

PREFACE

ECZEMATOID DERMATOSES OF THE HANDS  
WITH SPECIAL REFERENCE TO MYCOTIC INFECTION

THESIS

FOR THE DEGREE OF PH.D.

BY

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MAY 1948.



## PREFACE.

Eczematoid Dermatoses of the hands are becoming increasingly prevalent - due, one suspects in no small measure to the complexity of modern life. When such dermatoses are studied one must of necessity resort to a classification, and the one employed here is clinical and aetiological in type. It has been tested against 1364 cases, and has proved serviceable and sufficiently flexible for the purpose but it cannot be regarded as final or complete, particularly when one is dealing with such a complex biological reaction as that of the skin influenced as it is by so many factors, exogenous and endogenous.

The mechanism of production of lesions, the effect of various occupations, prevalence, and recalcitrancy factors, are considered when dealing with each subdivision of the classification.

Of these 1364 cases, 122 were selected and studied in detail. In the latter detailed study the origin was traced in many cases to mycotic infection of the feet. This in turn led to the study of immunity and sensitisation in mycotic infections. Towards this study, human and animal inoculations were performed and immunobiological investigations were made for the presence of humoral antibodies.

In the course of this work I also had the opportunity of observing an epidemic of ringworm infection, and from these observations a great deal of material and information were obtained.

This/

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PART I.

PREFACE: This work was undertaken in the skin department of the Royal Infirmary, Edinburgh, under the guidance of Professor G.H. Percival, and I am glad of this opportunity of acknowledging my indebtedness to him for his helpful and encouraging advice. I should also like to express my appreciation to Dr. R. Aitken and Dr. G.A.G. Peterkin for kindly placing their cases at my disposal. My thanks are also due to Professor Mackie for the provision of laboratory facilities at the Bacteriology Department, University of Edinburgh, and to Sister Toddie for her unstinting help in facilitating my examination of patients both in the wards and the Out-patient department. I wish also to thank my colleagues for their valuable assistance in the preparation of this monograph.

The photographs and the pathological sections were prepared by Mr. Dodds and the technical staff of the Pathology Department, and the typographical work of the final manuscript was undertaken by Miss Stewart, to whom I tender my sincere thanks.

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PART 1.INTRODUCTION.

Eczematoïd dermatoses of the hands are one of the most common types of cutaneous disorder encountered in dermatological practice. The factory worker, the housewife, and the clerk may complain in varying degree of disablement, and each case reveals a symptom complex requiring its own solution. For these individuals are inevitably rendered incapable of performing their normal duties, thus resulting in waste of man power, with tragic consequences for the sufferer, and for the family for which he or she is responsible.

Providing a solution is an intriguing task. It is not one problem which has to be solved but a seemingly interminable series of problems the solution to each of which is a revelation in itself. There is such a large mass of facts to be correlated that it may well appal the stoutest heart. But then, so it is with almost every department of modern research. New facts pour in a steady stream prompted and fed by the very thirst by which they seek to assuage, and for the honest student nothing remains but to select one aspect of his subject and deal adequately with it.

The investigator has neither the time nor the strength to deal with the forest as a whole. He sees the individual trees whereas the man of the eighteenth century with fewer facts to handle was paradoxically in many/

many respects better able to view the forest as a whole.

To arrive at a solution to any problem one must search out, submit to examination and dispose of all its causal factors. This however is not always easy in Dermatology. The skin is a biological system full of mysteries and queries. It is not static nor is it even uniform in its reactions. In biological processes there is no immutable stability or necessarily a repetitive form. A certain chemical may be harmless at one time and noxious at another, harmful to one individual and innocuous to another.

It is surprising how great is the interplay of factors when one considers eczematoid manifestations of the hands in particular. Personal intrinsic and external contactant factors lie at the back of every case reporting for advice. The worker in a chemical plant, the miner in the pit, the farmer in the field and the housewife in the home all report frequently with comparatively similar types of lesions, but each carries a variable interplay of aetiological factors which may be single in one case and multiple in another; may operate in the case of a worker in one factory but not in a worker in another factory, and these same individuals may react differently according to the season.

"We may conceive of this as the day of the jig-saw puzzle" says Stokes, "and though none can deny the importance of key pieces and clearly recognisable bits in the completion of the task of setting up, it is the fit-together of hundreds of often seemingly nameless bits, whose meaning derives less from themselves as such, than from/



from the way they can be placed in the integrated whole which, best defines the causal pictures of today. They are complexes put together by integrators at least as much as they are elemental wholes discovered by single-minded searchers along single trails."

Extensive study has in fact been done on eczematous dermatoses of the hands, but no agreement can be said to exist as to nomenclature, aetiology or therapy. The evolution of dermatology, like that of any other special classification of phenomena, began with the study of visible objective signs and what we now know to be distinct pathological entities were described by names coined purely according to morphological appearances hence the names Eczema - Out boil; Pompholyx - a bleb.

#### ECZEMA AND POMPHOLYX.

No other words in medical terminology are so loosely and indiscriminantly used as Eczema and Pompholyx. The first was coined about 1787 and Robert Willan defined it as "a condition generally due to the effect of irritation, whether internally or externally applied and - occasionally produced by a variety of irritants in persons whose skin is constitutionally very irritable. The second was coined by Jonathan Hutchinson in 1871 to describe a special type of vesicular eruption of the hands. The term Dermatitis has been employed recently in an attempt to remedy the state of affairs the use of the term eczema has created.

There is still great diversity of opinion as to what the term eczema includes and does not include. On the/

the other hand there is a large group of dermatologists to whom eczema and dermatitis are synonymous terms. Tilbury Fox in 1873 put forward the term dyshidrosis for the relationship of the sweat apparatus to the development of vesicles on the hands and feet. Although this theory was opposed by Hutchinson and disproved by numerous workers the term dyshidrosis still exists, to describe dermatological conditions which are in no way associated with disorders of the sweat glands.

In such a controversy one is often led to label dermatological entities whose classification as to aetiology and appearance is difficult to assess with the terms Dermatitis or Pompholyx without further qualification. Thus is created another dermatological scrap heap in which are embodied certain diseases of ill-defined nature. This want of order in the classification has resulted in the inclusion of many vesicular eruptions of the hands and feet under the name Pompholyx.

It is difficult to form a satisfactory definition of the word eczema and state precisely what it includes and does not include. If we accept the German definition of underlying specific or general hypersensitiveness we are confronted with the difficulty of explaining a large number of toxic and infective eruptions, and if we substitute the term Dermatitis we are no better off.

In this text the term eczema is used to indicate those cutaneous eruptions presenting the eczema pattern of reaction in its various forms, and in which the epidermis exhibits an intrinsic quality of hypersensitiveness produced by an external irritant or an internal constitutional/

constitutional predisposition, or both acting together. The term "Vesicular eruption of the hands and feet" has been substituted for those lesions in which no definite aetiology could be found and as far as our knowledge goes they cannot be placed in the classification of dermatoses dealt with below.

