a free fluid fraction and one consisting of the rudiments of degenerating prickle cells. As in the majority of vesicles examined, the only discernible rudiments present were pyknotic nuclei.

Comment

The specimen from which the above findings have been recorded demonstrates items of structure in a general manner, but now certain features will be analysed in greater detail and findings recorded from other specimens will be corellated with them under the following headings:-

1. The apparent elongation of cells in the vesicular walls and the apparent cleavage between them.

2. The vesicular contents.

The Apparent Elongation of Cells in the Vesicular Walls and the Apparent Cleavage between them

From examination of an isolated section such as demonstrated in the previous Plate 30, it is not possible to be certain whether or not apparent elongation of cells of the vesicular wall is due to actual elongation or is merely the picture produced by flattened cells cut longitudinally in section at right angles to their flattened surfaces and viewed on their cut edges.

Plate 15 and Plate 20 The areas marked "x" represent the walls of vesicles which have been cut tangentially. The cells on close examination, although their outlines in some cases have been rendered less clear on account of apparent degeneration, are seen to be elongated.

Plate 31 This microphotograph shows the cells in a vesicular wall, the section passing tangentially to its surface. The cells are clearly seen to be elongated in a direction longitudinal to the vesicular cavity and are similar in this respect to those of the lateral wall as shown in Plate 30. At every level of the vesicular wall cut tangentially in this specimen and most other specimens examined, the cells had an apparently elongated appearance. This finding would seem to indicate that the cells constituting the vesicular walls are probably essentially elongated. Had they been flattened, tangential sections to the vesicular walls would show mainly cells whose lengths and breadths were approximately the same.

Further examination indicates that definite spaces would appear to exist between the individual prickle cells of the vesicular wall. That some of the cells in the vesicular wall have undergone degeneration can be determined from the relative pallor of their staining reaction and from the reduced cell definition present.

Plate 32 represents another section taken tangentially to the wall of a small vesicle. Whereas the cells of the portion representing the lateral wall are less elongated than those of the previous plate, close examination shows that they have elongation in a direction longitudinal to the limits of the vesicular cavity and, in addition, marked spaces can be seen between some cells, apparently due to destruction of others. The spaces visible would appear to be greater than those between the apparently normal prickle cells on other parts of this photograph.

Plate 33 This specimen reproduces the common wall of two vesicles, the cells of which demonstrate apparent elongation as seen in longitudinal section, distinct spaces being visible between them. These again are apparently greater than those between normal prickle cells seen just to the right of the mid line in the upper portion of the photograph (marked "x"). As is the case with most vesicles examined, many cells in the vesicular wall are in a state of cytoplasmic degeneration.

Comment

It has been inferred, therefore, from serial sections taken

tangentially to vesicular walls that the cells forming these structures are probably elongated and not essentially flattened as might be suggested by the study of isolated sections through the vesicular walls. The cleavage between these cells would appear to be greater than that between normal prickle cells, many of which are observed to be in a state of degeneration. Further reference to the cleavages within the vesicular walls will be made subsequently in this section.

The Vesicular Contents

Plate 33 The vesicle (v) on the right hand side is seen to contain a free fluid fraction and one of degenerate prickle cells. As was characteristic of the great majority of vesicles, the only rudiments recognisable were the pyknotic nuclei of degenerate prickle cells, their cytoplasmic portion having in most cases disappeared.

Only rarely were migratory cells from the blood found within vesicles. These consisted mainly of lymphocytes, but occasionally polymorphonuclear leucocytes were found.

Plate 30 further demonstrates the components of the content of most vesicles, viz. the free fluid fraction and the rudiments of degenerate prickle cells consisting chiefly of pyknotic nuclei.

Comment

The two foregoing plates exemplify the nature of the vesicular content, as it was observed almost universally in all

vesicles examined, consisting, as it does, of a free fluid fraction and rudiments of degenerated prickle cells.

PROCESS OF VESICULATION

A striking feature was the lack of intermediate stages from foci showing early changes to vesicles of a fully developed type such as, e.g. Plates 30 and 33. Very few specimens of apparently early stages were seen in the many lesions examined, but the few discovered by serial sections of tissues serve as a link in the elucidation of the process which operates in vesicle formation.

In an endeavour to study the initial stages of vesiculation, the first aim was to examine in detail areas of spongiosis to establish, if possible, a similarity to the eczema vesicle. Numerous areas answering to the usual description of intercellular oedema were observed, but when followed by serial sections they were found to represent the walls of fully developed vesicles cut tangentially.

Plate 32 shows a focus of cells undergoing degenerative changes with increased fluid spaces between them, but subsequent serial sections indicate that the area shown represents the wall of a vesicle which has been cut in a tangential plane.

Similar findings have recently been recorded by Percival (1949). He has pointed out that areas of spongiosis, which have hitherto been regarded as the origin of eczema vesicles, are in fact, the appearances presented by the walls of vesicles cut in a

tangential plane.

In the present series, however, several early lesions were found in which the vesicular cavity had not formed. Though the prickle cells in these foci showed degenerative changes, some cohesion between the affected cells still remained and thus presented some insight into the early sequence of events occurring in the process of vesiculation.

Plate 35 shows a small area where a few prickle cells have degenerated to various degrees. It would appear in this specimen that the increased fluid spaces to a great extent represent areas which have been created by degenerating prickle cells. Apparently increased fluid spaces can be seen between normally staining prickle cells which still maintain continuity of prickle fibres, but examination of these cells indicate that they are more elongated than other surrounding prickle cells (elongated cell marked by arrowhead). Serial section of this lesion indicates that the cleavages between cells in the affected area are in communication with the surrounding tissue fluid.

Plate 36 This specimen would appear to demonstrate the process in operation at an intermediate stage of vesicle development for, though many of the rete rudiments suggest an advanced degree of degeneration, a fairly marked cohesion remains in the affected part. The cytoplasmic portion of the majority of cells has disappeared, but some cell rudiments still retain a fair bulk of their cytoplasm which, from its pallor of staining, suggests degeneration.

The cytoplasmic degeneration of the cells in the area uncovers what would appear to be much of the normal structure of the rete as a degenerative process at this stage has affected the rete cells in a selective manner causing degeneration of their cytoplasm, but leaving many of the tono-fibrils intact. From examination of this specimen, therefore, it would appear that the morbid process involved in the production of the sago grain vesicle is one, first of degeneration, affecting the cytoplasm of the cell, leading to its disintegration, being followed in turn by disruption of the tono-fibrils which causes solution in the continuity of the affected part of the rete.

Comment

It has, therefore, been deduced from the findings just exemplified that the morbid change initiating vesicle formation is probably that of a degeneration of foci of prickle cells, affecting them in the following sequence:- (1) Cytoplasm (2) Tono-fibrils (3) Nuclei.

Normal Structure of the Rete as deduced from changes seen in Cytoplasmic Degeneration

As a result of the selective degeneration which would appear to have occurred in the cytoplasm of the prickle cells shown in Plate 36, the fibril connections of the cells are particularly well demonstrated.

It has long been established that the network of spongioplasm

of the prickle cells stretches beyond the cells in the form of fine radiating protoplasmic threads which pass across the intercellular spaces as tono-fibrils and become continuous with the spongioplasm of neighbouring cells (MacLeod and Muende (1940)). According to Maximow and Bloom (1948) the intracellular fibrils are arranged in parallel bundles, particularly in the peripheral layer of the cell body. Their illustrations indicate that these fibrils are parallel to the cell surface.

Plate 36 shows fibrils in some cells arranged in a radial fashion and appearing to converge on the nuclear surface.

High power fields reproduced in Plates 37 and 38 demonstrate the same cell marked "x" in different focus. Fibrils are seen converging on a nuclear body and ramifying over its surface. Similar arrangements can be seen on other cells. Though not clearly shown on the photographs, the fibrils are seen under the microscope to have little nodal structures on their surface in relation to their course over the nuclear body.

Comment

The fibril connections of the normal rete have been demonstrated in a selective cytoplasmic degeneration. Confirmation of intercellular connections have been shown and radial convergence of fibrils from the periphery of the cells to their nuclei was observed. The fibrils on the nuclear wall appear to ramify freely.

The Corium

As has already been indicated, pages 81, 82, 83 most authorities agree that some degree of vascular dilatation is present within the corium together with cellular infiltration of varying degree, the majority maintaining that the predominant cell is the lymphocyte, whilst others lay stress upon polymorphonuclear leucocytes (vide pages 81,82,83). In the present series changes in the corium were moderate or minimal and consisted of slight vascular dilatation and round cell infiltration. One case (Biopsy No.8) examined, where clinically some lesions regional to those removed were obviously pustular, showed many polymorphonuclear leucocytes within the vesicular cavities and in the corium. In no case was oedema of the corium observed. The elastic tissue and collagen in all cases stained by orcein and Van Giesen stain reacted normally and had a normal appearance (vide appendix 2).

No essential change was ever observed in the glomeruli of the sweat apparatus or in the subcutaneous portion of the ducts. Some round cell infiltration was present around the structures of the sweat apparatus only when this represented part of a general infiltration.

Plate 15 shows no discernible reaction of the blood vessels and no infiltration in relation to the sweat gland.

Plate 30 presents only minimal vascular dilatation with slight round cell infiltration in the papillae and around deeper vessels.

Comment

From observations it has been deduced that changes in the corium are only slight and non-specific and the part of the sweat apparatus in this area shows no essential change. Oedema of the corium is not a feature in relation to the sago grain lesion.

MECHANISM OF VESICULATION

According to Robinson (1877) the mechanism of vesiculation consisted of fluid being forced into the rete from the corium pushing the cells aside and collecting as vesicles. Similarly Williams (1891) maintained that the fluid passed from the corium and that its presence there caused changes in the prickle cells consisting of compression and subsequent destruction. Neither of these authors substantiated their explanations by histological evidence though Robinson determined from biochemical examination that the concentration of albumin in the vesicular fluid was equal to that of blood serum.

From examination of specimens in this series no evidence could be brought to light in support of the contentions of Robinson and Williams which might suggest that the vesicle was essentially due to fluid influx from the corium. In specimens examined changes in this layer were often minimal and non-specific and no evidence existed to indicate that a fluid stream had its source from this part.

Percival (1947) regarded the "pompholyx" vesicle as being

identical with that of eczema as this is evoked by chemical irritation. In the same work he discusses the mechanism of vesiculation as applied to eczema and states "the factor which attracts fluid into the epidermis must, therefore, be some physico-chemical force which has developed as a result of localised necrosis and liquefaction of epidermal cells which is revealed by histological studies".

The conception of a physico-chemical force in this article received little substantiation. In 1949, after studying serial sections of eczema vesicles, he states "these serial sections give no indication as to how eczema vesicles are formed". This would appear to be pertinent to his conception of sago grain vesicle formation for he classifies "pompholyx" with reactions of the eczematous type.

In connection with sago grain vesicle formation, practically no reference, apart from statements such as those of Robinson and Percival, seem to be recorded in the literature except by those who have described the mechanism along the lines of sweat retention.

In the present series, however, it was considered that some indication as to the mechanism of sago grain vesicle formation could be deduced from the observations recorded.

From examination of specimens, it is apparent in each vesicle that many prickle cells have undergone degeneration. It can be deduced, therefore, that, as a result, a space must have been created

in the rete. An example is indicated in Plate 35 suggesting that the fluid spaces seen, to a great extent, might be attributed to cellular disintegration. Examination of a section such as Plate 34 indicates from the depth of the vesicle in comparison with the adjacent, apparently unaffected rete, that any potential space caused by cell destruction could only in part be responsible for the fluid space now present.

That the other factor is probably not physico-chemical (Percival), but of another nature, will now be shown. It has already been inferred that the cleavage between the cells of the vesicular walls might be greater than that between the normal rete cells. It would, therefore, seem that no barrier, even of a semi-permeable type which could induce an osmotic process, can be detected, as spaces between cells are clearly visible and the dissolved protein molecules are not. The suggestion is that the obstruction to the passage of fluid, into or out of a vesicle, is no greater than that between the normal prickle cells on the periphery of its wall. It follows, therefore, that, as the vesicular fluid is probably in continuity with that of the surrounding tissues, the pressures might be equalised throughout.

Having inferred that the intravesicular pressure may be equal to that of the surrounding tissue fluid, it is the intention to corellate this possibility with other findings and outline a possible mechanism of vesiculation.

That the vesicular and tissue fluid pressures are probably equal suggests that the vesicle is not the result of increased focal pressure, such as might result from a physico-chemical process. Corroboration of this deduction is offered by observations on the cells constituting the vesicular walls which suggest that they are mainly elongated (page 86). If this is so, it would appear that the roof and floor of the vesicles had moved apart as the result of some force causing elongation of individual cells. A force of compression from within on the other hand might be expected to produce flattening of cells and not elongation. If, therefore, the vesicle does not result from a focal increase in fluid pressure, it must result from a focal reduction of resistance to the already existing tissue fluid pressure.

Consideration of the normal rete might help to determine how such a reduced resistance operates in vesiculation. The prickle cells constituting this layer are bathed on all sides by the tissue fluid. They are linked together throughout this fluid and bind the upper impervious layers of the epidermis to the corium, attachment to this latter structure being formed by the stratum germinativum. The tissue fluid between the uppermost layers and the stratum germinativum by virtue of its pressure must be ever striving to drive these two layers apart, but under normal circumstances this is resisted by the cohesion of the prickle cells binding them. It has already been observed that, in early stages of vesiculation, a solution in the continuity of tono-fibrils occurs. By deduction,

therefore, it may be assumed that as a result, a concomitant weakness in the epidermis also develops. As there is now a reduced resistance to the tissue fluid pressure in the area, the upper portion might be expected to move away from the lower resulting in an increased cleavage in a vertical direction. With increase in the depth of the surrounding rete, the cells on the lateral periphery of the vesicle must elongate to accommodate it. Because of the existing cohesion between the prickle cells of the walls, roof and floor, the elongating force acting mainly on the walls becomes indirect at the points of junction of the roof and floor respectively. Therefore it should be expected that elongation of cells in these areas would be less marked. In support of this latter contention, examination of lesions in apparently early stages of vesiculation indicates that marked elongation of the cells of the lateral walls would often appear to take place before the cells of the floor become affected, e.g. Plate 14. In Plate 33 an apparently older vesicle("v") also demonstrates the marked elongation of cells of the lateral vesicular wall as compared with those of the floor.

The process of bulging in the epidermis is probably analagous in many ways to the mechanism of arterial aneurysm which demonstrates the manner in which a bulging can occur in a fluid space as a result of weakening of the wall, its contained pressure remaining unaltered.

Comment

From the above observations and considerations, therefore, it would appear that the mechanism of vesicle formation can be explained

on the basis of the resultant action of the normal tissue fluid pressure following a degeneration and solution in prickle cell continuity:-

1. By the creation of a passive space as the result of disintegration of foci of prickle cells.

2. Because of the resultant weakness thus created in the prickle cell layer, a bulging in the area is created because there is now reduced resistance to the tissue fluid pressure normally exerted between the basal layer of epidermis and its upper impervious layers.

Further Reference to cleavage in the Vesicular Walls

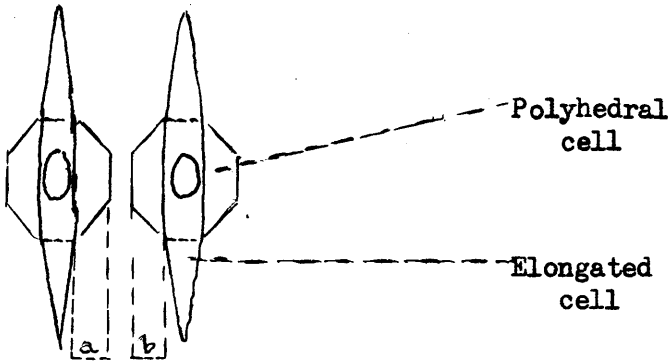
Earlier in this section it was observed that the spaces between the cells constituting the vesicular walls would appear to be greater than those between the normal prickle cells.

Percival (1949) pointed out that sections cut tangentially to vesicular walls presented the appearance of intercellular oedema in isolated sections, but when further serial sections were cut the cavity of the vesicle became evident. He further suggested that the description of eczema vesicle formation appearing in the literature would seem to be based on the study of such isolated sections. In sago grain vesicles cut serially my observations were in conformity with this finding. It was so constant that an area of apparent extracellular oedema, once found, one could usually anticipate that subsequent sections would pass through the cavity of a vesicle indicating that the original section resembling extracellular oedema represented the wall of a vesicle cut tangentiall

A few cases, however, presented the character of extracellular oedema at every plane (e.g. Plate 35) and these were taken to represent the process of vesiculation at an early stage. Even in these latter cases and in connection with the vesicular walls (vide Plate 32) cut tangentially, there was evidence that much of the apparent increased fluid could be attributed to spaces vacated by disintegrating cells, but this was not entirely the case as such fluid spaces were frequently found between cells which maintained their cohesion. Where apparently increased fluid spaces were observed between coherent and often apparently non-degenerating cells, alterations in shape were almost always observed. Thus the apparently early vesicle reproduced in Plate 35 and the walls of vesicles shown in Plates 31 and 33 indicate that apparently increased fluid spaces occur between cells which have suffered apparent elongation.

In the normal rete the cells would appear to be of polyhedral shape. If these cells should suffer elongation this could only be effected at the expense of their breadth. If their breadth should lessen, the spaces between adjacent cells would be anticipated to increase correspondingly, provided, as would seem to be the case, that elongation of cells occurred in a parallel direction. The

following diagram serves to illustrate the mechanism:-



a + b = distance which they have moved apart on account of elongation

Comment

From the above observations and considerations it would seem from many specimens examined in this series that the appearance of extracellular oedema can be accounted for by:-

1. Spaces vacated by disintegrating prickle cells
2. Increased space between adjacent cells effected by parallel elongation of these cells

It is deduced, therefore, that much of the fluid seen in relation to the vesicular wall and in early lesions is not of a primary nature, but is the result of degenerative and mechanical changes affecting the prickle cells. In other words apparent extracellular oedema results from degenerative changes and probably does not essentially cause them.

THE HISTOLOGICAL COMPARISON BETWEEN THE SAGO GRAIN VESICLE AND THE VESICLE OF DISCRETE SENSITISATION DERMATITIS

It is not the purpose of this thesis to analyse eczematous eruptions in detail, but serial sections of such lesions were

examined with particular reference to a case of discrete sensitisation dermatitis in association with a fungus infection of the feet. In this case every transition between the papulo-vesicular sensitisation eruption of the forearms to the discrete sago grain like eruption of the hands was apparent about the wrists.

Plates 39, 40 and 41 demonstrate sections of vesicles taken from the forearm from the last mentioned case. They demonstrate that no difference is apparent between them and lesions of the sago grain type affecting the hands. They are rounded cavities essentially confined to the prickle cell layers, the summit of their roofs being in relation to the stratum granulosum. Their walls consist of elongated cells, their vesicular content of free fluid and the rudiments of degenerate prickle cells, the nuclei of which would appear to be the last to degenerate.

Plate 41 shows the same fluid filled recess communicating through the roof of the vesicle with the under surface of the stratum corneum.

Plate 39 indicates a degree of perivascular infiltration of round cells and moderate dilatation of a blood vessel comparable with that of some specimens of sago grain like vesicles of the hand.

Plate 40 reproduces an apparently early vesicle marked "v" which demonstrates, as with all such vesicles examined in relation to nearby sweat ducts, an essential lack of communication. The vesicle is separated from the duct by a single layer of prickle cells at the level shown. This was the closest relationship of duct and vesicle

in all serial sections examined. Vesicle "vl" indicates, as with all other similar lesions, that the summit of the roof lies just under the stratum granulosum.

Many other vesicles examined had ruptured to the surface, thus presenting the only salient difference from sago grain vesicles. This would appear to depend on the relative thinness of the stratum corneum of the forearm as contrasted with that of the hand.

Comment

From the above findings it is deduced that the lesions of a discrete sensitisation papulo-vesicular dermatitis do not differ essentially in any way from the sago grain vesicles of the hand, the identity of the following features being apparent:-

1. Essential confinement to the prickle cell layer and communication through the cleavage in the roofs with the stratum corneum.

2. The relation of their roofs to the stratum granulosum.

3. Their identity of vesicular contents.

4. Their similar relation to the intra-epidermal course of the sweat ducts.

5. The non-specific changes in the regional corium.

THE SUBCORNEAL FLUID FILLED RECESS OF UNNA

A few writers have referred to an anatomical feature of the vesicular roofs in conditions variously described as "pompholyx," "cheiropompholyx" or "dysidrosis."

Robinson (1877) pointed out that the corneus layer became

involved in vesiculation at an early stage and remarked, that although it became partially eroded that process was never complete and resulted in a little fluid filled recess in communication with the vesicle. Attributing the same phenomenon to dilatation of a sweat duct, Fox (1878) stated that these globular dilatations were sometimes visible at the central points of the vesicular summits.

Again Unna (1896) described an invariable bottle neck like projection of the cavity of the vesicle into the area adjacent to the stratum corneum. This fluid filled flask like ante-chamber contained organisms which, according to him, were responsible for the production of the vesicle. They were often found in twos and threes behind each other, but occasionally they could be seen arranged in longer zig-zag threads. They resembled the tubercle bacillus, but were somewhat broader.

Muende (1934) referred to a dissolution of cells in the apices of vesicles which he attributed to pressure which he considered must be very great, owing to the resistance of the stratum corneum.

Percival (1949) published a microphotograph to show a similar phenomenon in the case of an eczema vesicle when he referred to a vertical tear which had occurred in the roof of a vesicle, followed by lateral stripping of the rete from under the surface of the stratum corneum. The tear was suggested by him to be due to pressure exerted by the vesicular expansion.

Observations from the present series of specimens indicate

that such breaches in the vesicular roofs are very frequent and in description, apart from the failure to demonstrate organisms (vide page 6), their structure in every way corresponds to Unna's.