#### ANATOMY AND PHYSIOLOGY OF THE SKIN OF THE HANDS.

So far as the skin is concerned the hands and feet show distinct anatomical features which gives them characteristic peculiarities additional to the specialised function they possess. The dorsum of the hand has few but important characteristics. The skin is thin as compared to that of the palms and the rest of the body and moves freely over the underlying parts. It contains groups of transverse creases which mark the location of the interphalangeal joints. Hair follicles, sebaceous glands and sweat glands are normally present on the dorsum of the hands and fingers. The nails guarding the dorsal surface of the end of each finger extend back to the proximal end of the distal phalanx lying on a soft matrix - the nail bed - from which it is formed, and covered on its proximal end by the eponichium. In contradistinction the skin of the palm is tough and thick and is covered with a thick layer of epidermis varying between 2-3mm. in thickness, less marked on the thenar eminences and the sides of the fingers. It is exceedingly sensitive and vascular but is devoid of hair and sebaceous glands. In it the sweat glands are plentiful as compared to other parts of the body. It is disposed/

disposed in numerous fine and coarse furrows in consequence of the arrangement of the papillae and the fibrous bundles which fix it to the underlying structures.

Embryologically the hands and feet resemble each other, being represented by a plate-like enlargement at the extremity of the bud from the lateral ridges at either side of the trunk. The skin and its appendages on the hands are almost anatomically identical with that of the feet, except for the higher selective functions of the skin of the palms. In spite of this marked resemblance the hands and feet have no other relationship in common except that both derive their nerve supply from the Anterior primary rami of the corresponding spinal nerves, otherwise physiologically they are different.

The hands are the instruments of qualification, they possess the most developed tactile sensibility of the skin as a whole. Nevertheless they are precious and necessary tools essential to everyday life. An eruption on the hand in contrast with such things as new growths or acute infections offers no threat to health, but it seriously handicaps an individual and places him at a considerable disadvantage, he may otherwise be perfectly healthy.

The palms by virtue of their thick and tough epidermis are capable of withstanding a wide range of noxious materials without showing any pathological changes. This anatomical feature backed by the specialized properties of sweating, acts as a barrier to infection. The backs of the hands are more liable to invasion by bacteria because, they lack the natural characteristics/

characteristics of the palms and contain pilo-sebaceous orifices which are vulnerable points through which bacteria may gain access.

The pH. of the skin over the hands, forearms and feet show a wide variation from day to day, and from one person to another. According to Pillsbury and Schaffer (1939) the pH. on the flexor surfaces of the forearm is 5.1, and on the extensor is 5.5. On the flexor surface of the index finger is 5.4 and in the 4th interdigital space on the feet is 6.5. About a quarter of the total loss of body fluids from the skin takes place from the hands and feet by insensible perspiration. The loss of moisture is about three times the rate of that from equal areas elsewhere. It is increased under direct nervous control or mental stress but not increased by rise of body temperature. Lovatt Evans (1945).

#### ECZEMATOID DERMATOSES OF THE HANDS.

Under the term "Eczematoid Dermatoses of the Hands", is included all cutaneous lesions which begin on the hands, and remain limited to the hands and lower parts of the arms, or appear on the hands secondary to a primary lesion elsewhere on the body and presents the "Eczema-Dermatitis" reaction.

To approach the study of aetiological factors in patients suffering from Eczematoid dermatoses of the hands the first question the investigator should ask himself is, "whether he is dealing with an allergic condition or not". The second question is, "what is the specific cause or causes of the signs and symptoms of which/

The answer to these queries is obtained only as a result of a study which comprises a detailed and intimate history, physical examination, laboratory investigations and close clinical observation.

In this paper the investigations have been undertaken by two methods.

Firstly. A study of cases, reporting to the Skin Department with eczematous lesions on the hands as regards, -

- a. Morphology and clinical appearance.
- b. Location and prevalence of the lesions.
- c. Occupation and relative contactants.
- d. Factors in recalcitrant lesions.

Secondly. A detailed study of selected cases with laboratory investigations, biological reactions and a regular follow up of progress, as in the following scheme.

Name	No.	Date.
Address	Age	Occupation
		Duration

- Family history including allergic history.
- Previous history. General and present complaint.
- Present illness (in chronological order).
- Social history - home, work, hobbies, habits, emotional life.
- Physical examination.
  - a. Skin in general.
  - b. Description of lesion.
- Relapse and causes.
  - Contacts - Vocational, hobbies.
  - Ingestants - Food, medicines.
  - Menstrual history.
- Any seasonal variation.
- Previous therapy and effects.
- Effect of Soaps.
- Any marked dietary deficiency.
- History of dermatophytosis - present and past.
- History of any other skin diseases.
- Evidence of any focal sepsis. Eyes, Ears, Mouth, Sinuses etc.
- Emotional and nervous stability.
- Endocrine history.
- Laboratory examinations
  - a - Bacteriological, cultural.
  - b - Skin tests
  - c. - Immuno-biological study.
  - d. - Pathological sections.

TABLE NO. 1.

This study was begun with a distinct appreciation of the difficulties ahead. It has been realised to a certain extent from previous experience, the difficulty in determining the etiology in these cases and the confusion existing over terminology. It was always my interest before I came to this country to examine fully, patients suffering from skin affections of the hands, for the simple reason that I was often unsuccessful in effecting a curative treatment, and occasionally patients reported for weeks on end, with the same complaint often exhibiting periods of remissions and exacerbations.

When first I started my work I encountered still more difficulties on account of the wide range of contributory factors in the causation of these dermatoses. The difficulty of insuring regular attendance of patients, the acute shortage of hospital beds and the exhausting task of follow-up, tend to blunt ones interest at the beginning of such a work. But in spite of all these difficulties, the material was available and facilities were freely provided to bring this study to a conclusion.

There are numerous factors that contribute to the causation of these dermatoses of the hand. They could be summarized into two groups.

1. Exciting Causes -

(a) External irritants.

External irritants, found to produce eczematous eruptions over the hands, are very numerous. They usually vary with different people in different occupations, and depend greatly upon the irritating characters of the substances encountered in everyday life. They are usually chemical in nature, simple or organic, but physical/

physical agents such as light, heat and cold are also capable of exciting an eczematous eruption.

(b) Internal agents.

These include food and medicaments as well as toxic products liberated inside the body from an infective process.

(c) Infections.

All organisms capable of exciting an inflammatory process contribute to the production of these dermatoses directly or indirectly. Pyogenic micro-organisms and fungi are commonly met with.

(d) Other causes.

Other causes such as trauma, nervous shock, parasitic infestation and insect bites are also capable of exciting an eczematous eruption.

2. Intrinsic predisposing causes.

Intrinsic or constitutional predisposing factors are concerned with the peculiarities of the individual and his relationship and adaptation to the particular environment in which he finds himself. These may be general, for example heredity, psychogenic or allergic factors, or local, such as surface bacterial and mycotic factor, pH. factor, sweat factor, traumatic factor etc. Stokes (1932) enumerates an illuminating list of factual analysis from which I quote those related closely to affections of the hands and feet.