Plates 30 and 42 demonstrate characteristic vesicles having continuity of their cavities through somewhat bottle neck like breaches in the roofs with somewhat flask shaped fluid filled spaces extending along a cleavage line corresponding to the stratum lucidum.

Plate 43 represents the same fluid filled recess as that shown on Plate 30 at a slightly different level and under higher magnification, to show greater cellular detail. Comparison of the cellular elements within the vesicle and those within the recess or ante-chamber reveals that those of the vesicle consist almost entirely of pyknotic nuclei, whereas those of the ante-chamber consist chiefly of a clump of prickle cells still preserving a fair degree of cohesion and, though some cytoplasmic degeneration is observed, this is much less advanced than that of the average cellular rudiment within the vesicular cavity. Under the floor of the recess large angular cells, having intact cytoplasm (one marked "x"), are lying free within the vesicular cavity. Their appearance is identical with those cells which constitute the floor of the ante-chamber and from which they would appear to have been detached.

The appearances presented indicate that the clump of cells within the recess has been carried there from the adjacent portion of the vesicular roof and that any intact cells adjacent to the

vesicular roof (or floor of the recess) have been detached from this structure. In the microphotograph under consideration the cells, forming the floor of the ante-chamber at the level shown, are seen to be continuous with the stratum granulosum on either side. At the vesicular summits the stratum granulosum was frequently seen to be adjacent to the vesicular cavity, but in these situations the cell granules were absent though this part of the layer became continuous with apparently normal granulosum cells more laterally.

Plate 44 demonstrates granulosum cells on the right of the section where a few layers of prickle cells separate them from the vesicular cavity, but this was unusual because in many specimens examined no granules could be seen in the granulosum cells in relation to the fluid filled recesses (e.g. in Plate 45).

Even with such change in granulosum cells, nothing comparable with the cytoplasmic disintegration of the prickle cells of the vesicular cavity was ever observed. The granulosum cells and those of the two or three layers of underlying prickle cells usually appeared to maintain some degree of cytoplasmic cohesion and, when a solution in continuity in the part occurred, it appeared to be effected by a separation between individual cells (vide Plate 43 and 44).

Plate 14 indicates an apparently early stage of vesiculation as serial sections demonstrate that at all levels the lesion consists of degenerating prickle cells which still retain a fair degree of

cohesion, but early cleavage between the affected cells is obvious. Even at this stage communication can be observed to have been established with the stratum corneum as a result of an apparent separation between the cells forming the vesicular roof. In consequence a little channel of communication between the vesicular cavity and the stratum corneum develops. The cells forming the walls of this channel appear normal in their staining reaction and no cytoplasmic disintegration is apparent. On the other hand in the vesicular cavity cell disintegration is seen to be very marked. Further examination of the vesicle suggests that at this stage it represents a passive fluid space which has resulted from this prickle cell disintegration.

From consideration of these findings it would, therefore, appear that this channel of communication between the vesicular cavity and the under surface of the stratum corneum originates in a manner different from that of the vesicular cavity. The channel would appear to arise as a separation between the cells of the vesicular roof in the absence of cell disintegration whereas the vesicular cavity, initially at any rate, would seem to result directly from prickle cell disintegration.

Plate 45 reproduces another vesicle in an apparently early stage of development. Serial sections demonstrate that no communication exists with the under surface of the stratum corneum. Although no loss of cohesion can be determined amongst the cells of

the stratum granulosum adjacent to the lesion, eosinophilic changes in their cytoplasm could be determined microscopically. The plate demonstrates an absence of the normal granules, suggesting that these cells have also been involved in the focal degenerative process affecting the adjacent prickle cells.

Plate 46 appears to demonstrate a lesion at a slightly later stage of development inasmuch as no marked recess has formed in relation to the stratum corneum. Communication has been established with the stratum lucidum and would appear to have been effected by a solution in continuity of the adjacent cells of the stratum granulosum in which loss of granules and eosinophilic change can be observed once more. These cells, though showing signs of degeneration, do not show the same degree of cytoplasmic disintegration as the deeper prickle cells. The underlying few layers of prickle cells corresponding to those of the normally slightly flattened cells of the rete, as in all specimens examined, fail to show the same degree of cytoplasmic disintegration as the deeper prickle cells involved, though their cytoplasmic disintegration would appear to be greater than that of the cells of the stratum granulosum.

Bacteriological Investigation

Specimens stained by the saline Gram method failed to reveal the presence of micro-organisms in or about the recess or within vesicular cavities. Similarly all other specimens on examination were likewise negative for the presence of micro-organisms. In

one specimen examined granules near a related granulosum cell slightly resembled organisms in the recess (vide Plate 44). The findings are, therefore, at variance with those of Unna who maintained that the presence of organisms was invariable.

Non-sudoriparous Origin of the Recess

In apparent contradiction to the observations of Tilbury Fox there was nothing to indicate that these lesions represented parts of sweat ducts or were connected with them.

Assessment of Findings in relation to the Fluid Filled Recess

In the case of the earliest lesions examined microscopically all but a few, e.g. Plate 45, showed communication with a fluid filled recess in relation to the lower border of the stratum corneum indicating that, although recess development would appear to be secondary to the presence of the vesicle, it usually appeared at an early stage of vesiculation. All vesicles, whether they were early or fully developed, were always observed to be in close proximity with the stratum granulosum when studied by serial sections. Although the cells of that layer usually preserved individual integrity, eosinophilic change and loss of granules at the earliest stage of vesicle development suggested that, as well as the deeper prickle cells, they too were involved in the primary focal degenerative process. The few layers of cells which immediately underlie the stratum granulosum and which in the normal rete are slightly flattened also offer some resistance to disintegration, though less

so than the stratum granulosum. Even at all stages, cells in relation to the fluid filled recesses showed a degree of disintegration which was always less advanced than that of the degenerate prickle cells of the vesicular cavity proper. This feature at a late stage is exemplified by examination of Plate 43. It would appear, therefore, that the degree of disintegration of cells in primary foci of degeneration diminishes from the level of the polyhedral cells to those of the stratum granulosum and corresponds with the morphological transition which occurs amongst cells at these levels.

Observations on early vesicles appear to indicate that separation between the cells of the stratum granulosum only occurs in the presence of visible degenerative changes, indicating that a resultant diminished cohesion might be, to a great extent, responsible for the separation occurring between cells. It is probable that this separation may be facilitated to some extent by the tension which would appear to exist in the vesicular wall, but the fact that it occurs only in areas showing degenerative change suggests that this degenerative change is the important factor.

That the recess, even in fully developed vesicles, is not very extensive can be deduced from examination of a specimen such as Plate 30. The fact that it would appear to extend laterally beyond the roof cleavage at the expense of the stratum lucidum is not surprising because Rényi and Chambers (1927) have demonstrated that the cells of the stratum lucidum possess no binding substance and,

that in comparison with the other cells of the rete they are easily separated as individual cells. The fluid filled recess mainly consists of a fluid extravasation along the stratum lucidum. It is possible that this natural lack of cohesion together with the vesicular fluid pressure to a great extent accounts for this extravasation. In all specimens examined the extravasation along the stratum lucidum was never very extensive and was constant in limitation to a small area. Though fluid had, therefore, extended a little way along this layer on either side of the communication with the vesicular cavity, its further passage was always resisted by the more peripheral stratum lucidum. This fact suggests that the area affected by fluid extravasation must have been less cohesive than the more peripheral stratum lucidum. It would seem, therefore, that a factor other than natural lack of cohesion and vesicular pressure must operate.

Referring again to the focal degenerative process, it has already been inferred that diminished cohesion of the stratum granulosum is dependent upon visible degenerative changes. The stratum lucidum lying immediately adjacent to this layer, probably at the same time, suffers some degree of degeneration which though invisible is the main factor reducing its cohesion and permitting of an extravasation of vesicular fluid limited in extent to the area so affected.

Comment

From these findings and deductions it appears, therefore, that

the limited dimensions of the fluid filled recess in the summits of the roofs of vesicles largely depends upon the extent to which the upper transitional layers of the epidermis have been involved in the focal degenerative process initiating the formation of the vesicle.

DEGREES OF MORBID CHANGE CORRESPONDING TO CELL MORPHOLOGY

It has already been recorded that the cells of the epidermis involved in initial foci of degeneration do not suffer the same degree of disintegration. In the case of the polyhedral prickle cells, disintegration is most marked, but diminishes in degree as the level becomes more superficial and is apparently least in the cells of the stratum granulosum and stratum lucidum. Similarly observations on the sweat ducts in relation to the same foci of degeneration indicate that these structures and their related prickle cells are spared the same degree of disintegration as affects adjacent prickle cells.

Comparison, therefore, of the pathological reaction of the upper transitional layers of the epidermis with that of the sweat ducts show them to be closely similar. The similarity of pathological reaction suggests that the cells of this portion of the sweat duct are probably histologically similar to those of the upper transitional layers of the epidermis.

This similarity would appear to be confirmed by the microscopic appearances presented in the specimen intravitally injected with

trypan blue.

Menkin (1940) showed that this dye had a particular affinity for inflammatory tissue.

Plates 23 and 24 are reproductions of sections of a multilocular vesicle intravitally injected with trypan blue. The deeply staining areas of the vesicular roof (clearly shown in Plate 24) represent the stratum granulosum and indicate its apparent special affinity for the dye. The upper portion of the intra-vesicular partition shown in Plate 24 is also seen to be deeply stained. The maximum intensity corresponds to the upper transitional layers and rapidly diminishes with the depth in the rete, the polyhedral cells being unstained.

A similar degree of affinity for the stain is noted in the intra-epidermal portion of the sweat ducts demonstrated in Plates 23 and 24.

This similar staining property when correlated with the previously demonstrated, similarity of histological appearances and of pathological reaction indicates that the component cells of the intra-epidermal portion of the sweat duct, if not identical to, are closely related in character to those of the stratum granulosum.

Conclusions 15 - 34 refer to the histopathological investigation. Please see Part 3, page 117 - 122.

PART 3

CONCLUSIONS

The aetiology and histopathology of one hundred cases of sago grain vesicular eruptions of the extremities have been studied and the following conclusions have been drawn:-

1. Sago grain vesicular eruptions of the extremities may be placed in certain aetiological groups corresponding to causal or associated factors. These groups and the frequency with which their corresponding factors operate are given as follows:-

(a)	Discrete sensitisation dermatitis	33%
(b)	Dermatitis venenata	14%
(c)	Scabetic	3%
(d)	Fungous	10%
(e)	Allergic	15%
(f)	Neurogenic	8%
(g)	Idiopathic	17%

2. The largest group is that of discrete sensitisation dermatitis. When added to the dermatitis venenata group, it is much greater than the combined group of McLachlan and Brown. This difference was suggested as being due to the possibility of these workers having omitted some cases filed under dermatitis venenata and infective dermatitis as a result of including some indexed as cheiropompholyx. Again the diversity of findings to a certain extent may have been due to the inclusion by these authors of some cases of this group under focal sepsis of external origin.

3. My figures regarding the operation of dermatitis venenata as a cause of sago grain vesicular eruptions confirm those of

Lehman.

4. The incidence of fungal infection associated with these eruptions would seem to be greater than that established by McLachlan and Brown. It is suggested that the difference of incidence could depend on seasonal factors. Variations between my figures and those of other workers is thought to be due to geographical factors.

5. In order to exclude ringworm infection, it is necessary to carry out both microscopic and cultural investigations as clinical appearances are often misleading.

6. My figures confirm the existence of an allergic group called the asthma, eczema, hayfever group by McLachlan and Brown. The relative incidence of this group of cases corresponds to that of McLachlan and Brown.

7. Findings confirm the existence of a neurogenic group where factors are probably functional, but there is no evidence to suggest that hyperthyroidism or other endocrinal disturbance is essentially connected with the production of these eruptions.

8. Gastric disturbances and internal focal sepsis would appear to play only a minor role in these conditions. No case to which drug or food idiosyncracy could be ascribed (McLachlan and Brown, Muende) was found in the present series.

9. 17% of cases can be placed in the idiopathic group although the greater majority have some associated factor common to cases classified within other groups (e.g. chilblain circulation or focal sepsis). These factors, however, are so infrequent and

indefinite in their mode of operation as not to place the cases in a definite group. It was considered on the other hand justifiable to sub-divide the idiopathic group into group 1 which included cases with indefinite associated factors and group 2 which embraced all those cases to which no causal or other factor could be ascribed.

10. The ratio of male to female affected is 1.5:1. That a preponderance of male over female, with one small exception (viz. 11-20 age group), is consistent throughout life is thought to indicate the operation of an innate factor in the male.

The age incidence in the various aetiological groups varied according as aetiological factors were exogenous or endogenous. When extraneous factors seemed to operate, generally speaking, most age groups were affected and the highest incidence occurred during the most active years of life (age 31-40). When factors appeared to be endogenous, patients were affected earlier in life. Three quarters of these patients were below the age of thirty.

11. A 14% complex aetiological group consisting of cases having sufficient criteria to place them in more than one group was brought to light. In these cases a predominating feature placed them in one group in preference to others.

12. Furthermore it has not been emphasised, hitherto, that in addition a 48% group exists in which the onset is conditioned

by one or more precipitating factors in the absence of which the eruption might never develop. These factors consist of (a) Warm weather (b) Medicaments applied to skin lesions resulting in discrete sensitisation dermatitis (c) Miscellaneous factors including surgical operations, exposure of the hands to sunlight, subjection to local heat and cold weather.

13. It is concluded, therefore, that there is evidence in more than half the cases of sago grain vesicular eruptions of the extremities to indicate that their causation is not a single factor, but the complex interplay of more than one causal, associated factor or group of factors.

14. There is no clinical difference between sago grain vesicles of different aetiological groups. Identity holds whether conditions are classified as "ids", "cheiropompholyx" or "discrete sensitisation dermatitis" of the extremities.

15. Sago grain vesicles of the hands and feet, despite apparently different aetiological origins, arise independently of the sweat ducts. The lesions are not due to sweat retention at the level of the rete Malpighii as maintained by Fox (1873), Crocker (1877), Nesterjewsky (1906), Sicoli (1924) and Pusey (1917) and apparently by Sulzberger and Baer (1948). There is further no evidence from specimens examined to indicate that some lesions are due to sweat retention as maintained by Duhring (1887), McCarthy (1931) and possibly Peck (1930). It is concluded, therefore, that

conditions variously described as "pompholyx" or "cheiropompholyx" are not dysidroses, a finding which is conformity with the views of A.R. Robinson (1877), .W. Williams (1891), Unna (1890), Sutton (1913), McLachlan and Brown (1934) and others.

16. Many specimens studied indicate that the intra-epidermal portions of the sweat ducts are relatively resistant to the disintegrative processes occurring amongst prickle cells in association with vesicles. Robinson (1877) and Unna (1896) have indicated that sweat ducts at times could be seen in the walls of vesicles. The investigations carried out in this series indicate that this occurrence is very frequent. Investigations show that the intra-epidermal portions of the sweat ducts, instead of being actually involved in the process of vesiculation, are in reality spared, except perhaps in the later stages. These findings correspond to those of Pinkus in his observations on other diseases confined essentially to prickle cells.

17. The greater extent of the intra-epidermal portion of the sweat duct from the stratum granulosum downwards, consists of granulosum or similar cells. Their granules would appear to be basophilic, but in the deeper parts a tendency is noted for them to be eosinophilic in some cases.

18. The immunity of the sweat ducts is dependent upon their cellular structure which, as already mentioned, is either identical or similar to that of stratum granulosum.

19. Sago grain vesicles of the hands and feet, differing aetiologically, are histologically identical.

20. They consist of rounded fluid filled spaces lying under the stratum granulosum. The surrounding prickle cells are elongated chiefly in the lateral walls and show signs of cytoplasmic degeneration. The vesicular content consists of fluid and prickle cell rudiments and occasionally lymphocytes and polymorphonuclear leucocytes. Vesicles are often multilocular.

21. The morbid process initiating the formation of sago grain vesicles of the hands and feet is that of multiple foci of degeneration affecting the prickle cell layer and overlying transitional layers of the epidermis. The prickle cells are affected in the following sequence (1) Cytoplasm (2) Tono-fibrils (3) Nuclei. All elements proceed to disintegration.

22. The prickle cells possess a system of radial intra-cellular fibrils which ramify freely over the cell nuclei where small nodal structures are present.

23. In accordance with the views of many authorities, changes in the corium in relation to sago grain vesicles are only slight and non-specific and oedema of this layer is not an essential feature of the lesion. The elements of the sudoriparous apparatus within the corium remain unchanged. There is no evidence to support the contention of Fox and Crocker that thickening or proliferation of the

glandular epithelium exists.

24. The mechanism of vesiculation consists of:-

(1) The creation of a passive space within the prickle cell layer as a result of the disintegration of a focus of prickle cells and

(2) Probably as a result of the weakness created, the potential space increases because of lessened resistance to the tissue fluid pressure.

25. Extra-cellular oedema associated with sago grain vesicles would appear to be secondary to degenerative changes and not their cause.

26. The histological nature of the lesion of discrete sensitisation dermatitis does not differ in any respect from that of the sago grain vesicle of the hands and feet.

27. As recorded by Robinson (1877) and Unna (1896), a fluid filled recess is present in the summit of most vesicular roofs and forms at an early stage of vesiculation. In opposition to the view of Unna, I conclude that, though its presence is frequent, it is not invariable. In shape it resembles that of an inverted flask and communicates with the vesicular cavity at its neck. It is bounded above by the stratum corneum, below by the stratum granulosum and laterally by the stratum lucidum. Lying in its fluid content are the degenerating cells of the upper transitional layers of the epidermis, viz. the upper somewhat flattened cells of the rete Malpighii, stratum granulosum cells and stratum lucidum cells which have been

involved in the initial degenerative focus.

28. The formation of the recess results from a degeneration of a small area of stratum granulosum which is always involved in the initial focus of degeneration. This causes loss of cohesion and permits access of fluid to the stratum lucidum. Because the cells of the latter layer have poor cohesion and are further disturbed by the initial focal degenerative process, extravasation of fluid is permitted to an extent limited by that of the focal degenerative process.

29. The dimensions of the fluid filled recess correspond largely to the extent to which the initial focal degenerative process involves the cells of the upper transitional layers of the epidermis.

30. The different degrees of disintegration apparent in the cells in relation to the fluid filled recess and in those of the prickle cells essential to the vesicular cavity correspond to the morphological differences between the cells at different levels of the epidermis affected, being most marked in the deeper prickle cells and diminishing correspondingly as the level becomes more superficial.

31. That the cells of the stratum granulosum are affected in the initial focal degeneration is indicated by the study of early lesions which demonstrate eosinophilic changes and loss of granules in the cell cytoplasm.

32. There is no evidence in or about the recess of micro-organisms as Unna (1896) had concluded.

33. There is no evidence to suggest that bulb-like dilatations in the roofs of vesicles are in any way connected with the sweat ducts. In all probability these recorded by T. Fox (1878) were the fluid filled recesses as already described and not portions of dilated sweat ducts.

34. It is concluded that the relative resistance of the intra-epidermal portion of the sweat ducts to the cellular disintegration noted in sago grain vesicles depends upon the fact that in these parts the ducts are composed of stratum granulosum cells or cells morphologically similar to them. That duct resistance to disintegration depends on its stratum granulosum structure is confirmed by the observation that the stratum granulosum proper adjacent to lesions offers a corresponding resistance to the disintegrative process.

APPENDIX 1

PROTOCOL OF CASES

In this appendix the following abbreviations are used:-

(M) = Male
(F) = Female
P.H. = Previous History
F.H. = Family History

Case 1

(F) E.M., age 28, Housewife , 9.6.48

History

Had suffered from dermatitis of right palm and wrists for four and a half months. Commenced as red itchy papules which spread peripherally. Latterly areas became raw and weeping and associated with itchy blisters on the fingers. No history of trauma or of contact with noxious substances. She was otherwise healthy.

P.H.

1942 - suffered from a similar skin condition. 1940 - left frontal herpes zoster. 1938 - tonsillectomy for recurrent sore throat.

F.H.

One brother suffered from recurrent dermatitis of the face and another from sycosis barbae.

Examination

She was an apparently healthy, well-nourished woman, but

appeared to be rather nervous. The tongue was moist and clean and no abnormality was apparent in the ear, nose or throat.

The palms were moist. A congestive, weeping, infectious eczematoid dermatitis involved the anterior aspects of the wrists and right palm and sides of the right third and fourth fingers. A discrete sago grain vesicular eruption bilaterally affected the lateral aspects of the fingers, the thenar and hypo-thenar eminences. The lesions were of pin head size, rounded and deeply embedded. The majority were clear, but some were opaque and others had dried and were exfoliating. The skin of the feet appeared normal.

Investigation

The following tissues were examined directly microscopically and culturally for fungus with negative findings:-

1. Roofs of vesicles.
2. Scales from edges of dermatitis.

Aetiological Group

Discrete sensitisation dermatitis.

Case 2

(M) McI., age 36, Furnace Cleaner, 1.6.48

History

Developed a hack on the left little finger five months previously. Surrounding area became red and scaly. Some weeks later it was treated with penicillin cream. After four days affected area became intensely itchy and little blisters appeared which rapidly spread over all the fingers of the left hand. Bilateral involvement soon followed. Since then the eruption constantly healed and relapsed and more recently had affected the feet. He had otherwise been healthy.

P.H.

Always suffered from hyperidrosis of the hands and feet in warm weather or in a warm environment. Two years previously had suffered from a vesicular eruption of the hands.

F.H.

Nothing relevant.

Examination

He appeared healthy and well-nourished. No apparent focal sepsis was evident. A fine finger tremor was noted.

A dry, well-defined, slightly squamous, erythematous dermatitis was present on the backs of the second, third and fourth fingers of the left hand. The dorsi-lateral surfaces of all fingers except the thumbs were affected with numerous discrete, but irregularly

shaped clear blisters of the deep seated variety. A similar eruption was present on the toes and on the insteps.