- 1- Heredity factor.
- 2- Infection-susceptibility factor.
- 3- Hypersensitivity and allergic factor
- 4- Ichthyotic and Xerodermatous factor.
- 5- Sweat factor
- 6- Psychogenic factor



- 7- Endocrine factor.
- 8- Metabolic factor.
- 9- Local and pH factor.
- 10- Surface bacterial and mycotic factor.
- 11- Traumatic factor.
- 12- Diathetic state factor.

Thus, all the evidence collected must be carefully and properly evaluated as regard its part in development of the dermatoses, and too much credence must not be placed on the history furnished by the patients, which may sometimes be at variance with fact. A general knowledge of the working conditions and a particular inquiry into the individual's work and environment, is of value and often necessary for diagnosis. When all this evidence is brought together and its relationship interpreted, clinical skill is all that is required to correlate the observations.

During the years 1946 and 1947, 12,680 new patients reported to the skin department of the Royal Infirmary, Edinburgh. There were 3657 cases or 28.8% suffering from Eczema-Dermatitis in general, and 1364 cases or 10.7% with a variety of eczematous eruptions of the hands. In general, the number of females was more than that of the males with a wide variation of age from a few days old to 85 years of age. Among the cases with eruptions over the hands there was a greater proportion in between the ages of 20-40, males showing a higher incidence. See table No. 4.

Seasonal prevalence of eczematous eruptions in general seems to show a high incidence during both autumn/

autumn and spring while eczematoid dermatoses of the hands, though they present the highest incidence in the month of July; they do not tend to show striking prevalence in any season, as can be seen from the accompanying table.

Eczematoid

<u>Dermatoses</u>	<u>Jan.</u>	<u>Feb.</u>	<u>Mar.</u>	<u>Apr.</u>	<u>May</u>	<u>Jne.</u>	<u>Jul.</u>	<u>Aug.</u>	<u>Sep.</u>	<u>Oct.</u>	<u>Nov.</u>	<u>Dec.</u>
1-On the hands	126	98	90	120	104	102	142	122	98	138	100	124
2-In general	312	254	319	343	326	263	293	271	300	386	340	250
3-General attendance	1005	900	1017	1089	1179	1066	1129	1151	1106	1171	1017	850

- 1- Eczematoid Dermatoses on the hands totaled 1364 10.7%
- 2- Eczema-Dermatitis in general totaled 3657 28.8%
- 3- New patients monthly attendance totaled 12680 100.0%

Table No.2 showing the ratio between Eczema-Dermatitis and general attendance for the years 1946 and 1947.

REVIEW OF LITERATURE

Dermatological literature contains a vast number of articles describing dermatoses of the hands. As a group they have been discussed by Chipman (1935), Andrews and Barnes (1934), Davidson and Birt (1943), Stokes, Lee, and Johnson (1943) and Blaisdell and Schwartz (1945) and Lane et al.(1945). Individual types of these dermatoses have been thoroughly investigated and widely discussed. Engman(1902), Fordyce, and Sutton (1920) described infectious eczematoid dermatitis, Pollitzer (1912) described "Recurrent Eczematoid Affections of the Hands" and differentiated it from Nummular Eczema. Mitchell (1929) emphasized the rôle played by streptococci in producing dermatoses simulating ringworm of the hands and feet. Barber ( 1936) and Ingram (1936) described a pustular dermatosis which they called Pustular/

"Pustular Psoriasis." Andrews and Mackacek (1935) also described a pustular dermatosis which they associated with a bacterial focus of infection, this they called "Pustular Bacterid." Jordan, Dolce and Osborne (1940) discussed housewife's eczema, Benedek (1946) described "Pompholyx" and attributed it to an endoparasitic haematogenous eruption due to *B. Endoparasiticus*. Blaisdell, Harper and Schwartz (1945) described a chronic vesicular eruptions of the hands and suggested a new clinical entity under the name of "Dermatitis Margaritata Recurrens." Becker and Obermeyer (1944) described "Exudative Neurodermatitis". Peck (1930) described "Epidermophytids" and Hopkins (1932) described "Monilids" of the hands, secondary to a primary fungus infection in some other areas of the body. Gross (1941) described "Nummular Eczema" and attributed it to vitamin A deficiency.

It has been increasingly evident throughout the study that the designation of many of the dermatoses do not conform to a common pattern, and what is called contact eczema of unknown origin by one, is called pompholyx by another. It is very difficult sometimes to classify a dermatitis and place it in a group or a subgroup of diseases- but this does not justify the creation of new terms whenever such a difficulty arises.

From the study of the morphology and clinical appearance and distribution of these eczematous eruptions, and the analysis of the data obtained from the patients' histories and laboratory studies, the following grouping is presented in an attempt to explain the pathogenesis and aetiology of these dermatoses of the hands.

1- POST-TRAUMATIC INFECTIVE ECZEMA.

2- TOXIC CONTACT DERMATITIS.

3- ALLERGIC CONTACT ECZEMA.

4- INFECTIVE ECZEMA.

5- ENDOGENOUS ECZEMA.

6- -ID ERUPTIONS.

I wish to make it clear that the grouping presented does not explain all eczematous eruptions of the hands. That will not be possible until our knowledge of the biological reactions of the skin and the body as a whole are more properly understood. I have attempted to cast some light on the aetiology of these lesions by presenting them in a different setting.

We have no standard device nor any special method by which we can discriminate between these cases; and as long as our judgement is restricted to objective phenomena, and the biological reactions are in progressive evolution, no accurate differentiation can be established.

#### POST-TRAUMATIC INFECTIVE ECZEMA.

In this group of eczematous lesions, trauma seems to be the basis if not the direct precipitating cause, and infection is a constant accompanying factor, but it has not been possible to identify any allergic phenomena. Some authors have attributed an aetiological importance to nervous factors (Becker 1944), others to vitamin deficiency (Gross 1941). Rowe (1946) is of the opinion that food allergy is an important cause of nummular eczema.

This group of eczemas is commonly found among workers, labourers and housewives in whose occupation dust and liquid is a major contact. Injury is thus produced/

produced by the mechanical action of gritty particles, by the toxic action of liquids evaporated from the skin surface or by direct irritant chemical action. Small amounts of these chemical substances may lodge in the natural folds of the skin and become more and more concentrated as a result of evaporation, so that what was originally, a safe concentration gradually acquires toxic properties. (Percival) 1947).

The part that micro-organisms or their allergic manifestations play is very difficult to assess. Haxthausen (1935) is of the opinion that the micro-organisms of the skin may be operative in the pathogenesis of certain allergic cutaneous eruptions, in as much as they represent the foreign protein which, in combination with substances applied to the skin, results in the formation of complete antigens capable of producing antibodies that are reactive with the simple compounds as well.

This group consists of eruptions described by some dermatologists as nummular eczema, streptococcal dermatitis and papulo-vesicular eczema of Brocq. Darier (1928) applied the name of "Eczematide" to such lesions when occurring on the body. Becker and Obermeyer (1944) uses the term "Exudative Neurodermatitis of Kriebek" for some of these eruptions which are microscopically vesicular, except when they affect the palms and show dyshidrotic vesicles.

#### CLINICAL FEATURES.

The eruption consists of one or more round or polycyclic plaques of minute discrete and confluent papules/

papules, papulo-vesicles and vesico-pustules which never retain their vesicular character as they are thin walled and easily ruptured. The lesions are usually seen in the oozing and weeping stage. Dry psoriasiform or pityriasi-form plaques resembling the eczematide of Darier are not uncommon, and also, impetiginisation and crusting not infrequently occur changing the picture into what is called impetiginised eczema. The advancing edges of these patches are sharply demarcated from the surrounding skin, they grow by peripheral extension sometimes tending to clear in the centre, thus resembling greatly a mycotic infection. The plaques may be single and the diameter of a fully developed disc may range from  $\frac{1}{2}$  to 8 cms. or more. The lesions remain discrete and recurrences and exacerbations are likely to occur in the same sites especially in the more discoid type where central recurrence occurs while the edges are still active. Pig-<sup>usually</sup>mentation/follows healing of these lesions. The more acute type presents multiple lesions varying in number from 2 - 32 on both hands as seen in one of the cases. Patches appear in crops probably due to auto-inoculation from scratching. Oedema with swelling of the parts and lymphangitis are occasionally met with. Pruritus is a very common complaint and in some instances very intense.

This type of eczema affects most often the hands and forearms but is also met with on the feet and legs. The sites commonly affected in order of frequency are the dorsal surfaces of the hands and fingers, the wrists and the extensors and flexors of the extremities. The nails are not affected except when the lesions extend to the nail fold or nail bed, resulting in an onychia or/

or onychoglyphosis.

Microscopic examination of scales' tops of papules and vesicles was made in a great number of these cases but they were always negative for fungi. Cultures on blood Agar plates were made and colonies of different strains of staphylococci and streptococci were grown.

FEMALES.

Age	1-10	10-20	20-30	30-40	40-50	50-60 & over	Total
P. T. I.	9	39	37	26	21	19	151
Toxic Contact	2	21	32	35	28	26	144
Allergic Contact	-	2	8	10	5	1	26
Infective	4	16	13	5	8	6	52
Endogenous	2	3	5	6	2	3	21
-Id.	1	4	6	5	4	3	23
							<u>417</u>
		<u>MALES.</u>					
P. T. I.	-	8	28	34	33	27	131
Toxic Contact	2	11	19	29	22	17	100
Allergic Contact	-	2	8	5	1	4	20
Infective	9	12	22	15	13	4	75
Endogenous	-	7	10	4	6	2	29
-Id.	-	5	8	13	4	5	35
							<u>390</u>

Table No.3 Showing age incidence of the different dermatoses of the hands.

Occupation contributes greatly to the production of Post-traumatic infective eczema, and also the area of predilection of these lesions seems to be related to the type of work the patient handles. (Refer to Tables No. 4 and 5). In occupations where oils or caustics are prevalent e.g. mechanical workers, welders, drivers, and housewives; the backs of the hands, fingers and forearms/

forearms are mostly affected and one can explain this distribution by studying the habits of these workers. e.g. A mechanical worker wearing his working apparel, his sleeves if not rolled up, are impregnated with oil he usually wipes his palms with a dirty rag, but never the backs of his hands or in between his fingers. A sedentary worker or an unemployed man, apart from his special hobbies, is more or less equally exposed over his body surface to the hazards precipitating this complaint and so the extent of the lesions takes a more widespread distribution. The miner and labourer are more exposed to dust than liquids. They often develop pustular eczematous lesions on arms and legs. This clears up when the man is off work but recurs immediately he returns to work again. Coal dust does not give a positive patch test, but this together with sweat and friction is undoubtedly a traumatising factor. In spite of the large areas exposed in these workers, the backs of the hands and fingers still bear the brunt of these lesions, probably direct trauma is a contributing factor.

The study of intrinsic or constitutional factors predisposing to the production of post-traumatic infective eczema has been very discouraging. Hereditary and diathetic factors have been ruled out completely from these cases. Ichthyotic and xerodermatous manifestations were strikingly noticeable. Most of these patients presented dry skin especially over the extremities. Psychogenic factors were not very suggestive for most of these patients were more of the pycknic type. Relationship to food or any articles of diet or habits were not noticed.

Patients/



Patients did not show any marked deterioration in health. There was no definite seasonal change in incidence.

Septic foci were found to be a contributory factor to the recalcitrancy if not the etiology of these lesions. In five cases the removal of septic teeth, and in three the treatment of septic tonsils and sinuses resulted in complete recovery in two; and in the remaining six recovery was followed by relapse. Lesions often improve on simple treatment alone and, only a small percentage of them especially the discoid or nummular type are resistant to treatment and tend to run a chronic course.



Fig.No.1. Post-traumatic infective eczema in a miner. (Nummular variety).

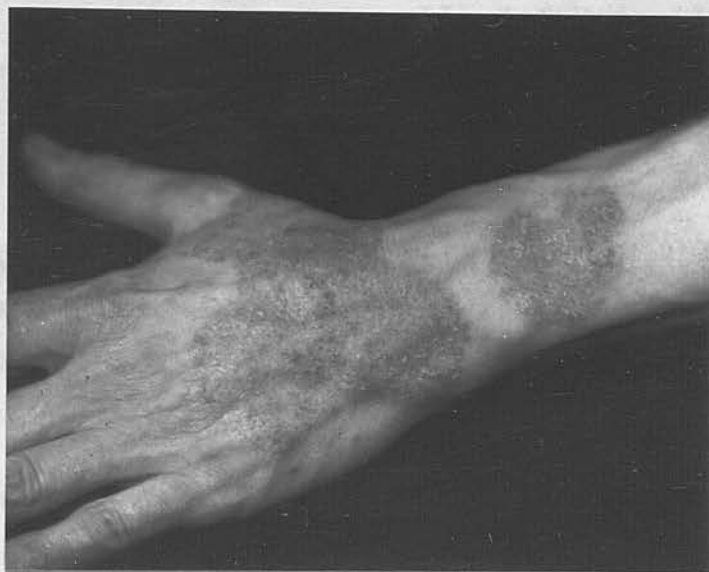


Fig. No.2. Post-traumatic infective eczema.

	PTI.	Tox.	All.	Inf.	End.	Id.	Total.
Mechanical	30	43	4	14	6	5	102
Paper, Rubber	3	2	1	-	1	-	7
Bakers	9	3	-	1	1	1	15
Builders	6	13	2	4	-	1	26
Unemployed	11	8	1	7	-	2	29
Waiters	5	-	-	1	1	1	8
Students	7	4	-	15	1	2	29
Butchers, Fishers	4	2	-	4	1	2	13
Sedentary	36	19	5	20	3	4	87
Labourers	37	23	3	8	-	1	72
Farmers	5	2	5	7	2	1	22
Drivers, Conductors	19	16	3	6	1	2	47
Chemical Workers	6	17	13	1	1	-	38
Miners	32	12	2	14	-	3	63
Al. Glass workers	3	3	1	2	-	1	10
Navy, Army	6	2	-	3	-	2	13
Barmen	6	7	1	2	-	1	17
Grocers	6	3	-	5	1	1	16
Barbers	3	5	1	1	-	-	10
Tailors	2	3	-	1	-	1	7
Doctors, Orderlies	1	12	3	1	-	2	<u>19</u>
							<u>650</u>

Table No.4. Showing the incidence of the different types of dermatoses of the hands among the different male occupations.