Aetiological Group

Discrete sensitisation dermatitis.

Case 3

(M) A.McL., age 2½, 20.5.48

History

Had suffered from a chronic vesicular eruption of the hands associated with a recurrent papular eruption of the trunk and limbs. No cause had been apparent and no drug or food could be implicated.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A typical discrete boiled sago grain eruption was present on the apposed aspects of the fingers. The skin on the affected parts was slightly reddened, apparently as a result of previous exfoliation. A typical discrete papular urticaria was present on the trunks and limbs.

Aetiological Group

Allergic

Case 4

(F) McK., age 23, Cake Packer, 25.5.48

History

Developed vesiculation around small fissures of the left little finger four weeks previously. Within a week similar lesions had become widespread over both upper extremities. No causal chemical agent could be implicated. She had no other complaints.

P.H.

Scabies several years previously.

F.H.

Mother had suffered from a recurrent vesicular eruption of the hands for four years.

Examination

Both hands and the fingers were covered in numerous small deep seated sago grain vesicles. The palms were warm and moist. A mild squamous interdigital intertrigo between the fourth and fifth toes was bilaterally present.

Investigation

The following tissues were examined microscopically and culturally for fungus with negative findings - scales from interdigital intertrigo.

Aetiological Group

Discrete sensitisation dermatitis.

Case 5

(M) A.M.C., age 17, Radio Mechanic, 23.5.48

History

Had suffered from a recurrent vesicular eruption of the hands chiefly in warm weather for about three years. Present attack commenced ten days previously. No other complaints.

P.H.

Chronic hyperidrosis of hands and feet since childhood most marked in warm weather. Nothing else relevant.

F.H.

Nothing relevant.

Examination

He appeared healthy and well-nourished, but was nervous and a fine tremor of the fingers was present. The pulse rate was 74.

Numerous small sago grain vesicles were present on the dorsi-lateral aspects of the fingers. Many were confluent and multi-locular. A few lesions were also present in the webs between the fingers and on the backs of the hands. Apart from hyperidrosis, the feet appeared normal.

Aetiological Group

Idiopathic.

Case 6

(M) F.Q., age 20, Unemployed, 22.5.48

History

Developed itchy blisters of the finger webs immediately after the use of carbolic soap and water seven years previously. Since then similar attacks frequently developed spontaneously during warm weather and always after using carbolic soap. Present attack occurred during warm weather several days prior to examination. He had no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He was an apparently healthy, well-nourished man with no indication of focal infection. The oral hygiene was good.

A desquamative erythematous and slightly moist dermatitis affected the apposed aspects of the fingers. Beyond the margins numerous sago grain vesicles in every stage from early vesiculation to exfoliation could be seen. The skin of the backs of the hands and of the fingers was dry as if subjected to fat solvent action.

The feet appeared normal.

Aetiological Group

Dermatitis venenata.

Case 7

(M) R.P., age 50, Machine Fitter, 21.5.48

History

Had noticed that caustics used for removing grease from his hands caused itching and blistering of his fingers three years ago. Blistering had occurred under similar circumstances a month prior to examination. There were no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He was a healthy well-nourished subject. No evidence of focal infection was present. The skin of the hands was very dry as if subjected to fat solvent action. The apposed surfaces of the fingers were slightly reddened and affected by numerous discrete sago grain vesicles of pin head size. No other abnormality was detected.

Aetiological Group

Dermatitis venenata.

Case 8

(F) A.A., age 20, Typist, 18.5.48

History

Developed an itchy vesicular eruption of the palms a few days previously. No causal contact agent could be implicated. Had been otherwise healthy and there were no other complaints.

P.H.

Dermatitis of face and limbs from infancy to puberty. Since then lichenified areas had persisted in the cubital fossae.

F.H.

Nothing relevant.

Examination

The palms were moist and over their surfaces were scattered typical discrete sago grain vesicles of lentil size. Lichenification of the skin was present in both cubital fossae. Hyperidrosis of the soles was present, but no skin lesion was detected.

Aetiological Group

Allergic

Case 9

(M) J.K., age 36, Cashier, 10.8.47

History

Developed a vesicular dermatitis of the left wrist under his watch strap during warm weather a month previously. Condition appeared on other wrist some days later following transfer of the watch. Areas treated with penicillin cream with immediate aggravation with spread and the appearance of a sago grain vesicular eruption on the hands and a concomitant papulo-vesicular eruption of other parts.

P.H.

Frequent axillary intertrigo. 1943 - infective dermatitis of the face following electro-cauterisation of a wart. 1946 - sycosis barbae - responded to ungt. Quinolor.

F.H.

Nothing relevant.

Examination

He was a healthy, well-nourished subject. There was no evidence of focal infection and the oral hygiene was good. A vesiculo-bullous dermatitis was present on both wrists and most marked anteriorly. A typical discrete sago grain vesicular eruption involved the dorsa of the palms and the apposed aspects of the fingers. A papulo-vesicular eruption of the discrete type was present on the forearms. The face and neck were red and swollen and covered in numerous papulo-vesicles. A few crusts were present here and there on these parts.

About the wrists every transition could be detected from the papulo-vesicular eruption of the forearms to the deeply embedded sago grain eruption of the hands.

Aetiological Group

Discrete sensitisation dermatitis.

Case 10

(M) J.A., age 37, Red Lead Worker, 7.9.48

History

Had suffered from a recurrent moist eruption between the toes for seven years. Attacks most commonly occurred in warm weather and were frequently associated with vesiculation of the hands and feet. The condition had recurred two weeks prior to examination.

P.H.

Tonsillectomy as a child. Plantar hyperidrosis throughout life. 1929-1942 suffered from peptic ulcer - healed following operation for perforation.

F.H.

Nothing relevant.

Examination

Bilateral pes cavus and much crowding of the toes with hammer deformity was present. The palms and soles were moist and affected b

discrete sago grain vesicles. The dorsi-lateral surfaces of the toes and fingers were also affected. The apposed surfaces of all the toes were congested and weeping and exfoliation was present. He appeared healthy in every other way. No focal infection was evident and the reflexes normal.

Investigation

The following tissues were investigated microscopically and culturally for fungus with negative findings:-

1. Roofs of vesicles of hands and toes.
2. Scales from webs of toes.

Aetiological Group

Idiopathic

Case 11

(M) H.H., age 56, Labourer, 14.6.48

History

A widespread dermatitis had affected the hands, face, flexures, groins and genitalia. No medicament, plant or other agent could be implicated. General health was good and he had no other complaints

P.H.

1933 - infective dermatitis of left shin following injury.

Periodically for ten years in the month of June he had suffered from sudden attacks of puffiness of the face and backs of the hands associated with blisters on the lower thirds of the fingers.

F.H.

Nothing relevant.

Examination

The backs of the hands were red and swollen. Sago grain vesicles were present on the sides and webs of the fingers. The face was red and the eyelids puffy. An ill-defined erythematous dermatitis was present on all flexures and on the forearms anteriorly. The groins were red and weeping and the genitalia greatly swollen. The appearances were those of an acute dermatitis venenata, but no allergen was ever implicated. A mercury ointment patch test was negative.

Aetiological Group

Dermatitis venenata.

Case 12

(F) E.M.D., age 37, Housewife, 16.6.48

History

Developed a dermatitis of both calves six months previously. Three weeks later an itchy eruption appeared on the forearms and backs of the hands. Weeping soon developed on the latter parts and was followed by the appearance of blisters on the dorsi-lateral aspects of the fingers and on the thenar eminences. She had otherwise been a healthy woman and there were no other complaints. No history of trauma.

P.H.

Nothing relevant.

F.H.

One of her children suffered from a weeping dermatitis of the leg at the age of eight months.

Examination

An infectious eczematoid dermatitis was present on both calves. A discrete papulo-vesicular eruption affected the forearms widely. An ill-defined squamous erythematous dermatitis was present on the backs of the hands. Numerous discrete sago grain vesicles affected the thenar eminences and the medial aspects of the index fingers. No other abnormality was detected. The skin of the feet appeared normal.

Aetiological Group

Discrete sensitisation dermatitis.

Case 13

(M) W.B., age 42, Labourer, 18.6.48

History

Had suffered from a recurrent vesicular eruption of the hands for six years. First attack occurred whilst engaged on a greasy job in the Army. A grease solvent mixed with black soap had been

supplied for cleansing the hands. Its use had caused severe burning and itching of his fingers. Since the onset attacks had occurred spontaneously in warm weather and following the use of Sunlight soap. Palmolive soap could be used with impunity. There were no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He was a well-nourished subject. The oral hygiene was good and no infection of the ear, nose or throat was apparent. The skin on the backs of the hands was very dry. The apposed surfaces of the fingers and the interdigital webs were affected by a scaly erythematous dermatitis. Numerous pin head size sago grain vesicles were present on the erythematous areas. No tremor was present on the fingers and there was no evidence of nervous upset. The skin of the feet appeared normal.

Aetiological Group

Dermatitis venenata.

Case 14

(M) H.B., age 35, Docker, 14.8.48

History

Developed a wet sticky spot on his chin following shaving cut two weeks previously. The face soon became involved in a weeping eruption and a rash appeared upon the scalp, arms and legs. Latterly blisters occurred on the hands and feet. No other complaints.

P.H.

Suffered from recurrent psoriasis of the points of the elbows. Five years previously whilst in the Army developed dermatitis of the right wrist as a result of friction from his battledress cuff.

F.H.

Nothing relevant.

Examination

A crusted impetiginous eruption affected the cheeks, chin and supra-orbital regions. The dorsa of the forearms were covered in numerous papulo-vesicles. Areas of crusting were also present on these parts. Large sago grain vesicles affected the backs of the fingers, their webs and the thenar eminences. A similar eruption affected the insteps.

Aetiological Group

Discrete sensitisation dermatitis.

Case 15

(M) F.McK., age 36, Labourer, 18.6.48

History

Sustained a burn to the back of the neck twelve days previously. The area had become raw and weeping and spread peripherally by the formation of papulo-vesicles. A widespread eruption had then occurred and vesicles had appeared on the hands and feet.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A congestive weeping infectious eczematoid dermatitis was present on the back of the neck. More peripherally numerous papulo-vesicles were present. Areas of grouped papulo-vesicles affected the chest and the abdomen. Numerous discrete papulo-vesicles involved the limbs. The hands, fingers and toes were affected by a discrete sago grain vesicular eruption. At the wrists every transition was noted from the papulo-vesicules of the forearms to the sago grain vesicles of the hands.

Aetiological Group

Discrete sensitisation dermatitis.

Case 16

(M) A.D., age 28, Builder's Labourer, 11.5.48

History

Had suffered from frequent attacks of flexural eczema of the cubital and popliteal fossae for several years. A relapse developed associated with vesiculation of the hands three weeks prior to examination. No other complaints.

P.H.

Chronic hyperidrosis throughout his life. 1942 - vesicular eruption of the hands associated with attack of flexural eczema.

F.H.

Nothing relevant.

Examination

An ill-defined finely squamous erythematous dermatitis affected the cubital and popliteal fossae. A few erythematous papules were noted on the extensor aspects of the forearms and calves. Sago grain vesicles of lentil size were present on the backs and palms of the hands. The skin of the feet appeared normal. No other abnormality was detected and there was no evidence of focal sepsis.

Aetiological Group

Allergic.

Case 17

(M) J.C., age 38, Labourer, 1.3.48

History

Developed an infectious eczematoid dermatitis of the left index finger following an abrasion of the part about a year previously. Similar dermatitic areas soon affected the neck and legs, but had remained localised. A month prior to examination "Biccolam" ointment was applied and the areas began to weep, and a widespread eruption occurred on the trunk and limbs, vesicles developing on the fingers.

P.H.

Hyperidrosis of the palms and soles had always been marked in warm weather.

F.H.

Nothing relevant.

Examination

He was a highly nervous individual. Fairly well-defined areas of congestive,exudative and superficially ulcerated infectious eczematoid dermatitis were present on the neck and backs of calves. A discrete papulo-vesicular eruption affected the trunk and limbs. All fingers, excepting the thumbs, were involved in a discrete sago grain vesicular eruption. The palms were moist and a fine tremor of the fingers was present. Apart from plantar hyperidrosis, the feet appeared normal. The oral hygiene was good and no evidence

of focal sepsis was apparent.

Aetiological Group

Discrete sensitisation dermatitis.

Case 18

(M) A.R., age 40, Labourer, 25.3.48

History

Developed a dermatitis on the backs of the calves on areas subjected to friction from Wellington boots four weeks prior to examination. Soon a widespread eruption affected the trunk and limbs and vesicles appeared on the hands.

P.H.

Hyperidrosis of the palms and soles in warm weather.

F.H.

Nothing relevant.

Examination

An infectious eczematoid dermatitis affected both calves. Numerous lesions resembling erythema multiforme involved the upper and lower limbs. Small papulo-vesicles were present on the trunk. The palms and backs of the hands and apposed surfaces of the fingers were affected by a typical sago grain vesicular eruption. The insteps were similarly affected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 19

(F) A.T., age 25, Housekeeper, 2.4.48

History

Developed a vesicular eruption of the hands and feet two weeks previously. Condition preceded by nausea and epigastric discomfort. Had always suffered from palmar and plantar hyperidrosis. No chemical contact agent could be implicated.

P.H.

Suffered from chilblains of the fingers and toes in winter.

F.H.

Nothing relevant.

Examination

She was a pale and anxious looking individual but the conjunctivae were of normal colour. The extremities were cold and clammy, but no abnormality was found in the chest or heart. The oral hygiene was good and there was no evidence of focal sepsis. The palms of the hands were moist and cold to the touch. A sago grain vesicular eruption affected the fingers, palms and soles. Areas of desquamation were also present on these parts and an intertrigo affected the fourth interdigital web of the toes bilaterally. No other abnormality was detected.

Investigation

The following tissues were investigated microscopically and culturally for fungus with negative findings:-

1. Macerated skin from between the toes.

2. Roofs of vesicles of sole.

Aetiological Group

Idiopathic

Case 20

(M) -. age 28, Assistant Medical Practitioner, 3.4.48

History

He was engaged in general practice in Scotland. There had been no previous history of skin trouble. He was confronted with a case of post-partum haemorrhage which had almost resulted in the woman's death. Within a few hours of the event he developed a deep seated vesicular eruption of the hands. He admitted that he had been severely frightened by the obstetric emergency. He was removed from midwifery duties for a few weeks and the hand condition healed rapidly. As soon as he resumed obstetric practice the condition immediately relapsed. Gloves, antiseptics, etc., had been excluded as possible causes. He went to practise in Westmorland where midwifery was conducted by the district nurse. The latter, on one occasion, had to suspend her duties for a time on account of illness as a consequence of which the doctor had to take over. Immediately upon the assumption of these duties vesiculation of the hands recurred.

Aetiological Group

Neurogenic

Case 21

(F) McE., age 16, Schoolgirl, 21.4.49

History

Had suffered from a recurrent sago grain vesicular eruption of the hands since the age of twelve coinciding with the onset of menstruation. Four weeks prior to examination her tonsils were noted to be chronically inflamed. A week later during a quiescent phase of the eruption tonsillectomy was performed and was followed by an immediate exacerbation of the skin condition of more than usual severity.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

The apposed surfaces of the second, third and fourth fingers of both hands were involved in a discrete sago grain eruption. Some scaling was also present in the areas. The skin of the feet appeared normal. Hyperidrosis and tremor of the fingers were absent. No other abnormalities were detected.

Aetiological Group

Idiopathic.

Case 22

(M) T.I., age 32, Marine Engineer, 12.6.48

History

Had suffered from a recurrent itchy vesicular eruption of the hands and feet for three months. There were no other complaints.

P.H.

Four years previously in the tropics had suffered from ringworm of the scalp and bearded region. Nothing else relevant.

F.H.

Nothing relevant.

Examination

He appeared a healthy well-nourished subject. The thenar eminences were covered in small deep seated sago grain vesicles of pin head dimensions. Slight exfoliation was present between the fourth and fifth toes bilaterally. No evidence of focal sepsis, hyperidrosis or tremor of the fingers.

Investigation

Scales from the affected areas between the toes and from the roofs of vesicles of the hands were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 23

(F) J.C., age 37, Housewife, 18.5.48

History

Seven weeks previously had developed a weeping dermatitis of both feet soon followed by recurrent vesiculation of the hands. There were no other complaints.

P.H.

A year previously had developed dermatitis of the hands around hacks with later widespread sensitisation. Condition healed in a month. Skin of the cubital fossae had been thickened and periodically itchy. Ingestion of strawberries always caused a sudden outbreak of urticaria. Skin sensitive to woollens. Dysmenorrhoea since puberty.

F.H.

Father suffered from bronchial asthma throughout life.

Examination

She was a sallow, slightly built subject presenting no evidence of focal infection or nervousness. Dorsally the feet and toes were covered by a weeping infectious eczematoid dermatitis. The interdigital webs appeared normal. Discrete sago grain vesicles were

present on the palms of the hands and the backs of the fingers. Some areas of exfoliation were present on the same parts.

Lichenification of the cubital fossae was also present.

Aetiological Group

Discrete sensitisation dermatitis.

Case 24

(F) M.P., age 55, Hairdresser, 11.8.49

History

Had suffered from a vesicular eruption of the hands and fingers for four days. Commenced as a severe itching between the fingers whilst working with "Inecto" hair dye. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A few rounded sago grain vesicles about the size of lentils were present on the palms and fingers. Some lesions were purulent .

Aetiological Group

Dermatitis venenata.

Case 25

(F) B.K., age 14, Schoolgirl, 23.8.48

History

Developed a sago grain vesicular eruption of the hands following mastoidectomy five years previously. Since then had relapses annually in warm weather. Had been a very nervous child throughout life. No other complaints.

P.H.

Tonsillectomy six years before.

F.H.

Sister suffered from hayfever and asthma. Grandmother (paternal) and aunt (paternal) similarly affected.

Examination

She was an intelligent girl, but very nervous, though tremor of the fingers and hyperidrosis were absent. Sago grain vesicles were present on the left palm, interdigital webs and fingertips. The right hand was not affected. A few vesicles of similar type were present on both insteps. A mastoidectomy scar was present behind the left ear. Hearing was good.

Investigation

Roofs of vesicles from the hand and feet were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Allergic.

Case 26

(F) M.J., age 34, Housewife, 11.11.48

History

Suffered from a recurrent itchy vesicular eruption of the left palm for five months first occurring spontaneously during warm weather. Attacks could be induced by washing the hands in soap and water. Suffered from chronic palmar and plantar hyperidrosis. There were no other complaints.

P.H.

Recurrent hayfever every year from May to September.

F.H.

Nothing relevant.

Examination

She was a nervous and anxious person. Sago grain vesicles were present on the centre of the left palm within a triangular area which had been denuded of horny layer as a result of previous exfoliation. No evidence of focal sepsis. Moderate hyperidrosis of the soles was present, but the feet appeared otherwise normal.

Aetiological Group

Allergic.

Case 27

(M) J.D., age 25, Milling Machiner, 18.5.48

History

A recurrent vesicular eruption had affected the hands and feet for about four weeks. There were no other complaints.

P.H.

Dermatitis of the left instep two and a half years before.

F.H.

Sister suffered from frequent asthmatic attacks and father from hat-band dermatitis.

Examination

Both palms were affected by a discrete sago grain vesicular eruption. Peeling was present on the apposed aspects of the fingers and around the nailbeds. Defined areas of exfoliation affected the insteps.

Investigation

Scales from the insteps and vesicles from the hands were investigated microscopically and culturally for fungus with negative findings.

Aetiological Group

Allergic.

Case 28

(M) J.H., age 6, 30.9.48

History

Had recently returned from a sanatorium where he had been under treatment for a tuberculous infiltration of the upper zone of the right lung. During warm weather three weeks previously he developed a vesicular eruption of the hands and a red rash on his legs. Hyperidrosis had been marked.

P.H.

Nothing relevant.

F.H.

Mother suffered from frequent bronchial asthma.

Examination

He appeared healthy and well-nourished. The oral hygiene was good and there was nothing to suggest focal infection of the ear, nose and throat. A sago grain vesicular eruption affected the palms. Desquamation was present on the apposed aspects of the fingers. An urticating erythema multiforme eruption involved the legs and forearms. Palmar and plantar hyperidrosis was marked.

Aetiological Group

Allergic.

Case 29

(M) V.G., age 27, Tram Conductor, 30.9.48

History

Five months previously small itchy vesicles had appeared around hacks on the fingers and since then recurrent vesiculation had involved the palms and sides of the fingers particularly of the left hand. No other complaints.

P.H.

Tonsillectomy five years previously on account of recurring sore throats.

F.H.

Nothing relevant.

Examination

On the centre of the left palm was present a triangular area of exfoliation. Sago grain vesicles were present on the denuded areas. The right hand appeared to be unaffected. No abnormality was seen on the feet and hyperidrosis was absent.

Aetiological Group

Discrete sensitisation dermatitis.

Case 30

(F) W.H., age 7, Schoolgirl, 30.9.48

History

Sustained a second degree burn from hot water on the right foot about a year previously. The lesion had no sooner healed without apparent complication when a sudden outbreak of itchy blisters appeared first on the feet and then the hands. Attacks of vesiculation had been recurring since. As a result of the accident the child had developed an abnormal fear of heat in any form e.g. warm water, the fire, etc., and consequently presented a great problem of child management.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

She was nervous and irritable. Both tonsillar glands were enlarged and the fauces injected. Moderate hyperidrosis of the palms and soles was present. A desquamating sago grain vesicular eruption affected the palms, thenar eminences and soles.

Aetiological Group

Neurogenic.