	PTI.	Tox.	All.	Inf.	End.	Id.	Total.
Housewives	147	178	15	30	11	13	394
Grocers	15	16	1	4	1	1	38
Farmers	3	4	2	4	-	-	13
Nurses	4	16	7	3	-	1	31
Mechanical Workers	8	3	1	3	1	-	16
Labourers	26	21	-	12	2	1	62
Sedentary	37	16	4	9	4	4	74
Tailors	8	4	1	1	1	-	15
Students	18	8	2	14	6	3	51
Hairdressers	2	5	-	-	-	1	8
Painters	3	6	2	1	-	-	<u>12</u>
							<u>714</u>

Table No.5. Showing the incidence of eczematoid dermatoses of the hands among the female occupations.

TOXIC CONTACT DERMATITIS.

Toxic Contact Dermatitis (Burckhardt 1940) or non-sensitisation dermatitis (Downing 1940), consists of a series of cutaneous manifestation caused by surface contact of the living epidermal cells with the excitant. The term toxic is employed here not in the narrow pharmacological meaning but rather in a broader sense as a cutaneous irritant. A primary cutaneous irritant is an agent that will produce a clinically manifested irritation at the site of contact on the normal skin of a majority of persons not previously sensitized to that substance if it is permitted to act in a given concentration, a given vehicle and after a given length of exposure. It forms a chemical combination with the skin or abstracts essential ingredients from it, thus resulting in total destruction, burn or inflammation, depending on the concentration of the chemical and the period of exposure.

PRIMARY IRRITANTS.

The lesions vary greatly according to the nature of the primary irritant. Keratolytics, consisting chiefly of caustics and alkalis, were found to be the cause of a large number of these toxic contact dermatitis. Fat solvents or toxic irritants themselves soluble in fat, lipoids and oils, form a second important group which is the cause of a good number of these eruptions. A more heterogeneous group consisting mainly of chemical irritants such as antiseptics, dyes, rubber accelerators etc. affects a more specialized group of individuals who come in contact with these primary irritants.

The/

The majority of cases report with erythemato-squamous or papulo-vesicular lesions and occasionally lichenified and bullous eruptions may be seen. The primary erythema frequently passes to vesiculation. The vesicles which may or may not rupture, are especially when seen on the palms tense and very closely set and sometimes they coalesce to form large blebs. In many cases the raw surface produced by the denuded vesicles become infected and impetiginised and crusted eczema results.

Toxic contact Dermatitis prevails in certain occupations in which primary irritants are commonly encountered. Tables No. 4 and 5 show the incidence of this type/among the various occupations.

#### TOXIC CONTACT DERMATITIS AMONG HOUSEWIVES AND ALLIED WORKERS.

The commonest history related by housewives suffering from toxic contact dermatitis runs as follows:- She is the mother 3 or 4 children and looking after a house of 5 or 6 individuals. She has suffered from this trouble for quite a long time but she is always too busy to go and see the doctor. It is most frequently during the winter months that these patients report for advice. The last time she was on her holidays or had less occasion to do housework her hands were perfectly clear, but since she obtained a packet of soap powder from the grocer or she has been very busy washing the dishes and doing the laundry, she developed an attack of dermatitis exactly similar to the one she had about a month ago, or her previous mild complaint became/

became worse.

In most instances, the lesions were erythematous-squamous or papulo-vesicular and confined to areas over the hands and wrists and occasionally the lower forearms. In subacute and long standing cases the palms and the palmar aspects of the fingers and finger tips are dry, scaly and fissured. The dorsal aspects of the hands and wrists are dry and may show red scaly patches, occasionally eczematous. The knuckles and the backs of the interphalangeal joints are dry and fissured. In acute cases the papulo-vesicular stage supervenes and the sides of the fingers and interdigital webs suffer greatly, very much resembling *Erosio interdigitalis Blastomycetica*. The lesions may also spread to the backs of the hands and palms as well.

The eruption seldom involves the entire hand completely. Affection of the palms of the hands with involvement of one or more fingers is commonly encountered. The next common area is the wrist with involvement of the palm or the lower forearm. (See Table 6.). The interdigital spaces and backs of the hands were almost always involved in the acute type. Usually both hands are affected symmetrically at the same time, but when the affliction is asymmetrical the right hand is more commonly affected than the left. Covered areas of the body were rarely affected; while the face and upper part of the chest may sometimes be affected together with the hands, in cases where the noxious agents have been carried to these areas by the hands or when patients have been exposed to gases and fumes of noxious substances.

By/

By far the most common agents encountered producing these toxic types/<sup>of</sup> irritations in housewives are soaps and other detergent cleansers and antiseptics.

Soaps are the sodium, potassium, or rarely ammonium salts of the higher fatty acids from vegetable and animal fat, varying greatly according to the type of fatty acid and the percentage used. Besides these mixtures soaps and soap powders contain a great number of salts and essential oils and perfumes.

All soaps in aqueous solution undergo hydrolysis to a greater or lesser extent and these are split up into free alkalis and free fatty acids. Even a neutral soap therefore liberates free alkali when in solution Jordan et Al. (1940). This free alkali is neutralized by the acidity of the normal skin and Blank (1939) found that the pH. of the skin after one lathering of soap rises up to 7.2 and it takes 2-3 hours for the skin to return to its normal pH. 5.4.

Whether the fatty acids, the alkali or the added ingredients is the active principle of soap to irritation is not yet well established. Patch tests were made with different soaps and soap powders in a number of cases. Either a soap solution or a thin paste was prepared and smeared on a piece of filter paper and was applied to the upper arm. Readings were done 24, and sometimes 48 hours after. In no case was an eczematous reaction obtained. In one case a trace of erythema was noticed which faded away in 24 hours after the removal of the test. The rest of the cases were either completely negative or showed whitish wrinkled/

wrinkled area at the site of the patch.

Caustic potash is not infrequently used by housewives in washing and laundry, and one occasionally sees cases with marked vesiculation and eczematous reaction after an excessive use of caustic soda in housework, but still no real sensitization to the patch was demonstrated.

In 15 cases Dettol, Glensol, and other anti-septics were suspected of being a precipitating factor, while patch tests with different dilutions were made and the results were negative.

Thieler (1941) studied 74 cases of dermatitis in housewives and found that in 46 cases alkaline washing agents and waxes containing turpentine were the causative agents.

Generally in most cases, the inflammation tends to subside upon the removal of the source of irritation and on abstaining from contact with soaps and water. The weeping dries up, unruptured vesicles resolve and after scaling and desquamation the tissues return to their normal character. Recurrences of lesions may occur but only after another prolonged or excessive exposure to the irritant responsible. Chronic fissuring with dryness of the palms is encountered among housewives in continuous contact with soaps and alkalis.