Case 31

(F) N.T., age 39, Housewife, 30.9.48

History

Had suffered from a dermatitis of the face, hands and open vest area for about six months. At times the face became very swollen and oedema of the eyelids had closed the eyes. During a holiday the condition had almost cleared in a fortnight, but had recurred on her return home. She latterly noticed that exacerbations had coincided with attention to a primula obconica which she had bought just prior to the onset of her dermatitis.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

The face was dry, erythematous and puffy. An erythematous dermatitis, in parts crusted and weeping, affected the open vest area. The fingers were slightly swollen and on their apposed aspects a sago grain vesicular eruption was present.

Note: Removal of the plant from her home was followed by the spontaneous disappearance of the eruption in two or three weeks.

Aetiological Group

Dermatitis venenata.

Case 32

(F) I.P., age 43, Housewife, 29.9.48

History

Had suffered from a recurrent vesicular eruption of the feet for five weeks first commencing during warm weather. There were no other complaints.

P.H.

Had suffered from friable, brownish, malformed nails of the fingers and toes throughout life. Had previous vesiculation of feet four years before.

F.H.

Mother suffered from friable nails.

Examination

Marked hallux valgus with much crowding of the toes was present. The toenails were brown, malformed and friable and suggested mycosis. A deep seated vesicular eruption involved the right instep and smaller vesicles were present on the dorsa of the toes bilaterally. Much peeling was present in the interdigital webs and over the metarso-phalangeal joints. There was no evidence of focal sepsis. Although excited and over-anxious, the pulse rate was only 70/min. Hyperidrosis was marked, but no finger tremors were present.

Investigation

A ringworm fungus culture was grown on Sabouraud's medium from a scale removed from between the toes.

Aetiological Group

Fungous.

Case 33

(F) E.McL., age 28, Housewife, 28.1.49

History

Had suffered from a recurrent vesicular eruption of the hands for four and a half months first commencing during her second puerperium. There were no other complaints.

P.H.

Contact dermatitis from newsprint in 1941.

F.H.

Sister suffered from recurrent attacks of bronchial asthma.

Examination

She was a well-nourished subject, but a little pale. There was no evidence of focal infection. A sago grain vesicular eruption affected the palms and sides of the fingers where exfoliation was also present. Hyperidrosis was absent and the skin of the feet appeared normal. A slight tremor of the fingers was present. The pulse rate was 74/min.

Aetiological Group

Allergic.

Case 34

(F) C.McF., age 12, Schoolgirl, 5.7.48

History

Had suffered from a recurrent vesicular eruption of the hands in warm weather for three years. The first attack had developed in association with a widespread sulphur dermatitis following treatment of scabies. At the time two other members of the household had been infected. There were no other complaints.

P.H.

Nothing relevant.

F.H.

Father suffered from lupus erythematosus.

Examination

She was a healthy girl. A marked deep seated sago grain vesicular eruption affected the centres of the palms within an area which had been denuded of horny layer as a result of previous exfoliation. There was no evidence of focal sepsis, hyperidrosis or of nervousness. The skin of the feet appeared normal.

Aetiological Group

Scabetic.

Case 35

(M) R.M., age 5, 19.8.48

History

Developed a vesicular eruption of the right foot around an abrasion about a month before. Vesiculation spread over the sole and a red rash appeared on the dorsum of the foot. The left foot then became involved in the same sequence. Vesiculation and exfoliation continued to occur on the soles, but a dermatitis intermittently weeping and scaling affected the dorsa of the feet. Recently a papular eruption had appeared on the arms and legs.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A discrete papulo-vesicular eruption was present on the extensor aspects of the forearms, knees and legs. The dorsa of the feet were involved in an excoriated scaly erythematous dermatitis having well-defined borders. Soles were affected by numerous vesicles of the sago grain type and exfoliation on some areas was marked. The apposed surfaces of the toes were moist, blanched and scaly.

Investigation

The following tissues were investigated microscopically and

culturally for fungus with negative findings:-

1. Roofs of several vesicles.
2. Scales from toes and soles.

Aetiological Group

Discrete sensitisation dermatitis.

Case 36

(F) J.A.A., age 19, Bank Clerk, 9.8.48

History

Developed a vesicular eruption of the hands preceded by much burning and itching. Had felt the strain of her work greatly during the previous month as in addition to her own work it was necessary to do that of a colleague who had been absent. She had otherwise been a healthy girl.

P.H.

Paronychia of the left index finger a month previously. Nine months before suffered from a similar vesicular eruption during an exceptionally busy period at the bank.

F.H.

Nothing relevant.

Examination

She appeared healthy, but had a fatigued look. A typical sago

grain vesicular eruption was present on the apposed surfaces of the fingers, palms and thenar eminences. Palmar and plantar hyperidrosis was marked. No lesion was seen on the feet.

Aetiological Group

Neurogenic.

Case 37

(F) C., age 48, Housewife, 2.7.48

History

Had suffered from a vesicular eruption of the hands and feet recurring in summer since the age of five. Palmar and plantar hyperidrosis had always been marked. During the previous year had become extremly nervous and lost weight. Bowels had been regular, but appetite exaggerated. Dysmenorrhoea since puberty.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

The face was flushed. Extremely nervous and excitable and weeping without provocation. She was very depressed. A diffuse swelling of the thyroid most marked on the right side was present. There was marked tremor of the fingers. Palmar and plantar hyper-

idrosis was severe. Numerous discrete sago grain vesicles were present on the palms. The pulse rate was 160, but no irregularity of rhythm was detected. B.M.R. was +70%

Aetiological Group

Neurogenic.

Case 38

(M) J.M., age 44, Labourer, 7.8.48

History

Had developed a red itchy eruption on the backs of the hands three weeks previously. Soon spread to involve the anterior aspects of the forearms and dorsa of the feet where crusting had occurred. Benicillin cream was applied to the latter area and soon vesiculation developed at the site of the dressing. Vesicles then appeared on the insteps.

P.H.

1942 - a similar eruption had affected the hands and forearms. Ran a self-limiting course in a month. 1945 - condition recurred and again healed spontaneously.

F.H.

Nothing relevant.

Examination

A weeping erythematous dermatitis was present on the dorsa of

both feet. The soles were involved in a discrete and confluent sago grain vesicular eruption. No peeling was apparent between the toes. A typical bullous erythema multiforme eruption was present on the backs of the hands and on the forearms. Iris forms could also be seen.

Aetiological Group

Discrete sensitisation dermatitis.

Case 39

(F) G, age 59, Hospital Maid Superintendent, 6.7.48

History

Had suffered from a recurrent vesicular eruption of the palms and fingers always induced by exposure of the parts to sunlight. During recent years she had been subjected to the humid heat of the laundry without ill-effect.

P.H.

Nothing relevant.

F.H.

Sister suffered from chronic dermatitis throughout life, first commencing in infancy.

Examination

She was a somewhat obese woman. She suffered from a chilblain circulation of the extremities. The skin of the hands was dry and cold. On the palms a sago grain vesicular eruption in the early exfoliative stage was present. A few discrete lesions involved the apposed aspects of the fingers and the thenar eminences. The feet appeared normal.

Aetiological Group

Allergic.

Case 40

(F) I.M., age 55. Housewife. 8.7.48

History

A vesiculo-bullous eruption had developed from an area of nummular eczema of the left wrist treated with copper oleate ointment two weeks previously. Several days later discrete papules had appeared on the face and scalp and vesicles occurred on the backs of the hands.

P.H.

Six years previously suffered from a generalised erythrodermia which had spread out from a similar area of nummular eczema. Five years before, developed infective dermatitis of leg following

injection for varicose vein.

F.H.

Daughter always developed urticaria after tomatoes.

Examination

Numerous crusts and ruptured bullae were present on both wrists particularly the right. Some crusting and numerous sago grain vesicles involved the backs of the hands. Discrete papulo-vesicles were present on both forearms, on the face and in the scalp. The feet appeared normal.

Aetiological Group

Discrete sensitisation dermatitis.

Case 41

(M) R.M., age 20, Marine Engineer, 9.7.48

History

Suffered from a recurrent vesicular eruption of the left middle finger and toes for two and a half months. Attacks had been induced by warm weather and aggravated by the warm environment of his job.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He was a well-nourished subject with no signs of nervousness. Hyperidrosis was absent. The sides of the left middle finger and dorsi-lateral aspects of the toes were exfoliating. Red glistening denuded areas were present on these parts and over their surfaces small pin head size sago grain vesicles were noted. A blanched squamous intertriginous condition affected the webs between all toes. The pulse rate was 68 and the B.M.R. -5%.

Investigation

The following tissues were investigated microscopically and culturally for fungus with negative findings:-

1. Scales from intertriginous lesions
2. The roofs of vesicles of toes

Aetiological Group

Idiopathic.

Case 42

(M) R.A.McC., age 5 months, 10.7.48

History

Had contracted scabies from the mother two weeks previously.

P.H.

Nothing relevant.

F.H.

Mother and other three children were suffering from scabies.

Examination

A widespread scabetic eruption was present. Burrows affected the soles, palms and finger webs. Numerous discrete sago grain vesicles were noted on the palms and soles and appeared to be unconnected with true scabetic lesions.

Aetiological Group

Scabetic.

Case 43

(F) H.L., age 39, Housewife, 29.6.48

History

Had suffered from a recurrent vesicular eruption of the hands and fingers for four weeks. No hyperidrosis and no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A sago grain vesicular eruption in the exfoliative stage affected the apposed aspects of the fingers. The centres of the palms were reddened and denuded, but typical sago grain vesicles were present on these parts. Slight peeling affected the skin

between the toes and the centre of the soles.

Investigation

Scales from between the toes and from the soles were investigated microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 44

(M) J.M., age 44, Electric Furnace Attendant, 22.6.48

History

Suffered from a recurrent vesicular eruption of the fingers for three years. The first attack followed the use of carbolic soap and since then its use had always resulted in an attack. Frequent attacks had also followed the use of other soaps which often had to be used vigorously because of the dirty greasy nature of his employment. A few weeks prior to examination a severe attack had occurred following the use of a coarse soap and an eruption had appeared on other parts.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He was an apparently healthy subject with no evidence of focal infection. The hands were dry as if they had been subjected to fat solvents. Patchy erythematous, scaly, denuded areas were present on the sides of the fingers. Over the surface of the latter, small sago grain vesicles were noted. A healing nummular sensitisation dermatitis and numerous discrete erythematous papules involved the lower limbs. The feet were apparently normal.

Aetiological Group

Dermatitis venenata.

Case 45

(M) J.W., age 50, Labourer, 20.6.48

History

Had suffered from a vesicular eruption of the fingers for two years. Condition commenced on right hand which was chiefly contaminated by a cutting oil which he had been using for about four months. Prior to the onset, he had noticed that contact with the oil had caused itching of his fingers. He had stayed off work for four weeks and the condition resolved spontaneously. Immediately on his return his eruption relapsed.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A sago grain vesicular eruption involved the sides of the fingers, the nail bases and palms. Slight scaling was present in the finger webs. An oil acne affected the thighs. The feet appeared normal.

Aetiological Group

Dermatitis venenata.

Case 46

(M) J.McN., age 38, Schoolteacher, 6.7.48

History

He had suffered from a recurring vesicular eruption of the feet for four weeks. The onset had followed local treatment of small infective eczematous patches of both heels which had been present for several years. The local application had been sulphonamide powder which had caused the areas to weep. He had been otherwise healthy.

P.H.

1942 - a diagnosis of epidermophytosis of the feet had been made in India.

F.H.

Nothing relevant.

Examination

Areas of denuded infective dermatitis were present on both heels. A sago grain vesicular eruption affected both soles. Lesions were at every stage of evolution and retrogression. He was a nervous and excitable individual. The tonsils appeared to be chronically inflamed.

Investigation

Scales and vesicles of the feet were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Discrete sensitisation dermatitis.

Case 47

(M) J.G., age 18, Shoemaker's Apprentice, 8.7.48

History

Had suffered from a recurring vesicular eruption of the feet for three weeks, the onset coinciding with warm weather. He had always been a nervous subject. No other complaints.

P.H.

Head injury a year previously. Since then had suffered from palpitation and fainting attacks on effort.

F.H.

Nothing relevant.

Examination

He was a nervous indolent and under-developed subject, in appearance more like fourteen than eighteen. A fine tremor of the fingers was present. No evidence of focal infection could be detected. An intertriginous dermatitis affected the area between the fourth and fifth toes bilaterally. A sago grain vesicular eruption with evidence of previous exfoliation was present on both soles. The pulse rate was 68.

Investigation

A ringworm fungus colony was grown on Sabouraud's medium from a scale from between the toes.

Aetiological Group

Fungous.

Case 48

(F) A.F., age 5½, 8.7.48

History

Developed a vesicular eruption of the hands first commencing around a fissure in the first left interspace three years previously. Since then attacks had been recurrent at several weeks interval. No other complaints.

P.H.

Tonsillectomy a year before for recurrent sore throats.

F.H.

Mother suffered from flexural eczema in childhood. Father suffered from chronic dryness and cracking of the skin of the hands.

Examination

Numerous lentil size sago grain vesicles were present on the palms and flexor aspects of the fingers. The nails were pitted and transversely furrowed. The hands were dry, but there was no evidence of tylosis or ichthyosis.

Aetiological Group

Discrete sensitisation dermatitis.

Case 49

(M) C.R., age 59, Labourer, 9.7.48

History

Had suffered from a chronic infective dermatitis of the forearms for two years. The condition had commenced as an irritation from the oily cuff of his overall. There had been a recent exacerbation with the appearance of papules on the forearms and vesicles on the hands. No other complaints.

P.H.

Eight and twenty-three years previously eruptions of the legs had been diagnosed as infective dermatitis.

F.H.

Nothing relevant.

Examination

A congestive weeping and squamous infectious eczematoid dermatitis was present on the anterior aspects of both wrists. The forearms were involved in a papulo-vesicular eruption and the palms in a deep seated sago grain vesicular eruption. A transition between the papulo-vesicles of the forearms and the sago grain vesicles of the hands was evident on the lateral aspect of the left wrist.

Aetiological Group

Discrete sensitisation dermatitis.

Case 50

(M) A.McK., age 5, 10.7.48

History

Had suffered from a recurrent vesicular eruption of the hands in warm weather. At the onset a widespread eruption diagnosed as urticaria had also been present, but had cleared in about two weeks.

Since then in warm weather vesiculation of the hands had occurred.

P.H.

Frequent hyperidrosis of palms and soles. Nocturnal enuresis.

F.H.

Nothing relevant.

Examination

A sago grain vesicular eruption in the exfoliative stage was present on both palms. No other abnormality was apparent.

Aetiological Group

Allergic.

Case 51

(F) E.R., age 20, Grocer's Assistant, 11.7.48

History

Suffered from an itchy vesicular eruption of the hands and feet commencing during warm weather two weeks previously. Always had been a nervous individual who suffered from chronic palmar and plantar hyperidrosis. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

On the palms and apposed aspects of the fingers numerous dry

areas denuded of stratum corneum could be seen. On these areas many typical discrete sago grain vesicles were present. A few also involved the non-exfoliating parts of the palms. A similar eruption was present on the dorsa of the toes, but the skin of the interdigital webs appeared normal and did not suggest mycotic infection. The palms and soles were moist and a slight finger tremor was present. The pulse rate was 68/min. and the B.M.R. -10%.

Investigation

A ringworm fungus colony was grown from a vesicular roof from a toe.

Aetiological Group

Fungous

Case 52

(M) H.S., age 48, Milk Roundsman, 27.7.48

History

Three months previously developed a scaly dermatitis on the backs of the knuckles around small fissures from which he suffered periodically. Penicillin cream was applied causing the areas to weep and a vesicular eruption occurred on the palms. The lesions soon healed, but three weeks prior to admission a relapse developed and a dermatitis occurred on the back of the neck. No other complaint

P.H.

Frequent asthmatic attacks since the age of eleven.

F.H.

Nothing relevant.

Examination

Moderate pityriasis capitis and an associated corona seborrhoeica were present. A dry ill-defined slightly scaly dermatitis involved the nail beds and areas over the interphalangeal joints. A healing sago grain vesicular eruption was present on the apposed aspects of the fingers. A furfuraceous infective dermatitis affected the back of the neck. The skin of the feet appeared normal.

Aetiological Group

Discrete sensitisation dermatitis.

Case 53

(M) R.I., age 24, Electric Cable Maker, 10.7.48

History

Had suffered from a vesicular eruption of the hands and feet preceded and accompanied by itching for five days. No other complaints.

P.H.

Vesicular eruption of the feet in India two years before.

F.H.

Nothing relevant.

Examination

He was a healthy, well-nourished individual. A discrete sago grain vesicular eruption was present on both insteps and on the apposed aspects of the fingers. Nervousness, hyperidrosis and intertrigo between the toes were absent.

Investigation

The roofs of vesicles of the hands and fingers were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 54

(F) E.W., age 4½, 30.6.48

History

Suffered from a vesicular eruption of the feet recurring in warm weather for four years. No other complaints.

P.H.

Nothing relevant.

F.H.

Mother frequently suffered from Migraine hemicrania associated with spots before the eyes, dimness of vision and rippling across the visual fields and vomiting. Headaches induced chiefly by excitement.

Examination

She was a temperamental child, but well-nourished. Palmar and plantar hyperidrosis were marked. The insteps were involved in a discrete and confluent sago grain eruption. No other abnormality was detected.

Investigation

Vesicles of the feet were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Allergic.

Case 55

(M) W.A., age 33, Probation Officer, 29.6.48

History

Developed a recurrent vesicular eruption of the fingers eight weeks previously.

P.H.

1940 - Suffered from psychoneurosis after a head injury.

F.H.

Nothing relevant.

Examination

He was well-nourished, but exceedingly nervous. Marked tremor of the fingers, palmar and plantar hyperidrosis were present. The apposed aspects of the fingers were denuded of horny layer, but over the denuded areas typical sago grain vesicles were noted. No lesion was detected on the feet.

Aetiological Group

Neurogenic.

Case 56

(M) J.G., age 67, Retired Seaman, 31.7.49

History

Developed a vesicular eruption of the hands and feet as part of a widespread sensitisation eruption resulting from treatment of an area of infective dermatitis with penicillin cream ten days previously. No other complaints.

P.H.

Dermatitis medicamentosa around an appendicectomy wound thirty years before. Several attacks of prickly heat in the tropics. Sensitive to adhesive plaster and wool.

F.H.

Nothing relevant.

Examination

He was a well-nourished individual. A widespread papulo-vesicular eruption dermatitis affected the limbs and trunk. A discrete sago grain vesicular eruption was present on the palms and insteps. The primary lesion was a congestive and exudative infective dermatitis of the lower third of the left leg. No other abnormalities were detected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 57

(M) R.S., age 54, Butcher, 2.8.48

History

During warm weather two weeks previously he had developed a small area of weeping dermatitis over the anatomical snuff box of the left hand. Within a few days vesiculation had occurred on backs of the hands and over the fingers. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He was a well-nourished individual. A widespread papulo-vesicular sensitisation dermatitis affected the limbs and trunk. A discrete sago grain vesicular eruption was present on the palms and insteps. The primary lesion was a congestive and exudative infective dermatitis of the lower third of the left leg. No other abnormalities were detected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 57

(M) R.S., age 54, Butcher, 2.8.48

History

During warm weather two weeks previously he had developed a small area of weeping dermatitis over the anatomical snuff box of the left hand. Within a few days vesiculation had occurred on backs of the hands and over the fingers. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A partially denuded congestive and exudative infectious eczematoid dermatitis affected the dorsum of the left thumb. Numerous discrete and confluent sago grain vesicles, about the size of split peas, were present on the backs of the hands, sides and backs of the fingers. Some lesions were purulent. No other abnormalities were detected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 58

(F) M.R., age 35, Housewife and Wool Spinner, 24.1.49

History

Suffered from a recurrent vesicular eruption of the toes for about six months. Palmar and plantar hyperidrosis throughout life. No other complaints.

P.H.

Dermatitis of face eighteen years before.

F.H.

Nothing relevant.

Examination

She was a pale, but well-nourished woman. No evidence of nervousness, but hyperidrosis of the palms and soles was marked.

A healing vesicular eruption of sago grain type was present on the soles and a moist scaly interdigital intertrigo was noted. Pulse 76/minute.

Investigation

A ringworm fungus colony was grown from scales from between the toes.

Aetiological Group

Fungous.

Case 59

(F) S.O'H., age 40, Housewife, 7.7.48

History

Developed a sudden vesicular eruption of the insteps and toes during warm weather twelve days prior to admission. There were no other complaints.

P.H.

1938 - similar attack. A further occurrence in 1947. Several severe attacks of chilblains during adolescence.

F.H.

Nothing relevant.

Examination

On the medial thirds of both insteps large irregular multilocular bullae were present. Some were clear, but others were purulent. The dorsa and plantar aspects of the toes were scaly

and erythematous, but the apposed aspects appeared normal. Several small sago grain vesicles were present on the palms and the apposed surfaces of the fingers. Hyperidrosis was not evident, but the extremities were cold and slightly cyanotic and of the chilblain type. No cardio-vascular abnormality was detected.

Investigation

Several vesicles of the insteps and toes were examined micrcoscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 60

(M) J.W., age 38, Restaurant Owner, 28.6.48

History

A vesicular eruption had affected the left palm and fingers for six months. Three days prior to examination the fingers of the right hand became involved. Since the onset several attacks of lymphangitis had affected the left arm. He had been extremely nervous since 1941. Had had psychotherapy for anxiety neurosis several years previously. Suffered from chronic insomnia and had been addicted to alcohol since the onset of his nervous state.

P.H.

Duodenal ulcer 1941.

F.H.

Nephew suffered from eczema at the age of two.

Examination

He was an exceedingly nervous and anxious individual, but finger tremors and hyperidrosis were absent. A well-defined area of exfoliative sago grain vesicular lesions was present on the left palm. Small clear deep seated sago grain vesicles were noted on the apposed aspects of the fingers of both hands. The skin of the feet appeared normal. No other abnormalities were detected.