We have so far incriminated soap and water and other alkalis detergents with the etiology of toxic contact dermatitis in housewives. Other toxic substances may be encountered e.g. vinegar, citric acid, etc. One housewife was found to develop marked scaling with fissuring of the palms and fingers every time she used Henna/

Henna to dye her hair. The dyes in woollen gloves and the use of dyes in dyeing clothes and curtains were found to be responsible in 5 cases. Wearing rubber gloves during washing precipitated an attack in two housewives.

But to accept that soaps excite an eczematogenous reaction in every housewife is definitely not correct, because not all housewives condemn soap as an irritant and even those that condemn it vary greatly in the degree of susceptibility to it. Therefore, there should be an inborn predisposition behind these cases which is expressed by the use of soap or other alkaline detergents. Schwartz (1939) suggests the possibility that diet has an influence on susceptibility to external irritants. He believes that this is achieved chemically by affecting the pH. of the sweat which in turn affects the ability and capacity of sweat both in its action as a solvent for, and as a neutralizer of external irritants.

In the discussion of Jordan et al, Joseph V. Klauder (1940) believes, that the role that soap plays in the causation of dermatitis in housewives and others, concerns the defatting action of soap, and especially to the prolonged exposure to soap as an alkaline substance. Burckhardt's studies (1938) suggest that the eczematogenous action of soap is inherent and is due to the impairment of the functions of the skin to neutralise alkali, whereby an alkaline becomes an irritant in a concentration to which the normal skin does not react.



	Mechanical		Sedentary		Miners- Labourers		Housewives.	
	PTI.	TC.	PTI.	TC.	PTI.	TC.	PTI.	TC.
Hands & Fingers Right	2	1	1	-	2	-	4	4
" " Left	2	1	1	-	3	-	5	-
" " Both	11	15	5	7	19	7	19	29
Back of Right Hand	-	-	-	-	1	1	9	1
" " Left Hand	1	-	-	-	2	-	1	-
" of Both Hands	10	6	3	1	6	1	4	2
Fingers, Hands, Forearms	10	12	6	5	5	8	10	7
Fingers Right Hand	-	-	1	-	-	-	7	1
" Left Hand	2	-	-	-	-	-	4	1
" Both Hands	-	5	6	-	6	3	2	8
Palms of Right Hand	-	-	1	-	-	-	1	2
" Left Hand	1	-	-	-	1	-	1	2
" Both Hands	-	4	5	2	3	3	3	13
Wrists	1	1	3	-	2	-	1	1
Hands and Wrists	1	-	5	2	2	1	4	6
Wrists and Fingers	-	-	1	-	2	-	2	5
Hands and Legs	4	3	2	-	3	2	2	1
Hands and Face	1	2	2	2	2	4	-	-
Forearms	3	3	3	5	4	2	1	1
Forearms and Legs	3	6	1	2	6	3	-	1
Total	52	59	46	26	69	35	80	85

Table No.6. Showing the relation between the incidence of Post-Traumatic Infective Eczema (PTI.) and Toxic Contact Eczema (TC.) on the different areas of the hands and body.

#### TOXIC CONTACT DERMATITIS DUE TO CHEMICALS.

Victims of this group are individuals who handle chemicals during the course of their work. They include Doctors and allied professions, workers in chemical factories, dyers, tanners, rubber workers, French polishers, Painters etc. They are more prone to this type of dermatitis than post-traumatic infective, because many of the chemicals employed in these occupations are known primary irritants.

Doctors/

Doctors, nurses and orderlies are subject to skin trouble from the toxic effects of large numbers of antiseptics and chemicals. Two cases with toxic type of contact dermatitis due to mercuric biniodide, 3 to dettol, 4 to iodine, 2 to formalin, 5 to soap were encountered. The lesions were more or less wide spread over the hands and forearms and of an eczematous type.

Of the chemical workers, one case was due to cantharidine showing marked bullous type of lesions over the hands and forearms and localised only to areas of contact. Another laboratory worker showed a wide spread erythematous-vesicular lesion on hands, forearms, face and neck due to contact with BAL. appears to be a toxic type more than an allergic one, for the patient is still handling the same preparation with caution and no relapse occurred recently.

Polishers, dyers and painters use acids, alkali and defatting substances such as turpentine, petroleum distillates etc. in their work. They suffer from a more scaly eczematous type of lesion over the backs of the hands, especially between the fingers.

Victims of this group may at any time show a change of reaction to any of these chemicals by developing a specific hypersensitivity which changes the picture into that of the allergic type of reaction.



Fig. No. 3- Toxic Contact Dermatitis in a chemical worker due to contact with cantharidine.



Fig.No. 4- Toxic Contact Dermatitis , same as Fig.No.3 .

TOXIC CONTACT DERMATITIS AMONG MECHANICAL  
WORKERS.

In this group of workers which consist of engineers, fitters, joiners, drivers, garage workers etc. oils, greases and alkalis act as the primary irritant. Skilled and unskilled workers both saturate their hands and clothes; especially their sleeves with oil and gasoline. Moreover, the solvents, used to clean their hands, act as primary irritants as well. Most cutting oils contain a slight amount of free sulfuric acid (Downing 1939). Others are compounds of petroleum oil in an alkaline soapy solution.

In most cases the lesions are erythemato-squamous or vesicular on the back of the hands and fingers which are often the sites of cuts and abrasions incurred during work (see Table No.6.). The webs of the fingers are commonly affected, owing to the frequent collection of oils in the folds, and improper washing and drying. They tend to show a sodden vesicular skin affecting the root of the thumb and sides and webs of the 2nd. 3rd. and 4th fingers. The palms and wrists may also be affected and show marked thickening and fissuring.

As regards their liability to cutaneous disturbances, members of this group are more prone to show Toxic contact dermatitis of the hands than post-traumatic infective dermatitis (see Table No.4), because of their frequent contact with primary irritants, while the fore-arms and the rest of the body show lesions of either type with equal frequency.

Secondary infection and folliculitis are common complications/

complications, but the chances of developing specific hypersensitivity is not great. Many workers resume duty after being cleared by local treatment, and continue to handle these substances without ill effect, as long as they abstain from prolonged exposures, or excessive use of the noxious substances. Other chemicals used for specialised purposes; such as alkali, potassium cyanide, tetraethyl lead in gasolene etc. may contribute as other causative agents, in the production of this type of dermatitis in this group.

#### ALLERGIC CONTACT ECZEMA .

Allergic contact eczema or sensitisation dermatitis, Downing (1949), is by far the most important of the skin affections of our present time. It prevails among certain types of occupations more than others. In a survey of 11,760 workers in various factories Schwartz (1940) found that the percentage of what he calls occupational Dermatitis in a period of one year, was about 1.2%. This figure does not include burns, splashes of acids, alkali or pyogenic infection of occupational skin wounds.