Aetiological Group

Neurogenic.

Case 61

(M) R.W., age 26, Labourer, 6.6.48

History

Had suffered from a vesicular eruption of the soles, palms and fingers commencing in warm weather a week previously. No other complaints.

P.H.

1942-1946 - recurrent interdigital intertrigo between toes

whilst serving in the Far East. Palmar and plantar hyperidrosis for several years.

F.H.

Nothing relevant.

Examination

A squamous intertriginous dermatitis was present between the toes. Numerous discrete sago grain vesicles affected the insteps, the palms and apposed aspects of the fingers. Hyperidrosis was present on the hands and feet, but no finger tremor was noted.

Investigation

Scales and vesicular roofs from between the toes and soles were investigated culturally and microscopically for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 62

(M) A.S., age 39, Fireman, 29.7.48

History

Recurrent vesicular eruption on the palms in warm weather for several years. Suffered from chronic vertigo which had been attributed to a functional basis by several specialists.

P.H.

Apart from vertigo there was nothing to note.

F.H.

Nothing relevant.

Examination

He seemed an inadequate person who trembled a great deal. No abnormality was detected in the central nervous system and no focal sepsis was evident. Hyperidrosis of the palms was marked. On these parts an area of exfoliation was present. In parts the horny layer appeared to be absent, but several sago grain vesicles affected these areas. The feet appeared to be normal. Pulse rate was 68/min.

Aetiological Group

Neurogenic.

Case 63

(F) F.L., age 42, Housewife, 15.7.48

History

Had suffered from a recurrent vesicular eruption of the hands first occurring during warm weather six weeks previously. Apart from recent mental depression, there were no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

An exfoliative sago grain vesicular eruption was present on the apposed aspects of the fingers and on the palms. Bilaterally a squamous intertrigo was noted between the fourth and fifth toes.

Investigation

A ringworm fungus colony was grown from the intertriginous scales from between the toes.

Aetiological Group

Fungous.

Case 64

(M) A.M.McC., age 24, 20.7.48

History

Had suffered from a recurrent vesicular eruption of the hands and feet in warm weather for several years. First attack occurred in Iraq during summer. He suffered from chronic palmar and plantar hyperidrosis. There were no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

Small sago grain vesicles were present on the dorsilateral edges of the fingers. A fine finger tremor was noted. An exfoliative sago grain vesicular eruption involved both insteps. The pulse rate was 74/min.

Investigation

Scales from the insteps were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 65

(M) J.Y., age 51, Engineer, 29.7.48

History

Had suffered from an itchy vesicular eruption of the hands for four days following the use of a coarse soap. There were no other complaints.

P.H.

During previous year had several attacks of itching between the fingers following the use of soap to remove grease from his hands. Several months previously vesiculation had occurred.

F.H.

Nothing relevant.

Examination

The backs of the hands and fingers were dry and warm and suggested contact with fat solvents. Small pin head size sago grain vesicles were present on the apposed aspects of the fingers and interdigital webs. The thenar eminences were also affected. The feet appeared normal.

Aetiological Group

Dermatitis venenata.

Case 66

(F) P.McA., age 11, 6.8.48

History

Had suffered from a vesicular eruption of the fingers and toes for several weeks. No other complaints.

P.H.

Always been a nervous child with marked palmar and plantar hyperidrosis.

F.H.

Nothing relevant.

Examination

Sago grain vesicles and bullae were present on the dorsi-

lateral edges of all the toes. A moist, but non-scaly, intertrigo involved the interdigital clefts. Hyperidrosis was marked and foetor was very offensive. Around the nailbeds of the little fingers numerous small discrete sago grain vesicles were present. Palmar hyperidrosis was marked. She was nervous, tense and irritable. There was no evidence of focal infection. No other abnormalities detected.

Investigation

The roofs of the vesicles and specimens of intertriginous skin were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 67

(M) J.S., age 54, Labourer, 6.8.48

History

Developed a widespread sensitisation eruption following the application of sulphonamide powder to a deep wound of his right calf several weeks previously. The eruption had become more severe some days prior to admission and sago grain vesicles had appeared on the hands and feet. There were no other complaints.

P.H.

Suffered from pityriasis capitis throughout life. Infective dermatitis following injury to right calf - 1944. Condition healed rapidly.

F.H.

Nothing relevant.

Examination

He was a seborrhoeic subject with marked pityriasis capitis. A widespread papulo-vesicular eruption and numerous crusted areas affected the trunk, arms and buttocks. Sago grain vesicles were present on the apposed aspects of the fingers. The feet were unaffected. No other abnormality was detected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 68

(M) J.B., age 23, Labourer, 20.6.48

History

Developed a vesicular eruption of the insteps and toes following the wearing of another person's boots a month previously. Some days later vesicular lesions appeared on the fingers. The onset coincided with a warm spell of weather. Nausea and vomiting

preceded and accompanied the onset and since then had coincided with mild exacerbations.

P.H.

Dermatitis upper lip at the age of nine. Periodic attacks of palmar hyperidrosis in warm weather. Contact dermatitis of hands from petrol and grease - 1943.

F.H.

Brother suffered from bronchial asthma and mother from a recurrent vesicular eruption of the hands.

Examination

Scaling and dried sago grain vesicles were present on the apposed aspects of the fingers. A similar eruption involved the apposed surfaces of the great and second toes bilaterally. No interdigital intertrigo was present. Marked palmar and plantar hyperidrosis was noted.

Investigation

A ringworm fungus colony was grown from a vesicle from the right great toe.

Aetiological Group

Fungous.

Case 69

(F) M.L., age 38, Housewife, 19.6.48

History

Recurrent attacks of vesiculation of the hands and feet occurring in warm weather for five years. Patient stated that vesiculation could be induced on the feet by holding them near the fire or by wearing warmed slippers. Concomitant anorexia and nausea frequently accompanied attacks. There were no other complaints.

P.H.

Inecta hair dye dermatitis of face seven years before. Always developed urticaria from rhubarb and oranges.

F.H.

Brother suffered from bronchial asthma.

Examination

A discrete sago grain vesicular eruption was present on the apposed aspects of the fingers and on the soles. No other abnormalities were detected.

Investigation

Vesicles of the hands and feet were examined microcopically and culturally for fungus with negative findings.

Aetiological Group

Allergic.

Case 70

(M) A.R., age 45, Labourer, 12.7.48

History

Had suffered from a widespread sensitisation dermatitis and vesiculation of the hands for four weeks. Followed exacerbation of an old varicose eczema of right leg.

P.H.

Widespread dermatitis following application of elastoplast to the skin - 1940. Dermatitis of the face following the use of atropine eyedrops - February 1948. Chronic palmar and plantar hyperidrosis throughout life.

F.H.

Twin brother suffered from chronic dermatitis of left leg. Sister suffered from asthma.

Examination

The face, neck and limbs were involved in a nummular vesicular dermatitis. Crusting had occurred in many areas. The backs and palms of the hands and the apposed aspects of the fingers were affected by discrete sago grain vesicular eruption. At the wrist all transitions were present from the sago grain vesicle of the hands to the more flaccid and more easily ruptured vesicle of the forearm. A congestive exudative infective dermatitis was noted on the medial aspect of the right leg. Varicose veins were bilaterally present.

Aetiological Group

Discrete sensitisation dermatitis.

Case 71

(M) J.D., age 40, Railway Telegraph Linesman, 4.10.48

History

Had been very depressed for several months as the result of domestic strife. Had been suffering from a recurrent vesicular eruption of the hands and feet for about three months first commencing during warm weather. No other complaints.

P.H.

Dermatitis of left forearm ten years previously. Palmar and plantar hyperidrosis throughout life.

F.H.

Nothing relevant.

Examination

He appeared very depressed and frustrated. No evidence of focal infection was detected. Marked pityriasis capitis was present. Hyperidrosis of the palms and soles was marked and an exfoliating sago grain vesicular eruption involved these parts. Early lesions were present on the thenar eminences. No intertrigo was present between the toes.

Investigation

The roofs of vesicles from the feet were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Neurogenic.

Case 72

(M) A.G., age 32, Clerk, 9.12.48

History

Ten weeks prior to examination received a blow from a ruler on the outer aspect of the left elbow. According to the patient there was no visible evidence of skin damage, but after a few days the area became itchy and red. The condition persisted for a few weeks and penicillin cream was applied followed by an increase of the reddened area and the appearance of a widespread papulo-vesicular eruption of the trunk, face and limbs. The areas affected on the legs became moist and a vesicular eruption occurred on the extremities No other complaints.

P.H.

Plantar hyperidrosis in warm weather throughout life. Occasional mild vesiculation of feet.

F.H.

Nothing relevant.

Examination

A widespread sensitisation eruption consisting of patchy areas of exfoliating erythematous dermatitis, papules and papulo-vesicles affected the arms, face and legs. A sago grain vesicular eruption affected the palms, the fingers and backs of the hands. The lesions were discrete and confluent. At the wrist transitions from the papulo-vesicle of the forearms to the sago grain vesicle

of the hands were noted. The feet appeared normal.

Aetiological Group

Discrete sensitisation dermatitis.

Case 73

(F) R.M., age 32, Housewife, 31.149

History

Had suffered from a recurrent vesicular eruption of the feet for seven months first commencing in warm weather. At the onset the hands had been similarly affected, but healed in a few weeks. No other complaints.

P.H.

Palmar and plantar hyperidrosis throughout life.

F.H.

Nothing relevant.

Examination

The insteps were affected by a defined area of dry exfoliation denuded of stratum corneum in places. Numerous small sago grain vesicles were present on the denuded areas. A moist squamous intertrigo affected the areas between the toes. No lesions were present on the palms. Palmar and plantar hyperidrosis was marked. No evidence of nervousness, focal infection or finger tremors. No other abnormalities were detected. Pulse 88/min.

Investigation

A ringworm fungus colony was grown from scales from between the toes.

Aetiological Group

Fungous.

Case 74

(M) G.S., age 31, Unemployed, 12.12.48

History

Had suffered from a chronic vesicular eruption of the extremities for five years. First commenced on feet, but soon appeared on the hands. The onset followed soon after being shipwrecked whilst serving with the Royal Navy. Condition rapidly healed, following hospitalisation. Always recurred when contact with the enemy was imminent. As a result was never fit to complete a naval operation. Finally discharged from the service on account of his skin condition.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He was healthy and well-nourished, but nervous and irritable. A typical exfoliating sago grain vesicular eruption was present

on the thenar eminences, palms and sides of the fingers. Discrete sago grain vesicles were scattered irregularly over both palms. An erythematous, scaly and vesiculo-pustular dermatitis affected both insteps. The upper edge was sharply defined and consisted of numerous small vesicles and scales. The margins appeared more active than the rest. Moist intertrigo between toes. Moderate palmar and plantar hyperidrosis. Fine finger tremor noted. Pulse rate 100/min.

Investigation

A fungus of the epidermophyton type was grown from scales from between the toes.

Aetiological Group

Fungous

Case 75

(F) P.McN., age 1 year 9 months, 28.2.49

History

Suffered from a recurrent vesicular eruption of the hands and feet for two months. Since the onset an eczematous eruption had affected the legs. Plantar hyperidrosis had been present from birth. Child otherwise healthy.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

She was well-nourished. Sago grain vesicles were present around the nailbeds. Exfoliation was noted on the sides of the toes and fingers and a discrete papulo-vesicular sensitisation eruption was present on the legs. The toenails were brown, opaque, friable and malformed.

Investigation

A ringworm fungus colony was grown from an avulsed toenail.

Aetological Group

Fungous.

Case 76

(F) E.C., age 9, 3.3.49

History

Suffered from a recurrent vesicular eruption of the palms, fingers and insteps for seven months. Lesions commenced around septic abrasions of the palms resulting from a fall. A nervous girl, but hyperidrosis was absent.

F.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He appeared healthy. There was no evidence of focal infection. An exfoliating sago grain vesicular eruption affected the palms and insteps. An ill-defined weeping dermatitis was present on the lower third of the right leg. Numerous discrete papulo-vesicles were noted around the periphery of the dermatitic area. The skin of the feet appeared normal.

Aetiological Group

Discrete sensitisation dermatitis.

Case 77

(M) P.R., age 2, 28.8.48

History

Sustained a third degree burn of the left calf and thigh three months previously. Penicillin cream induced healing, but its use was continued. Five weeks prior to examination redness and vesiculation appeared around the scar on the left calf. A papulo-vesicular eruption then appeared over the limb, soon becoming bilateral. The face and arms became involved and a vesicular eruption simultaneously affected the hands and feet.

P.H.

Nothing relevant.

F.H.

Father suffered from a chronic eczematous eruption of the hands.

Examination

Numerous discrete papulo-vesicles affected the face, arms and legs. Areas of crusting were also present on these parts. The palms and soles were involved in sago grain vesicles in every stage of evolution and retrogression.

Red scars were present on the anterior aspect of the left thigh and calf. Around the latter a moist weeping ill-defined dermatitis was noted.

Aetiological Group

Discrete sensitisation dermatitis.

Case 78

(M) V.C., age 66, Plater's Helper, 14.9.49

History

Had suffered from a varicose dermatitis of the right leg for six months. Four weeks prior to admission sulphonamide powder was applied and severe weeping and spread occurred. Several days previously a widespread discrete sensitisation eruption occurred and a vesicular eruption involved the extremities. No other complaints.

P.H.

Dermatitis (? infective) of hands twenty years previously.

F.H.

Nothing relevant.

Examination

He appeared healthy and well-nourished. No focal infection was evident. The lower third of the right leg was embraced in an ill-defined congestive weeping dermatitis. The trunk and limbs were involved in a discrete papulo-vesicular dermatitis. The face was red, slightly oedematous and finely scaly. A petaloid seborrhoeide affected the presternal region. A discrete sago grain vesicular eruption was present on the hands and feet. At the wrists every transition from the papulo- vesicle of the forearm to the sago grain vesicle of the hand was noted.

Aetiological Group

Discrete sensitisation dermatitis.

Case 79

(F) M.M., age 47, Housewife, 25.1.49

History

Four weeks previously cut left thumb with a tin. Covered area with adhesive plaster and a few days later little blisters appeared

under the dressing. An eruption spread over the back of the hand and soon became bilateral. A widespread sensitisation eruption then developed and a vesicular eruption occurred on the extremities. Anorexia had been marked since the onset of the sensitisation eruption. There were no other complaints.

P.H.

Dermatitis of hands from washing soda on several occasions.

F.H.

Brother's child suffered from infantile eczema.

Examination

A pale woman. Had marked pyorrhoea alveolaris and dental caries. The fauces were markedly injected. A weeping congestive infectious eczematoid dermatitis was present on the back of the left thumb.

A subsiding discrete sensitisation eruption of the limbs was noted and large sago grain vesicles affected the palms, apposed aspects of the fingers and the first and second toes bilaterally. No interdigital intertrigo was present.

Aetological Group

Discrete sensitisation dermatitis.

Case 80

(M) J.B., age 31, Labourer, 15.4.49

History

A recurrent sago grain vesicular eruption had affected the hands and fingers for nine months. The condition commenced around fissures on the thenar eminences, a few hours after the application of an ointment, the nature of which was unknown. There were no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

Exfoliating areas denuded of horny layer were present on the thenar eminences and the apposed aspects of the fingers. Numerous pin head size sago grain vesicles were noted on the denuded areas. The skin of the feet appeared normal. No other abnormalities detected

Aetiological Group

Discrete sensitisation dermatitis.

Case 81
(F) M.R., age 27, Cotton Worker, 15.4.49

History

Suffered from a recurrent vesicular eruption of the hands for

six months. No history to suggest extraneous cause. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

Exfoliation and discrete sago grain vesiculation bilaterally affected the centres of the palms. Hyperidrosis, nervousness and focal infection appeared to be absent. There was no evidence of abnormality of the skin of the feet.

Aetiological Group

Idiopathic.

Case 82

(M) E.S., age 19, Jeweller, 14.6.49

History

Sustained a second degree burn of both hands from burning magnesium powder two years previously. Lesions had almost healed, when a vesicular eruption developed on the hands. The latter eruption soon healed, but since then there had been several

recurrences always during warm weather. He had been otherwise healthy.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A typical discrete sago grain vesicular eruption was present on the palms and the apposed aspects of the fingers. Hyperidrosis and nervousness were absent. There was no evidence of focal infection. The skin of the feet appeared normal.

Aetiological Group

Discrete sensitisation dermatitis.

Case 83

(F) E.E., case 35, Housewife, 14.6.49

History

During previous year had developed several attacks of sago grain vesiculation of the hands following contact with soap powder and water. She had been otherwise healthy.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

The backs of the hands and fingers and anterior aspects of the wrists were rough, warm and dry and suggested the action of fat solvents. Hyperidrosis and nervousness were absent. Deep seated sago grain vesicles of lentil size, discrete and confluent, were present in the interdigital webs and on the lower thirds of the apposed aspects of the fingers. The skin of the feet appeared normal. No other abnormalities were present.

Aetiological Group

Dermatitis venenata.

Case 84

(M) W.McD., age 26, Labourer, 14.6.49

History

A diagnosis of epidermophytosis of the feet had been made two years previously. More recently he had developed a recurrent vesiculation of the left palm. He had been otherwise healthy.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He appeared a healthy individual with no evidence of nervousness, hyperidrosis or focal infection. Discrete lentil size sago grain vesicles were present on an exfoliative area of the left palm. No other abnormalities were detected, and the skin of the soles and between the toes appeared normal.

Aetiological Group

Idiopathic.

Case 85

(M) R.D., age 61, Locomotive Driver, 30.6.49

History

Sustained a scald from escaping steam on the left wrist two weeks previously. Lesion became infected and failed to heal. An ointment was applied and resulted in severe weeping of the part. Three days prior to examination small blisters developed on the sides of both little fingers. He had been otherwise healthy.

P.H.

Plaster of Paris dermatitis four years before.

F.H.

Nothing relevant.

Examination

An exudative crusted infectious eczematoid dermatitis was present on the medial aspect of the left wrist. Discrete papulo-vesicles surrounded the lesion. Discrete and confluent sago grain vesicles were present on the apposed aspects of the fingers. No other abnormalities were detected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 86

(F) J.A.B., age 51, Housewife, 31.5.49

History

Two weeks prior to examination a vesicular eruption appeared on the hands preceded and accompanied by itching following the use of "Arpidol" which she had been applying to a boil on her husband's neck. She was otherwise healthy.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

Both hands were affected in a sago grain vesicular and exfoliative eruption. The right hand was more markedly involved

than the left. No other abnormalities were detected.

Investigation

An"Arpidol" patch test was strongly positive.

Aetiological Group

Dermatitis venenata.

Case 87

(F) H.S., age 53, Housewife, 23.6.49

History

Had developed a weeping dermatitis of the anterior aspect of the right wrist about a year previously following the use of "soda ash" for cleansing linoleum. The eruption had always recurred thereafter following contact with washing soda and water. Two weeks previously the condition recurred after washing clothes with washing soda and soap powder. Several days prior to examination a vesiculation of the hands occurred.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

A well-defined exudative dermatitis was present on the right wrist and papulo-vesicles involved the adjacent area of the forearm.

A bullous eruption affected both hands. The face was red, puffy slightly scaly and warm. Sago grain vesicles were present on the plantar aspects of both great toes. No other abnormalities were detected.

Aetiological Group

Dermatitis venenata.

Case 88

(F) E.P., age 28, Housewife, 30.6.49

History

Suffered from a recurrent vesiculation of the hands for nine months. Lesions always commenced around fissures of the palms. She had been otherwise healthy.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

She appeared a well-nourished subject. Areas of exfoliation were present on both palms. Discrete sago grain vesicles affected the skin, peripheral to these areas. The skin of the feet appeared normal. No abnormalities were detected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 89

(F) E.L., age 28, Waitress, 30.6.49

History

She had noticed that the constant use of soap and water over a period of several years had caused drying of the skin of the hands. For about three years she had suffered from fissuring of the parts in winter and vesiculation in summer. The condition always healed spontaneously and rapidly with the avoidance of soap and water. There were no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

The back of the hands and the anterior aspects of the wrists were dry, rough and warm and suggested fat solvent action. Small sago grain vesicles were present on the apposed aspects of the fingers. Hyperidrosis and nervousness were absent and the skin of the feet appeared normal. No other abnormalities were detected.

Aetiological Group

Dermatitis venenata.

Case 90

(M) J.P., age 10 months, 20.3.49

History

The mother and child had suffered from a widespread itchy eruption for several weeks. About a week before, the mother had been much relieved by the use of benzyl benzoate emulsion.

P.H.

Nothing relevant.

F.H.

As above.- mother also affected.

Examination

The child suffered from widespread scabies. Numerous burrows were present on the insteps and palms. A group of discrete sago grain vesicles involved the outer aspect of the right heel. No apparently scabetic lesions were seen in relation to these vesicles.

Note: The generalised scabetic eruption cleared rapidly by the use of benzyl benzoate emulsion, but the sago grain vesicles continued to recur for many weeks.

Aetiological Group

Scabetic.

Case 91

(M) T.E.R., age 48, Office Manager, 2.6.49

History

Had suffered from a recurrent vesicular eruption of the hands for about twelve years, attacks occurring at several months interval. Ten days prior to examination he abraded the left sole on a nail. Within a few days blisters occurred around the area, soon spreading and becoming bilateral. No other complaints.

P.H.

Developed urticaria from fish.

F.H.

Sister suffered from chronic eczema, and Migraine hemicrania associated with bilious vomiting.

Examination

He was an apparently healthy subject. A discrete sago grain vesicular eruption involved both soles. Some lesions had dried and were beginning to exfoliate. A moist scaly intertrigo was present between the toes.

Investigation

The following tissues were examined microscopically and culturally for fungus with negative findings:-

1. Scales from intertrigo of toes.
2. Vesicular roofs removed from soles.

Aetiological Group

Allergic.