It cannot be denied however that it is often difficult to determine whether a given eruption is one of toxic or allergic contact eczema, especially at the start, when the clinical picture of some cases is identical. The principal difference is that in toxic contact eczema, patch tests with non toxic concentrations of the causative substances are negative, while in the allergic type they are positive. Moreover, it is quite possible that a toxic irritation often paves the way for a/

a specific allergic reaction, and as we shall see later, that time and frequency of exposure are variable factors.

Allergic contact eczema is a complex biological reaction produced by the action of an allergen on a skin in the allergic state. The allergic state consists of an increased irritability of the body cells, to a specific cutaneous sensitizer called the allergen. The characteristics of this specific pathological process lies in the fact, that when a normal unsensitized body cell comes in contact with a cutaneous sensitiser it develops a state of hypersensitivity to that specific allergen. If this allergic state is brought about by the mediation of an antibody then the particular allergen is acting as a haptén. But, if the sensitization is brought about by the stimulation of specific antibody, then, and only then, may the allergen be called an antigen. Goldsmith (1936).

It is widely accepted that true allergisation can be induced in any human being or animal. Bloch (1929) using primroses induced the allergic state in 100% of cases who have never suffered from eczema or any metabolic disturbance, and produced in them every clinical and microscopic appearance of true eczema. Similarly Sulzberger and Baer (1939) using nitrochlorbenzine, and Low (1924) by repeated rubbing of primula leaves produced a hypersensitization in some previously non reacting individuals. He showed that this hypersensitivity was specific, but only a group of individuals were sensitisable and they tended to be grouped in families.

Under/

Under natural conditions, only a small percentage of the population show an alteration in the capacity to react to the substances they come in contact with. There are two main factors which determine this percentage, namely individual predisposition and exposure factor.

Individual predisposing factors consist according to Doerr (1929) in a pathological increase of the physiological sensitisability, and this could either be inherited or acquired. Some of the predisposing factors have been mentioned in the introduction of this paper. But there is no doubt, that there are many other factors that operate in a more specialised manner, often temporary, seasonal, or geographical. Individuals with excessively dry and easily fissured skin, as well as those with soft, moist and easily macerated skin, are candidates for eczematous sensitisation provided they undergo the risk of exposure.

It has been shown by many observers that first exposure of the skin to certain allergens is usually tolerated with impunity, except if the allergen is a primary irritant Low (1924), Bloch & Jadassohn, Straus (1934), Simon et al (1934), Landsteiner (1935), Sulzberger & Baer (1938). Therefore an excematogenous substance exerts an allergic type of eczema only after a previous exposure, at which, sensitisation started, followed by a period of refractoriness which varies between a week and three weeks, or over years in some cases. Then, a flare up of eczema type of reaction appears, either spontaneously or after a subsequent exposure.

A substance which is capable of producing the eczema/

eczema reaction, is at first absolutely specific, but as allergisation progresses, it appears to be relatively non specific in the sense that substances which are chemically related, also become capable of producing the reaction. It is found that later all attempts at specificity, either absolute or relative are lost, and the skin then reacts to a large variety of substances which have no apparent chemical affinity. Thus, a reaction which was monovalent at first becomes polyvalent.

The finding of the substance, producing the allergic contact eczema, depends greatly on the energy expended in searching for it. It is only after a careful search and evaluation of the case history, that exposure to a certain substance which fulfills the requirements of being the possible allergen in the particular case can be detected. There are no organic changes or disease pictures which are pathognomonic of allergy. The eczema reaction may be produced by an allergic as well as non-allergic mechanism. (See Toxic Contact Dermatitis.) Moreover an allergic mechanism can be the basis of almost every known form of reaction and disease process; and it is only after prolonged observation, clinical study and laboratory investigation, that an allergic skin reaction can be detected.

To incriminate a substance as the cause of a particular eczema, certain conditions should be fulfilled.

1. The suspected substance should be a known allergen.
2. Exposure to the suspected substance should have taken place 12-48 hours before the appearance of the lesion.



3- Removal of the suspected substance results in subsidence of the acute symptoms.

4- Patch tests with nontoxic doses exert a positive reaction in the particular hypersensitive individual.

It should be pointed out that in some cases the previous exposure is one to two weeks before the outbreak of the eczema, and the acute symptoms started without a reexposure. This is well demonstrated in one of the cases. Sulzberger (1940) labels such conditions as "Spontaneous Flare Ups", and he attributes them to the fact that the first application has started a specific sensitisation, and when this is complete; a quantity of allergen is still present at the first site enough to excite the allergic reaction.

Sometimes the removal of the suspected substance fails to produce an abatement of the eczema reaction, or a flare up may appear without exposure to the suspected substance. This may be due to a severe affection of the epidermal cells by the allergen; and it must be remembered that a sensitisation to one substance is often accompanied by sensitisation to other substances, related or even unrelated, (Bloch, Sulzberger(1939) and Wedroff and Dolgoff ). In another words a sensitisation to one substance may render the skin susceptible to any irritant irrespective of sensitisation.

#### PATCH TEST.

The patch test is a useful test to confirm the presence of hypersensitivity in the epidermis of an individual to a certain substance, and to prove that the substance is the cause of the given eczema. It operates only/

only when the epidermis is the tissue where the shock reaction is taking place. A positive patch test with the suspected substance as revealed from the history should reproduce some phase of the eczema reaction. Thus, when a substance suggested from the history, is capable of repeating some phases of the eczema reaction in the area applied, it can be safely presumed that, that particular substance is probably the causative agent.

#### CLINICAL PICTURE

Allergic contact eczema is commonly encountered in the acute eczematous stage. It begins with a generalized erythema and swelling of the parts accompanied by the feeling of heat and extreme irritation. Generalized vesiculation soon appears, covering all the area of contact with equal intensity. The backs of the hands are more severely affected than the palms owing to their thin skin and soft underlying tissues. The lesions have no limited border, they are confined at first, usually to the areas of contact, but spread later beyond this area, and scattered spots may be seen all over the body. The vesicles may rupture and oozing appears, but very often they remain unruptured and disappear by absorption provided the precipitating cause has been removed. It takes between 4-6 weeks for the process to clear up depending on the severity and extent of the area of contact, provided no other factors are present to keep the process going indefinitely.

In subacute and chronic cases oedema and vesiculation is less marked or even absent. The skin of the hands, particularly that of the backs and the wrists show/

show scaly papules with thickening and lichenification with predominant localization in the folds of the skin. Occasional outbreaks of acute eczema reaction is not uncommon, and this changes the picture into an acute weeping stage of eczematous patches or deep seated vesiculation.

Of 1364 cases of dermatoses of the hands, only 74 cases or 5.4% with allergic contact eczema were encountered. While this at first glance appears to be low, it must be pointed out that, it represents only established cases, confirmed either by patch tests or trial and abstinence of the suspected contacts. Even so only in 46 cases, were the noxious agents discovered, for one should not forget that noxious substances are ubiquitous.