Case 92

(M) R.B., age 28, Civil Servant, 2.9.49

History

Recurrent vesiculation of the hands and feet first occurring in Singapore three years previously. Attacks usually induced by warm weather. Had been free from eruption for several months, but ten days prior to admission the condition recurred on the soles. No other complaints.

P.H.

Skin sensitive to adhesive plaster and elastoplast.

F.H.

Nothing relevant.

Examination

He appeared healthy. Had one carious tooth, but otherwise no evidence of focal infection was detected. A typical discrete sago grain vesicular eruption affected the anterior thirds of both soles. The hands and the areas between the toes appeared normal. Hyperidrosis was absent and no other abnormalities were detected.

Investigation

The roofs of vesicles from the soles were investigated microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 93

(F) M.E.Q., age 22, Typist, 25.5.49

History

Had been taking a hundred thousand units of calciferol daily for two weeks as treatment for recurrent chilblains. Several days prior to examination a vesicular eruption appeared on the fingers.

P.H.

Recurrent chilblains in cold weather for several years.

F.H.

Nothing relevant.

Examination

The extremities were slightly cyanotic. The hands and feet were cold to the touch, but no evidence of hyperidrosis was present. No abnormality was detected in the lungs or cardio-vascular system. A discrete sago grain vesicular eruption affected the apposed aspects of the fingers and the interdigital webs. A moist scaly intertrigo was present between the fourth and fifth toes bilaterally.

Investigation

Scales from the intertriginous areas were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case94

(F) McC., age 30, Housewife, 1.7.49

History

Suffered from several attacks of vesiculation of the hands following contact with Dettol during the previous two years. Two weeks prior to examination she had added a little to water used for scrubbing and immediate vesiculation had occurred. There were no other complaints.

P.H.

Dermatitis of right leg following abrasion, eight years before.

F.H.

Nothing relevant.

Examination

She appeared healthy. A sago grain vesicular eruption was present on the backs of the hands and the sides of the fingers. Hyperidrosis and nervousness were absent. A moist squamous intertrigo was noted between the toes. No other abnormalities were detected.

Investigation

Scales from the intertriginous areas were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Dermatitis venenata.

Case 95

(F) D.L., age 34, Housewife, 31.3.49

History

Laceration of right thumb covered with elastoplast ten days previously. Area became raw and weeping in twenty-four hours. A day prior to examination a widespread sensitisation eruption occurred and vesicles appeared on the hands. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

She appeared well-nourished. A denuded exudative congestive dermatitis involved the back of the right thumb. Discrete sensitisation papules were present on the dorsa of both hands and anterior aspects of the forearms. Sago grain vesicles involved the palms and sides of the fingers. No other abnormalities were detected.

Aetiological Group

Discrete sensitisation dermatitis.

Case 96

(M) V.D., age 10, 5.8.48

History

Recurrent vesicular eruption of the soles in warm weather for three years. Was a regular attender at the swimming baths. There were no other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

Numerous deep seated rounded sago grain vesicles affected the insteps. Areas of exfoliation were also present. Plantar hyperidrosis was also noted. No other abnormalities were detected.

Investigation

A ringworm fungus of the epidermophyton type was seen microscopically in a vesicular roof. No colony was grown culturally.

Aetiological Group

Fungous.

Case 97

(M) T.S., age 18, Steelworker, 28.5.49

History

Suffered from a recurrent vesicular eruption of the hands and feet since the age of ten. Attacks occurred at several month intervals without apparent cause. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

He appeared healthy. There was no evidence of nervousness or hyperidrosis. A discrete sago grain vesicular eruption was present on the apposed aspects of the fingers and on the backs of the hands. A moist scaly intertrigo was noted between the fourth and fifth toes bilaterally. No other abnormalities were detected.

Investigation

Scales from between the toes were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Idiopathic.

Case 98

(F) J.M., age 9, 21.12.48

History

Suffered from a recurrent vesicular eruption of the hands in cold weather for four years often with concomitant chilblains. No other complaints.

P.H.

Nothing relevant.

F.H.

Maternal grandmother suffered from lichenfied dermatitis throughout life and maternal aunt from recurrent dermatitis of the hands.

Examination

She was a pale girl. The lower thirds of the legs were cyanosed and the palms were moist, cold and clammy. No abnormality was detected in the heart or lungs. The pulse was 68/min. There was no evidence of undue nervousness or of focal sepsis. The apposed aspects of the fingers excepting the thumbs and ulnar aspects of the little fingers were involved in a sago grain vesicular eruption. Discrete sago grain vesicles were present on the insteps. No intertrigo of the toes was noted.

Aetiological Group

Allergic.

Case 99

(M) A.Mc.L., Age, 37, Electric Driller, 5.7.49

History

Burned his left wrist five months previously. A dermatitis developed in about ten days and soon blisters occurred on the fingers. The original dermatitic area had healed, but vesiculation of the fingers had been recurring every few weeks. No other complaints.

P.H.

Nothing relevant.

F.H.

Nothing relevant.

Examination

Exfoliation was present on the apposed aspects of the fingers. Some areas were reddened and denuded of horny layer. Over these areas numerous small sago grain vesicles were noted. A course tremor of the fingers was present. The pulse rate was 80/min. The feet appeared normal.

Aetiological Group

Discrete sensitisation dermatitis.

Case 100

(M) W.S., age 56, Electrical Engineer, 5.7.49

History

Repeated attacks of a vesicular eruption of the hands for eight months. A recent attack had coincided with warm weather. No other complaints.

P.H.

Chronic dermatitis of the face from age of seventeen to twenty-four.

F.H.

Nothing relevant.

Examination

Clear sago grain vesicles were present on the backs of the hands and fingers. A moist squamous intertrigo with associated fissures were noted between the fourth and fifth toes bilaterally. A coarse tremor of the fingers was present. The pulse rate was 66/min. No other abnormalities were detected.

Investigation

Scales from the intertrigo of toes were examined microscopically and culturally for fungus with negative findings.

Aetiological Group

Allergic.

Case 101

(M) J.M., age 24, 27.10.48 (Case of Eczema)

History

A patch of eczema had been present on the left calf for five years. Latterly the area had become moist and areas of nummular vesicular eczema had appeared on the right leg and forearm.

APPENDIX 2

METHODS AND TECHNIQUES

Biopsies

All tissues were excised using local 2% Novutox anaesthesia care being taken not to infiltrate the piece of tissue to be excised.

Fixation of Tissue

70% alcohol was used as the fixative.

Preparation of Tissues

The fixed tissues were placed in the following fluids for the periods indicated and in the following sequence:-

1. 80% methylated spirit for 6 hours)
2. 8% phenol in methylated spirit and left overnight) to soften
3. Absolute alcohol (1) for 3 hours then)
   Absolute alcohol (2) for 3 hours) to dehydrate
4. Equal parts absolute alcohol and chloroform until tissues sank.
5. Chloroform (1) overnight)
6. Chloroform (2) 3 hours) to clear

Blocking of Tissues

The tissues were then placed in paraffin wax (melting point 54°C) as follows:-

1. Molten paraffin wax (1) in oven at 56°C for 4 hours.
   Molten paraffin wax (2) in oven at 56°C overnight.
2. Molten fresh paraffin wax - section properly orientated and wax cooled in cold water.

Cutting of Sections

The blocks were trimmed and placed in a Cambridge rocker microtome set to cut at a thickness 6-8 μ.

Sections were cut in ribbons of ten and floated in tepid water and in turn floated on slides in strict serial. The first section of each series was placed near an end of the slide which had previously been marked and at which the slide was subsequently labelled.

The slides were then placed on a hot plate and allowed to drain and dry at 45-50°C. They were then transferred to an oven at 56-60°C for one to two hours.

Preparation for staining

The sections were then treated as follows:-

1. Paraffin wax dissolved out with xylol for 3-5 minutes.
2. Xylol removed with 98% alcohol for 3-5 minutes.
3. Alcohol removed with methylated spirit for 3-5 minutes.
4. Washed in running water for 5 minutes.

Staining

Tissues were stained as follows:-

1. By intra-vital methods.
2. Ordinary methods.

Intra-vital Methods

At the outset it was considered feasible that fluid injected into a vesicle might be expected to pass into any sweat duct having

continuity with it.

Fluids which were hoped to show up microscopically were chosen as follows:-

1. A suspension (Indian ink) used in Case 14 Biopsy 2.
2. Non diffusible dye (carmine in gelatine (after Carleton and Leach (1938)) used in Case 15 Biopsy 3.
3. Diffusible dye (0.5% trypan blue) used in Case 18 Biopsy 6.

These substances were allowed to run passively into vesicles after aspiration of a few drops of fluid. The gelatine carmine was fluid at body temperature, but solid at room temperature. The syringe, therefore, had to be warmed slightly to maintain the temperature above melting point.

The vesicles were then excised in the normal way.

These methods of intra-vital staining of the vesicular fluid were abandoned because only relatively large vesicles could be used. It was considered in these cases that the vesicle expansion alone might often have ruptured ducts to cause continuity of a secondary nature.

Ordinary Methods

The following stains were used:-

1. Mayer's haemalum and eosin was used in by far the majority of specimens.
2. Carmalum was used as a counter stain for trypan blue in sections from Case 18 Biopsy 6.

3. Saline Gram stain was used in a few isolated sections to determine the presence or absence of organisms described by Unna.

4. Several other stains were used in isolated sections.

   (a) Van Giesen to study fibrous tissue.

   (b) Orcein to study elastic fibres.

   (c) Tri-chromic stain (eosin methylene blue) was used experimentally in an endeavour to find a contrasting stain for sweat ducts.

Having prepared the sections as already indicated, they were stained as follows:-

Mayer's Haemalum and Eosin

1. Haemalum filtered on section and allowed to remain for 5 minutes.

2. Washed in water 3-5 minutes.

3. Placed in Scott's tap water for 5 minutes.

4. Washed in ordinary water for 5 minutes.

5. Eosin filtered on section and allowed to stain for 5-10 minutes.

6. Rinsed in water.

7. Dehydrated in methylated spirit and alcohols and then cleared in xylol.

8. Mounted.

Carmalum

Sections after preparation for staining were placed in carmalum solution for 15 minutes then dehydrated with methylated spirit and

alcohols. Cleared in xylol and mounted.

Saline Gram

1. Stained in carmalum for 15 minutes.
2. Rinsed in water.
3. 0.5% crystal violet filtered on and allowed to remain for 2-3 minutes.
4. Washed off with 10% saline which was allowed to act for 10 minutes.
5. Dried with filter paper. Placed in aniline oil until differentiation was complete (1-3 hours).
6. Cleared in xylol and mounted.

Van Giesen Stain

1. Stained in Celestin blue for 10 minutes.
2. Rinsed in water.
3. Haemalum filtered on and allowed to remain for 10 minutes.
4. Rinsed in water.
5. Rinsed in saturated aqueous picric acid.
6. Rinsed in water.
7. Excess wiped off and placed in Van Giesen solution for 3-5 minutes.
8. Excess wiped off and then dehydrated with methylated spirit and alcohols. Cleared in xylol and mounted.

Orcein Stain

1. Placed in orcein solution for 1-2 hours.
2. Rinsed in methylated spirit.

3. Differentiated in 1% hydrochloric acid in methylated spirit until elastic fibres were browny black and the background translacent.

4. Washed in water.

5. Stained with haemalum for 3 minutes.

6. Rinsed in water.

7. Placed in Scott's tap water until blue.

8. Washed in water for 5 minutes.

9. Slide washed with cellosolve.

10. Tartrazine - cellosolve poured on and allowed to remain for 5 minutes.

11. Washed in tap water 2-3 minutes.

12. Dehydrated in methylated spirit and alcohols, cleared in xylol and mounted.

Trichromic Stain (Eosin Methylene Blue)

1. Stained in eosin (5% alcoholic) for 10 minutes.

2. Rinsed in water.

3. Stained in polychrome methylene blue for 10 minutes.

4. Rinsed in water.

5. Differentiated in equal parts - absolute alcohol and colophonium resin to saturation.

6. Finally differentiated in pure acetone.

7. Cleared in xylol and mounted.

Mounting

The medium used was D.P.X.

MYCOLOGICAL METHODS

Fungus Medium

The fungi were grown on Sabouraud's medium slopes prepared in glass universal containers with screw caps. The ingredients were in the following proportions:-

Pure tap water	1000 cc.
Maltose ("brute de Chanut")	40 gm.
Peptone ("granulée de Chassaing")	11 gm.
Agar	18 gm.

Preparation

The method of preparation was in accordance with that outlined by Muir and Ritchie (1932) as follows:-

1. Agar soaked in water for ½ hour.
2. Other ingredients added and dissolved by gradual heating to 120°C in an autoclave.
3. Thoroughly mixed by stirring.
4. Filtered into sterile 500 cc. flasks.
5. Contents of flasks mixed.
6. 8-10 cc. placed in each glass universal container (sterile).
7. Containers placed in Koch steriliser at 100°C for 2 minutes on 3 successive days. (Container screw cap slightly loose)
8. On removal from steriliser on the third day, containers were left tilted and medium allowed to congeal as slopes.

Medium Controls

To test the efficacy of the medium so prepared, scales from

typical tinea circinata lesions were inoculated on slopes and cultures were grown. Plate 7A shows a culture from the type of lesion selected.

Examination for fungi

The lesion was gently cleansed with 70% alcohol and the affected epidermis removed by a sterile scalpel and inoculated on three Sabouraud medium slopes in each case. A piece of tissue was also placed on a microscopic slide.

The prepared slopes were allowed to stand at room temperature for periods up to three months before a negative reading was recorded.

The tissue on the slide was covered with a large drop of 20% liquor potassae and heated for a few seconds under a coverslip and then examined microscopically.

APPENDIX 3

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"Dermatophytosis and Dermatophytids." Arch. Derm. Syph., N.Y. 34, 1.

Wittkower, E. (1948)

Modern Trends in Dermatology, edited by MacKenna, R.M.B.; 1st series, Butterworth's Medical Publications, Lond., page 247.

Plate 1 Case 95 Discrete Sensitisation Dermatitis Group (contact origin, Elastoplast)

Plate 2 Case 72 Discrete Sensitisation Dermatitis Group (contact origin, penicillin cream), demonstrates transition of lesions at the wrist

Plate 3 Case 24 Dermatitis Venenata Group ("Inecto" hair dye)

Plate 4 Case 86 Dermatitis Venenata Group ("Arpidol")

Plate 5 Case 87 Dermatitis Venenata Group (Washing Soda)

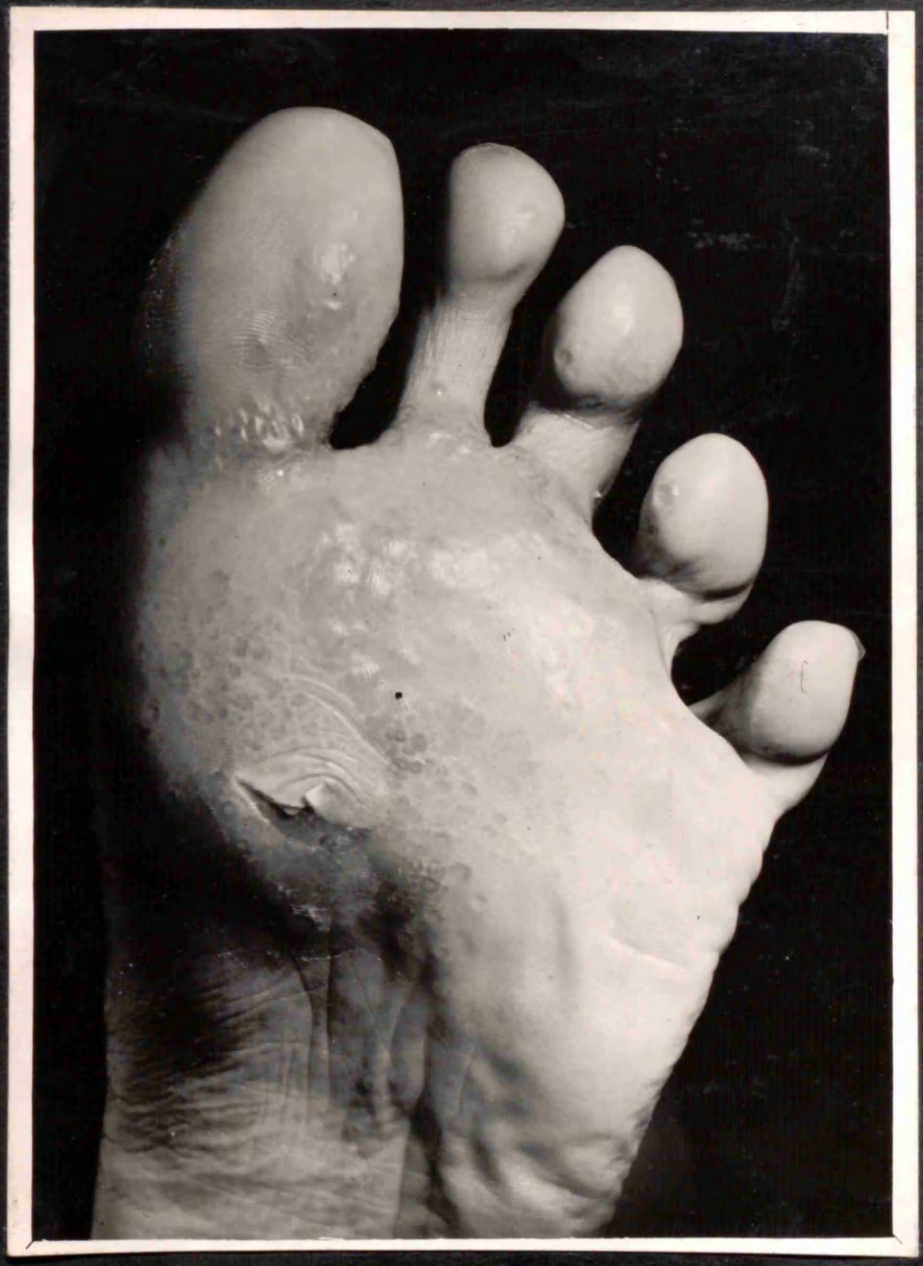
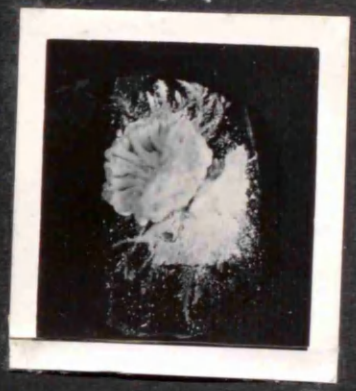


Plate 6 Case 92 Idiopathic Group

A



A. Female M. Tinea circinata control

B

Case 32 Interdigital intertrigo

C

C. Case 51 Vesicle of toe

Plates 7 Fungus Cultures. Lesions from which fungi were grown are indicated.

D

D. Case 63 Interdigital intertrigo

E

E. Case 68 Vesicle of toe

F

F. Case 73 Interdigital intertrigo

G

G. Case 74 Interdigital intertrigo

H

H. Case 75 Toenail infection

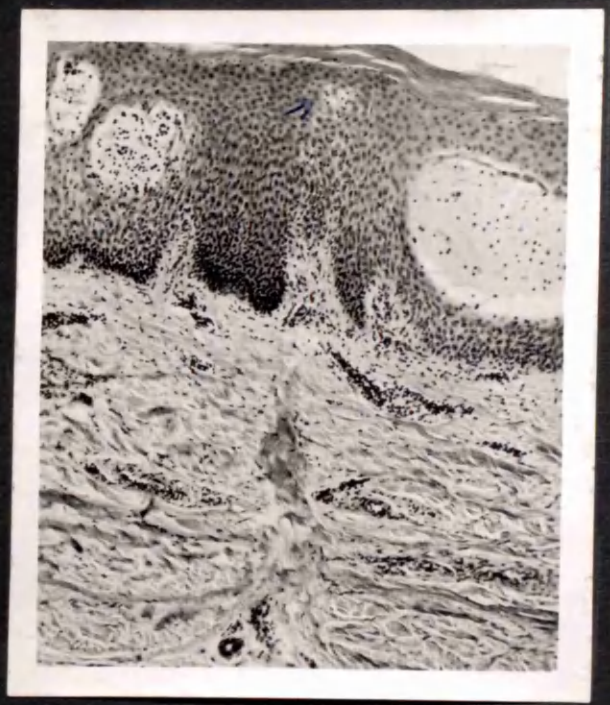


Plate 8 Biopsy 9 Case 72 Slide 4 Section 9
(haemalum and eosin) x 65

Plate 9 Biopsy 9 Case 72 Slide 4 Section 8
(haemalum and eosin) x 65

Plate 10 Biopsy 9 Case 72 Slide 4 Section 7
(haemalum and eosin) x 65

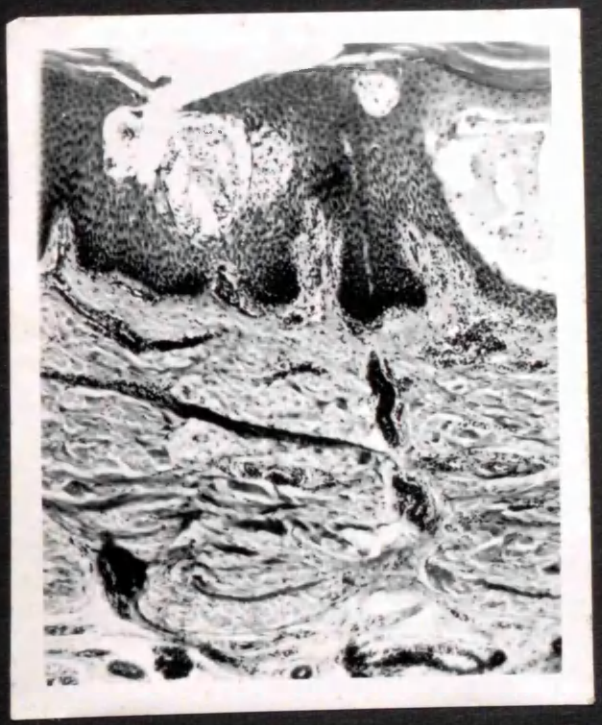


Plate 11 Biopsy 9 Case 72 Slide 4 Section 6
(haemalum and eosin) x 65

Plate 12 Biopsy 9 Case 72 Slide 4 Section 5
(haemalum and eosin) x 65

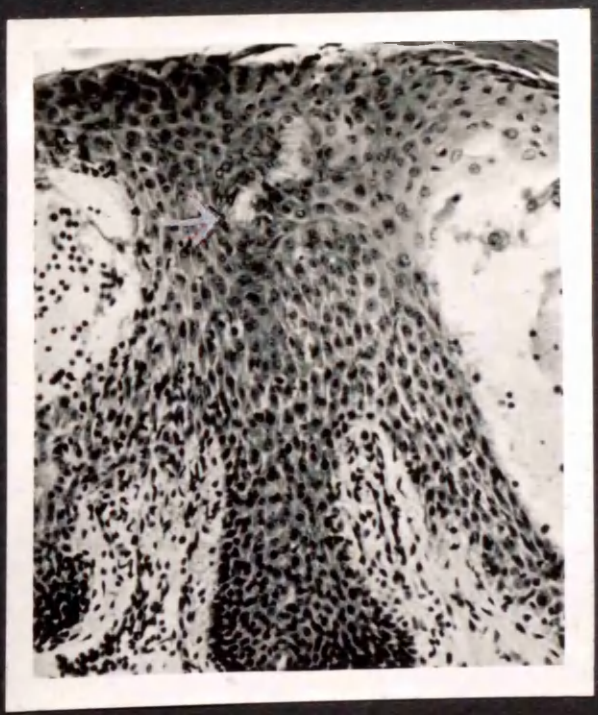


Plate 13 Biopsy 9 Case 72 Slide 4 Section 5
(haemalum and eosin) x 160

Plate 14 Biopsy 9 Case 72 Slide 6 Section 7
(haemalum and eosin) x 210

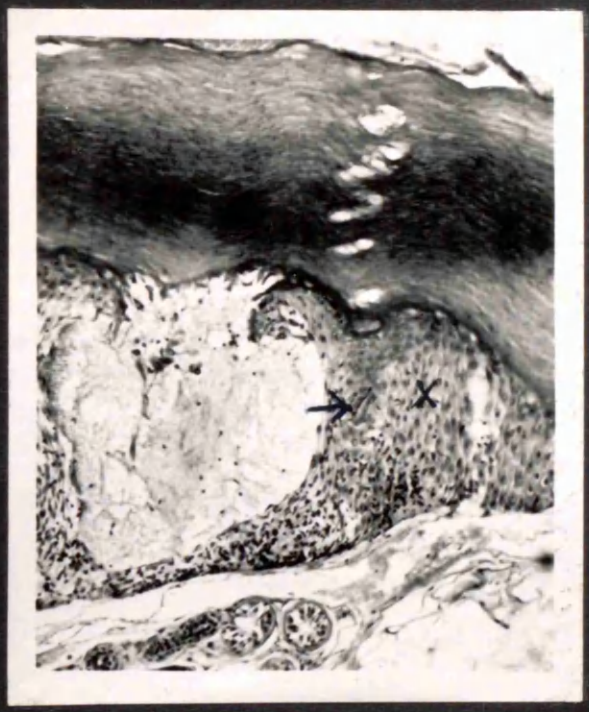


Plate 15 Biopsy 7 Case 19 Slide 4 Section 10
(haemalum and eosin) x 130

Plate 16 Biopsy 9 Case 72 Slide 14 Section 6
(haemalum and eosin) x 120

Plate 17 Biopsy 7 Case 19 Slide 2 Section 2
(haemalum and eosin) x 45

Plate 18 Biopsy 7 Case 19 Slide 8 Section 9
(haemalum and eosin) x 50

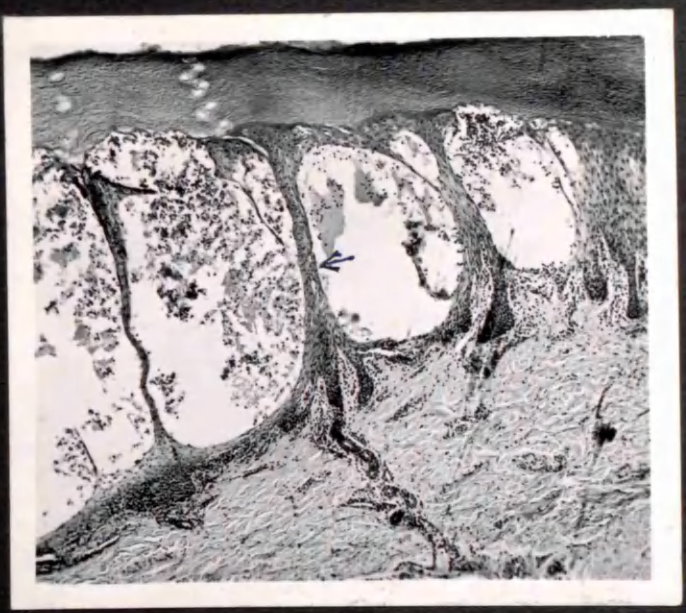


Plate 19 Biopsy 7 Case 19 Slide 3 Section 7
(haemalum and eosin) x 55

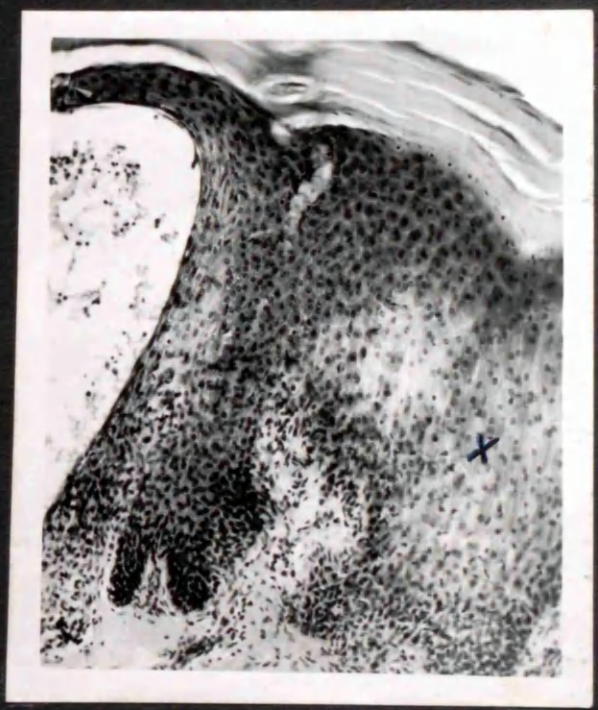


Plate 20 Biopsy 9 Case 72 Slide 7 Section 8
(haemalum and eosin) x 120

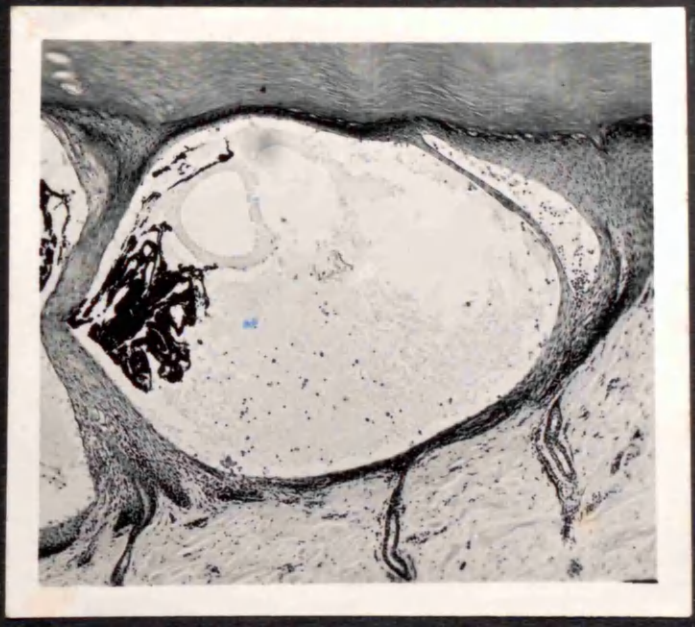


Plate 21 Biopsy 2 Case 14 Slide 5 Section 2
(Intra-vital Indian ink, haemalum and eosin,
vide Appendix 2) x 55

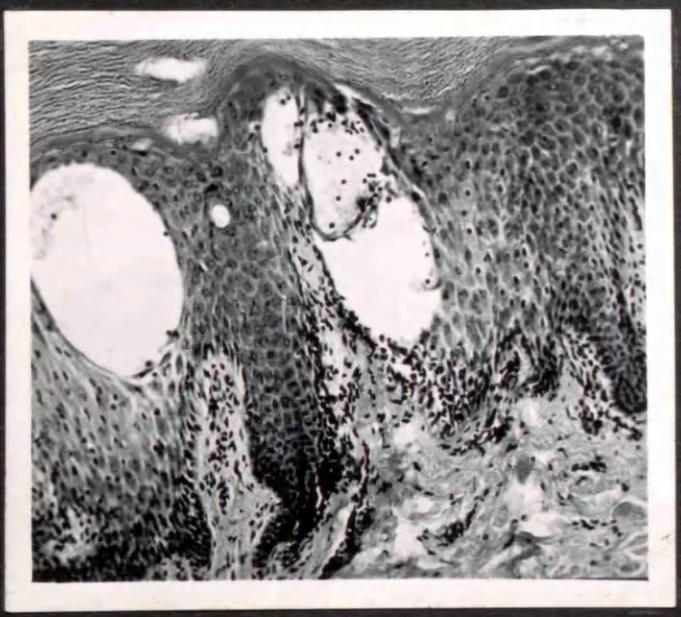


Plate 22 Biopsy 7 Case 19 Slide 15 Section 5
(haemalum and eosin) x 140

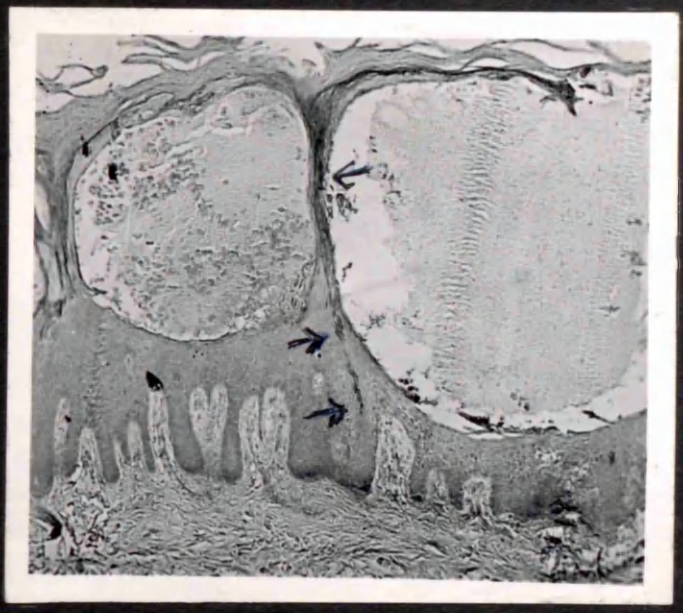


Plate 23 Biopsy 6 Case 18 Slide 17 Section 10
(Intra-vital trypan blue, carmalum, vide
Appendix 2) x 45

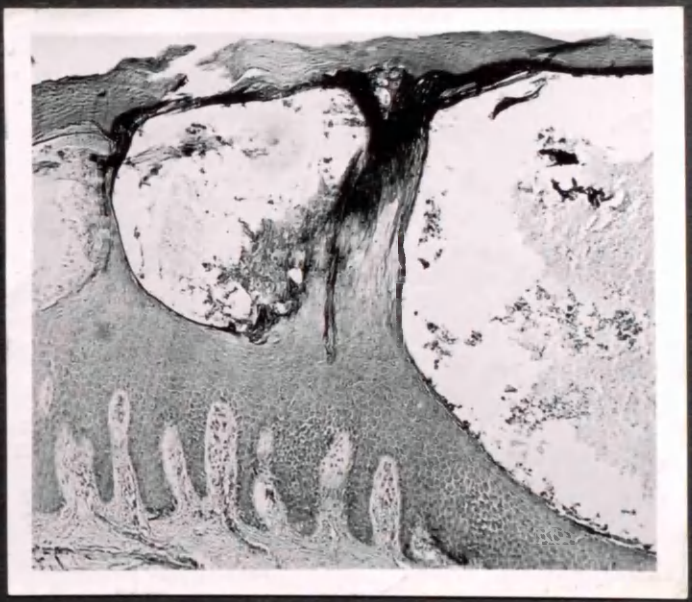


Plate 24 Biopsy 6 Case 18 Slide 13 Section 8
(Intra-vital trypan blue, carmalum, vide
Appendix 2) x 55

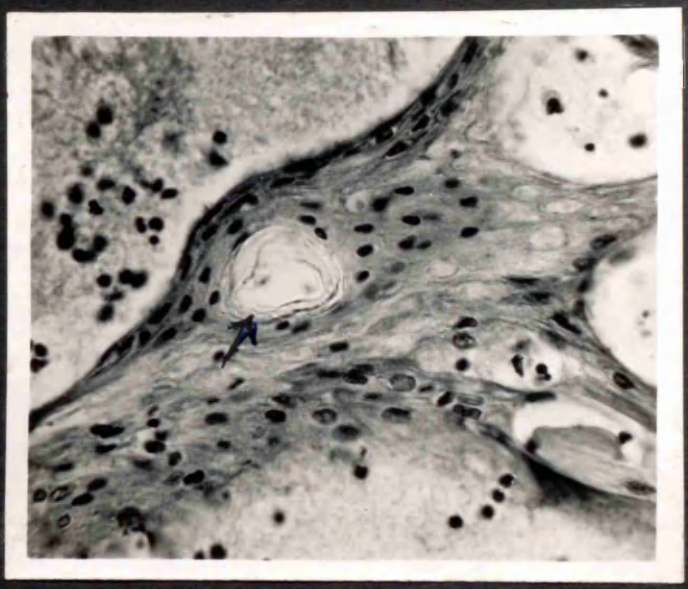


Plate 25 Biopsy 3 Case 15 Slide 15 Section 4
(haemalum and eosin) x 420

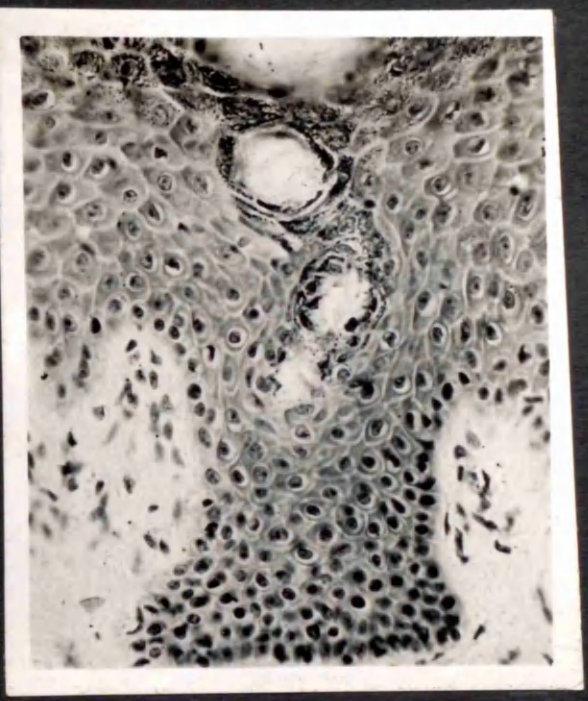


Plate 26 Biopsy 2 Case 14 Slide 3 Section 7
(haemalum and eosin) x 420

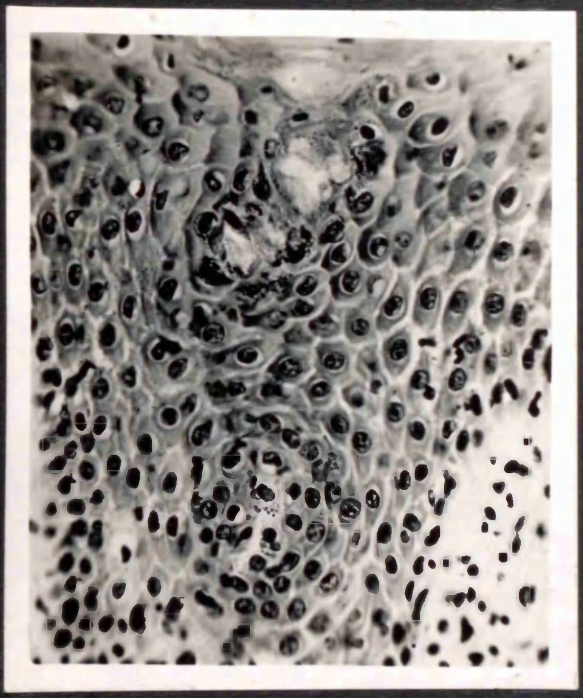


Plate 27 Biopsy 7 Case 19 Slide 3 Section 4
(haemalum and eosin) x 420

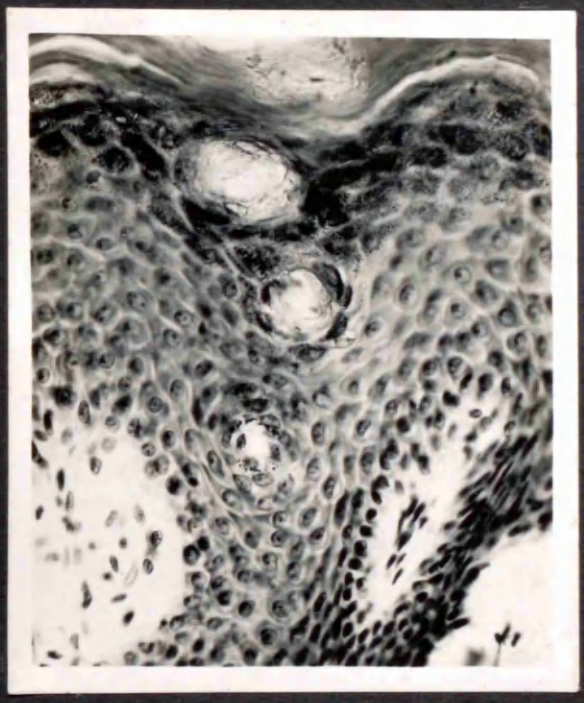


Plate 28 Biopsy 2 Case 14 Slide 2 Section 3
(haemalum and eosin) x 420

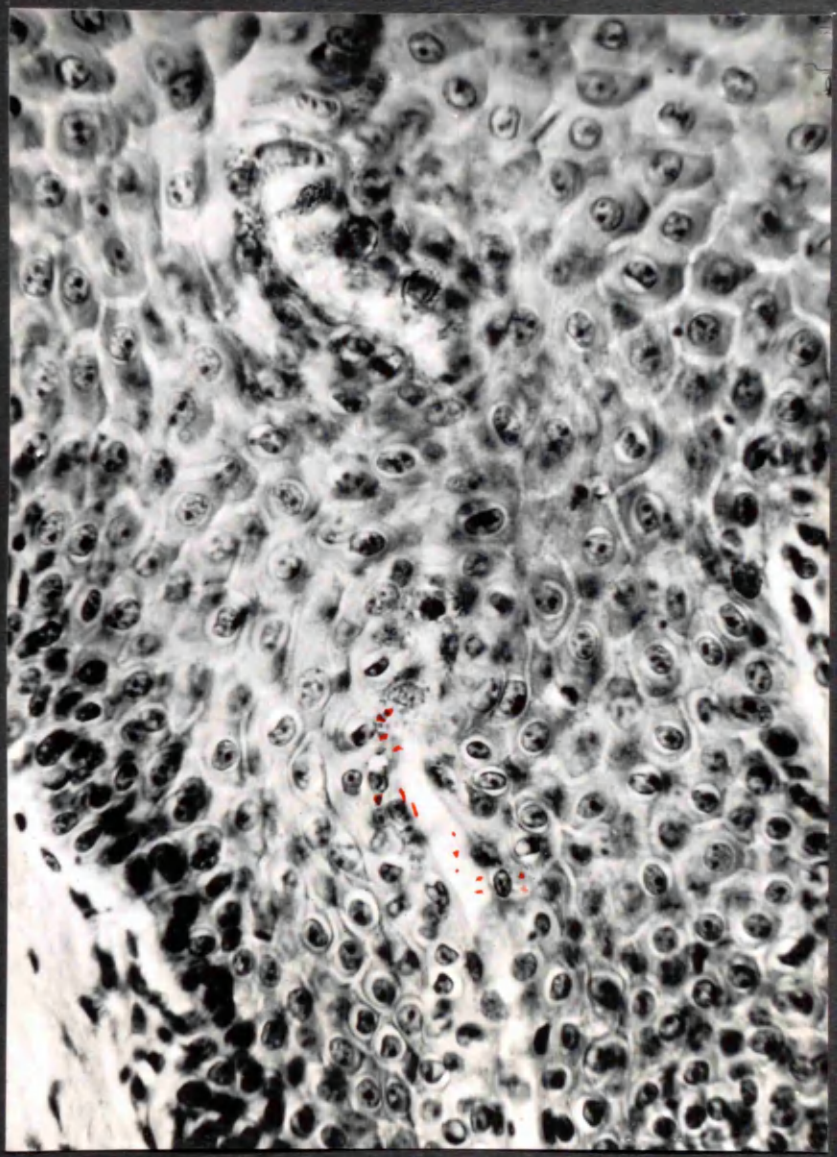


Plate 29 Biopsy 9 Case 72 Slide 9 Section 6
(haemalum and eosin) x 500

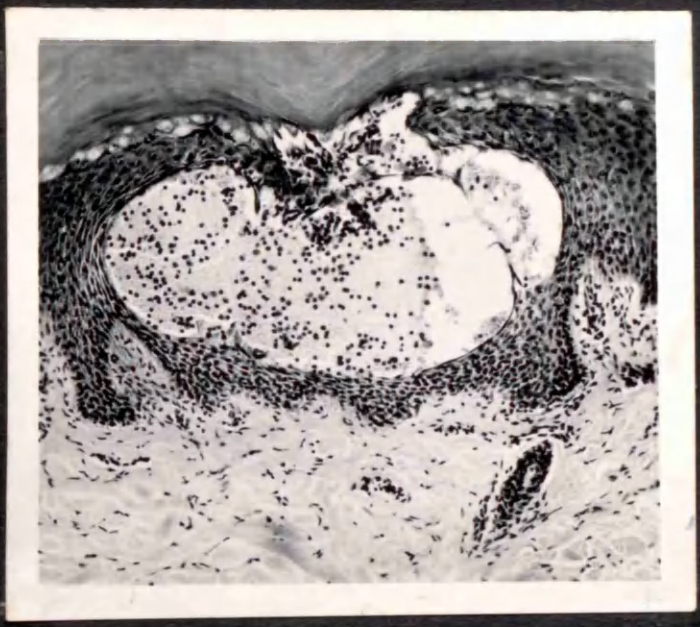


Plate 30 Biopsy 2 Case 14 Slide 9 Section 5
(haemalum and eosin) x 120

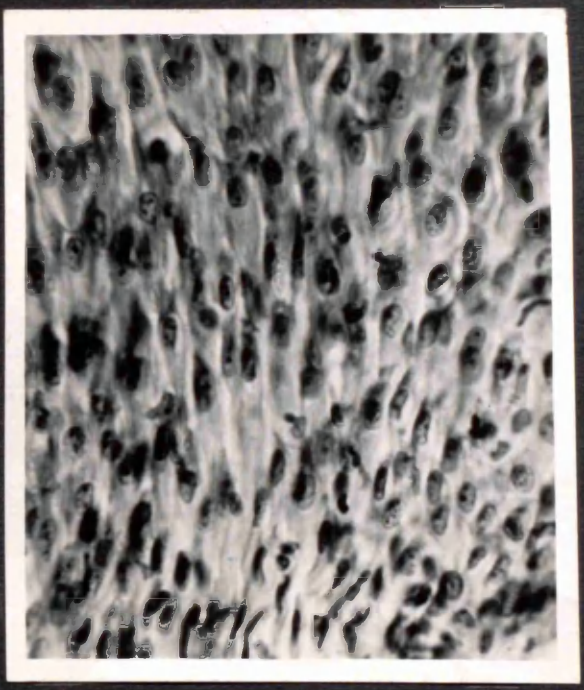


Plate 31 Biopsy 2 Case 14 Slide 8 Section 7
(haemalum and eosin) x 300

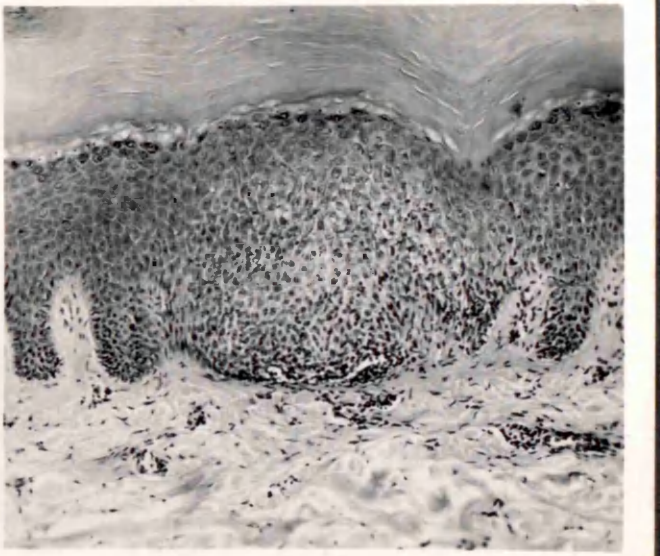


Plate 32 Biopsy 2 Case 14 Slide 14 Section 5
(haemalum and eosin) x 120

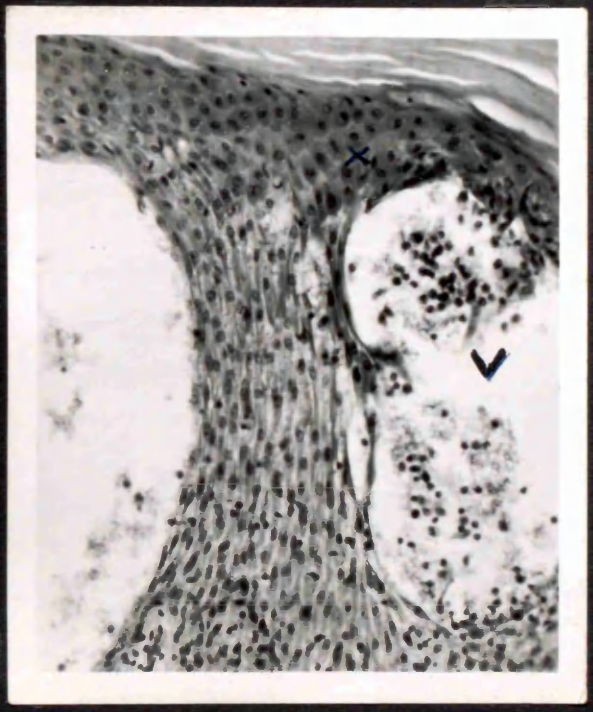


Plate 33 Biopsy 9 Case 72 Slide 7 Section 4
(haemalum and eosin) x 210

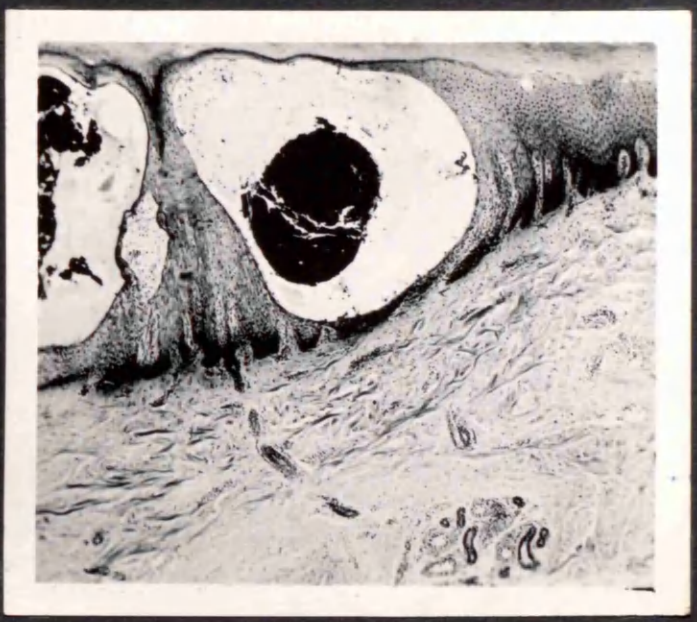


Plate 34 Biopsy 2 Case 14 Isolated Section
(Intra-vital Indian ink, eosin methylene blue,
vide Appendix 2) x 40

Plate 35 Biopsy 2 Case 14 Slide 13 Section 2
(haemalum and eosin) x 420

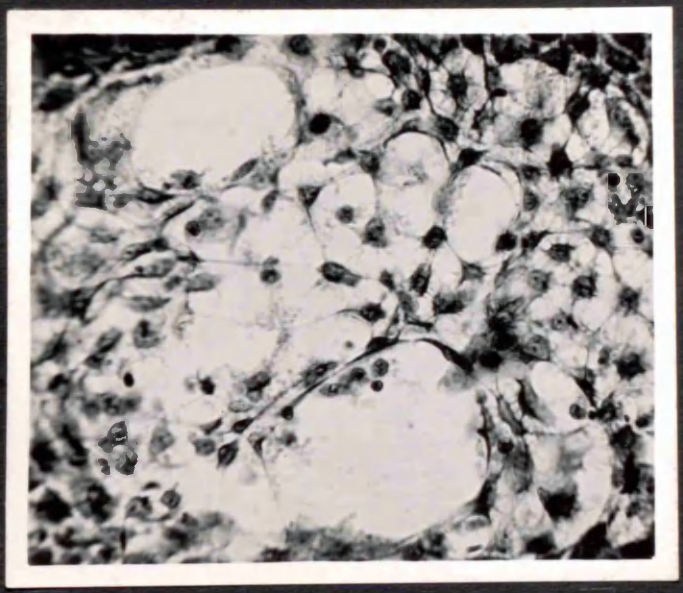


Plate 36 Biopsy 9 Case 72 Slide 18 Section 6
(haemalum and eosin) x 280

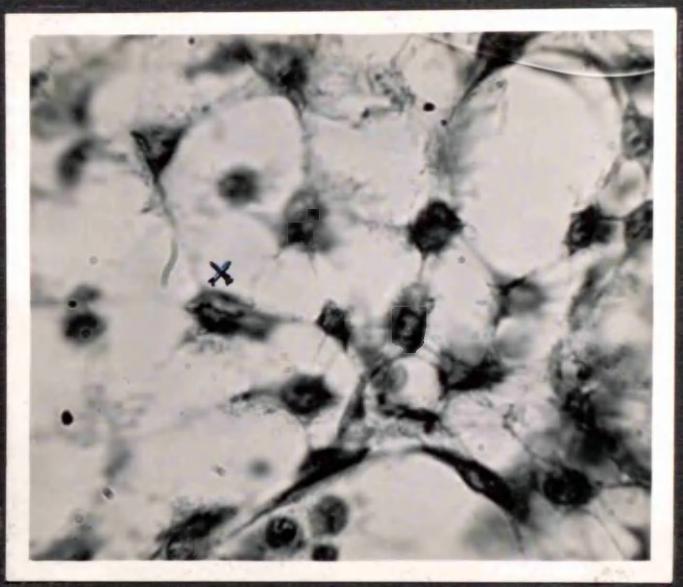


Plate 37 Biopsy 9 Case 72 Slide 18 Section 6
(haemalum and eosin) x 420

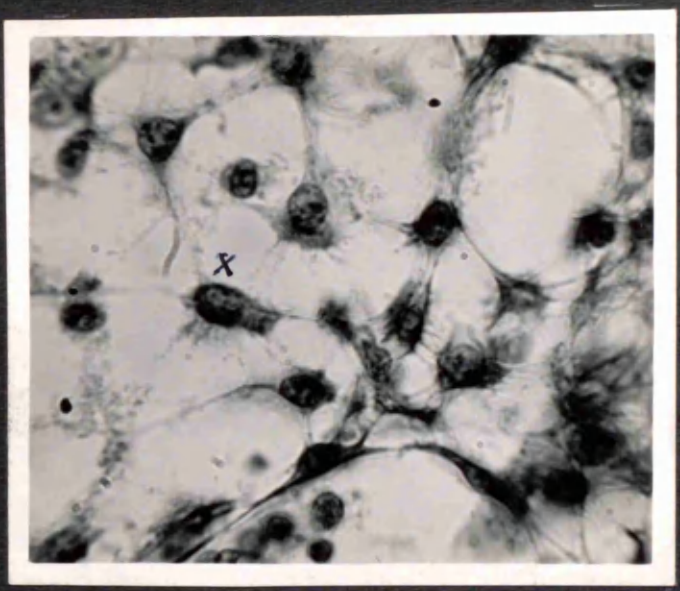


Plate 38 Biopsy 9 Case 72 Slide 18 Section 6
(haemalum and eosin) x 420

Plate 39 Biopsy 10 Case 73 Slide 8 Section 7
(haemalum and eosin) x 280

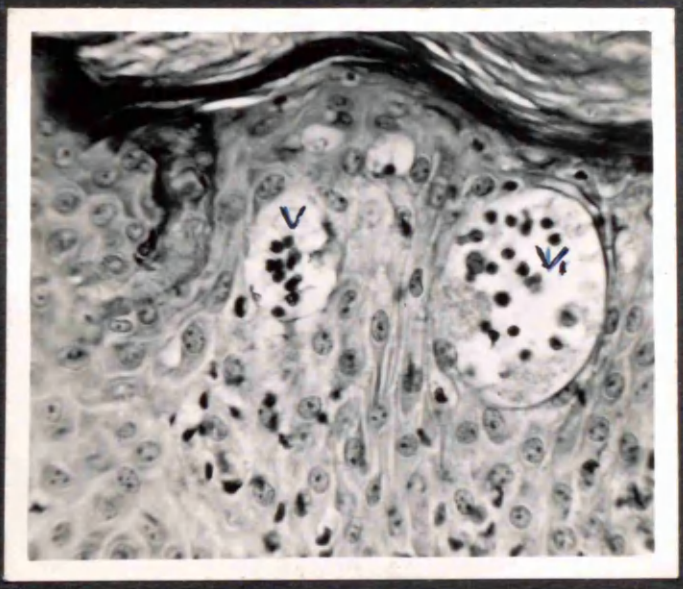


Plate 40 Biopsy 10 Case 73 Slide 4 Section 3
(haemalum and eosin) x 300

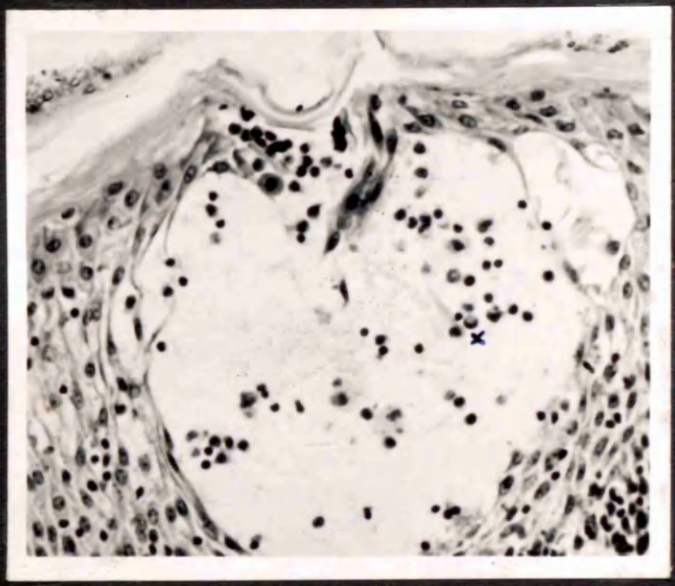


Plate 41 Biopsy 10 Case 73 Slide 7 Section 7
(haemalum and eosin) x 280

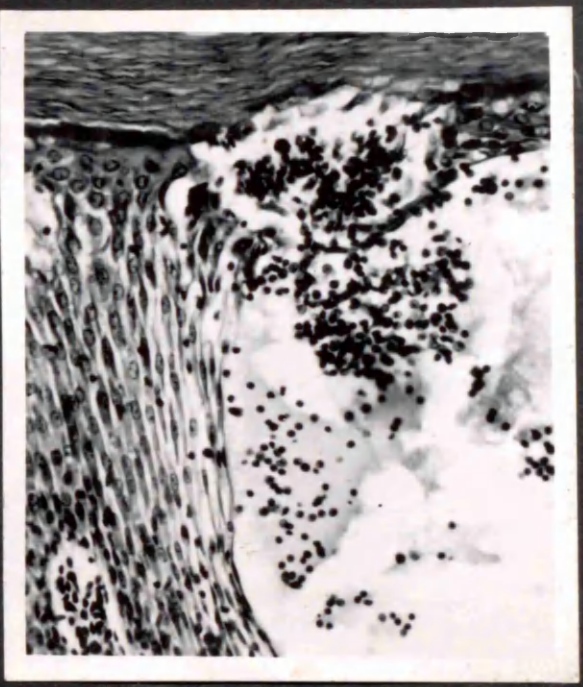


Plate 42 Biopsy 7 Case 19 Slide 5 Section 9
(haemalum and eosin) x 200

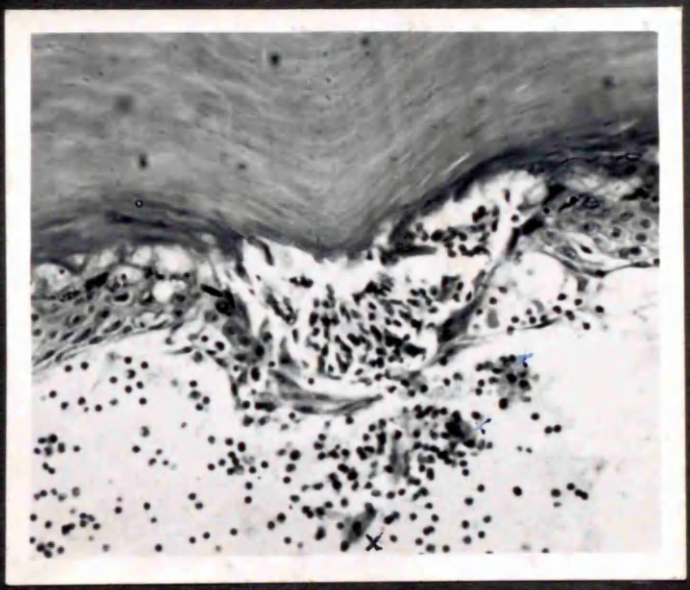


Plate 43 Biopsy 2 Case 14 Slide 9 Section 6
(haemalum and eosin) x 360

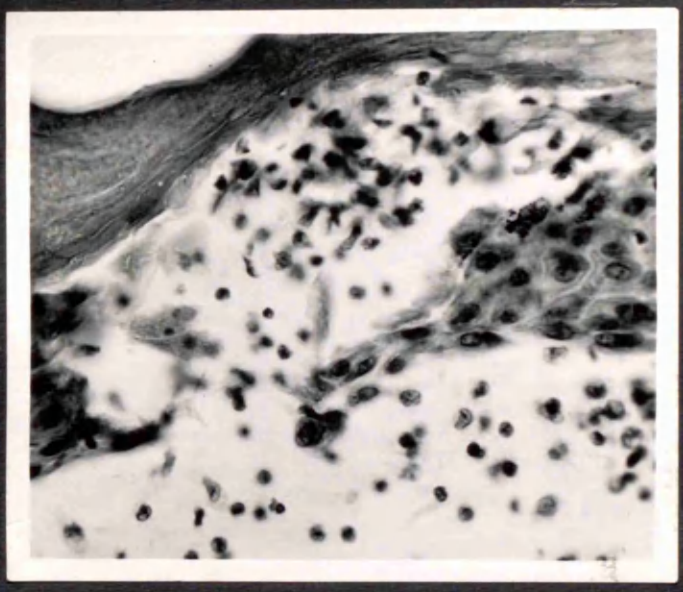


Plate 44 Biopsy 9 Case 72 Slide 15 Section 5
(haemalum and eosin) x 280

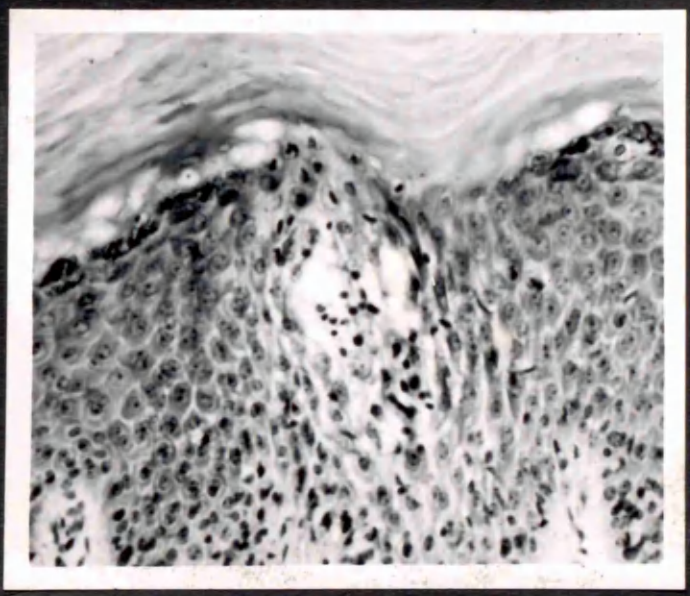


Plate 45 Biopsy 2 Case 14 Slide 14 Section 2
(haemalum and eosin) x 275

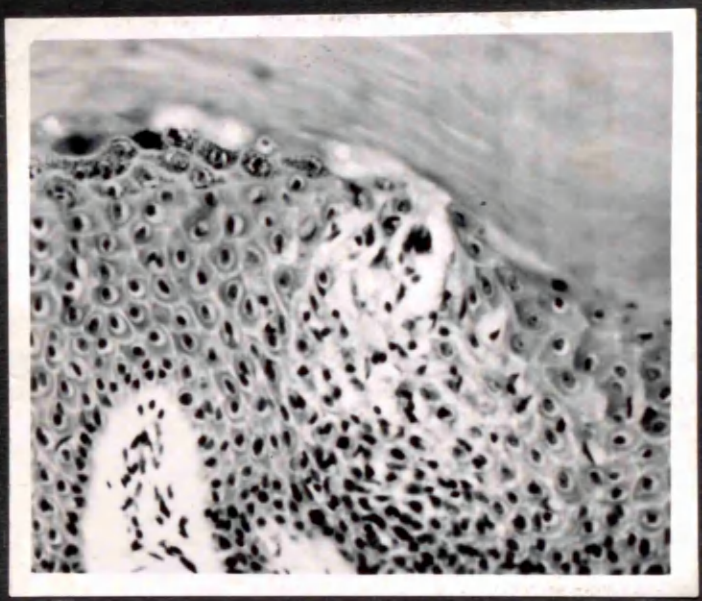


Plate 46 Biopsy 2 Case 14 Slide 5 Section 9
(haemalum and eosin) x 275