It will be seen when studying table No. 4 and 5 that allergic contact dermatitis prevails in certain individuals and occupations more than others. For example, of 63 miners with eczematous lesions on the hands only 2 cases or 3% were of allergic contact, of 167 sedentary individuals only 9 cases or 5.6%, of 394 housewives only 14 cases or 3%. While on the other hand of 38 workers in chemical processes 13 or 34%, of 47 doctors and allied profession 10 or 21%, and of 34 farmers and gardeners 7 or 20%, were affected with allergic contact eczema.

Some of the different agents encountered in the production of the allergic contact group, were the following, Turpentine, Iodine, Dutch Tulips, Rubber accelerators, Nickel, Chrysanthemum, Orange peel, Paraffin, Hair dyes, Sulphur, Tar, Picric acid and Sulphathiazole.



Fig. No. 5- Allergic Contact Eczema due to Turpentine five days after acute attack.



Fig. No. 6- Allergic Contact Eczema

Undoubtedly there are many other noxious substances, which are difficult to pick out from <sup>among?</sup> between a large number of others, especially with an unintelligent patient, and more so, if the noxae were ingestants; and one should resort to skilled clinical observation, and hospitalization to help to confirm the diagnosis. So far, no special histological picture is as yet described as pathognomonic of allergic contact eczema, but there is much to expect from careful histopathological work and it <sup>is</sup> not beyond possibility that such study will be fruitful (Percival 1948).

Three cases are briefly presented and discussed as examples to show typical histories and clinical behaviour of allergic types of contact eczema.

B.A. female, student, age 18, fell accidentally and sprained her left wrist. On her mother's advice she rubbed on Liniment Terebinthine five times in three days, after which she was very much better. On the evening of the ninth day after the accident she developed a severe itch and burning sensation on both hands and forearms. On the tenth day, she reported with a severe swelling of both hands and forearms with wide spread vesiculation, slight oedema of the eyelids and scattered spots over the arms and chest. The picture was a typical case of acute contact eczema. On questioning the patient, no history of any more recent contact to a suspected irritant could be obtained than the Liniment Terebinthine. A patch test with this substance diluted five times with olive oil gave a very strong reaction.

This is a clear example of a spontaneous flare up/

up of acute allergic contact eczema, seven days after the last application of the irritant. Liniment Terebinthine was rubbed on only five times in three days. Over the left wrist four times by the patient's mother, and only once by the patient herself, but both hands broke out with similar lesions. The whole skin surface was hypersensitive to the liniment. The patient recovered completely with simple applications. There has been no recurrence. There was no history of allergy or diathetic state in the family.

M. S. female age 21, a rubber worker, reported with red and slightly swollen hands showing deeply seated vesicles, limited to the palmer surface and sides of the fingers, and the hypothenar eminences of both hands. She had been working in the rubber factory for seven months, and this was the first time that she had complained of such a trouble. She stated that she was an asthmatic, but had not had an attack during the past six years.

Contact to rubber at work was suspected, and a patch test was applied over the upper arm which showed an eczematous reaction in 36 hours after application.

Two days after the test, she reported with an itchy patch over the medial side of her left thigh, and on examination it was discovered that the piece of her suspender corresponding to that area, was made of rubber, while the other pieces of the suspender were made of other material.

Simple applications were advised, with strict guard against handling rubber by keeping off work for four weeks. Both hands cleared completely. After two weeks /

weeks, she went back to work and on the night of the first day she developed itchy hands, and two days later reported with the same picture. At this time the lesions were very resistant to treatment. Wearing of woollen gloves resulted in exacerbations of symptoms and spread of lesions up the forearms. A patch test showed that she was sensitive to the dye in her gloves. Three weeks later she reported with an erythematopapular eruption on the neck; this was found to be due to her scarf.

This is an example of an allergic contact eczema in a girl with an allergic diathesis, showing at first a specific sensitization to rubber. Later this specific sensitization ushered in a state of polyvalent nonspecific hypersensitivity to the dyes in the gloves and scarf which she had been wearing for some time.



Fig.No. 7  
Patient M.S.with  
Allergic Contact  
Eczema due to  
Rubber. Palm showing  
fading vesicles  
with exaggeration  
of the furrows.



Fig. N. 8  
Same case showing  
positive patch  
test with rubber.

M.B. female, housewife, age 45. An Asthmatic, giving a history of hypersensitivity to orange and tangerine skin, of ten years duration. The mere handling or the peeling of oranges, resulted in an outbreak of acute vesiculation and weeping on both hands. Eating oranges and tangerines does no harm. She reported one day with wide spread papulo-erythematous eruption over the body, resembling urticaria in certain areas and eczematous type of reaction over the hands and the lower forearms. There was no history of any contact with oranges or tangerines. The characters and distribution of the eruption however, did not suggest a contact type or any parasitic infestation.

Going carefully into the history of ingestants, the patient revealed that she had been eating a new orange peel marmalade for the last few days. Abstaining from this marmalade, with administration of a laxative, cleared up the rash completely in a few days, except for the eczematous lesions over the hands. A prick test was made by applying to the skin the juice from a piece of fresh orange peel. The area was then pricked with a needle, and the excess of the juice was removed. A wheal the size of a sixpence developed in 5 min. time, surrounded by an areola of erythema. A patch test was done by rubbing a piece of the orange peel thoroughly over a small area over the arm. An acute vesicular eruption appeared in less than 24 hours, spreading to three times the area on which the peel was rubbed.

This is an example of acute hypersensitiveness to the essential oil in the orange peel, demonstrated both in a hypersensitivity of the epidermis as the shock tissue/



tissue for the eczematous reaction and, a hypersensitivity of the blood vessels in the dermis, by the urticarial wheal.

From the last two examples of individuals with diathetic predisposition, one can presume that, in spite of the fact that hereditary and atopic tendencies do not influence the production of idiosyncrasy to external agents, it can be seen that they influence some of these nonspecific and persistent cases.

To this group of eczemas, allergic photosensitivity should be included. It is not an uncommon skin affection, but strangely enough it is a rare disease in the East. Some patients who have spent the summer months in the East with no complaint, suffer from skin eruptions when they expose themselves to the sun in this country.

Skin eruptions from photosensitivity affect exposed surfaces equally, when the photosensitiser is operating internally. Our series includes three cases with photosensitivity, one occurring after local application of tar, and two others after sulphonamides. It should be admitted that there may be many other cases of photosensitivity that are not detected, because there are no pathognomonic signs or symptoms, and very often patients' histories are very misleading.

#### INFECTIVE DERMATITIS.

The normal flora of the skin surface has been studied by a large number of workers, Kock. Mitchell (1937), Topley & Wilson (1946), etc. and it is widely accepted that the normal skin contains a large number of known pathogens. Downing et al (1937) reported that from/

from the study of cultures, normal skins revealed many strains of staphylococcus, albus and aureus, streptococcus diphtheroids, gram positive bacilli, and various saprophytic fungi. In another series of 100 cases with normal skin, scrapings taken from several areas recovered only two pathogenic fungi, one trichophyton and one epidermophyton, both were isolated from the toes. Maxted & Johns found haemolytic streptococci on the hands of 7 of 181 persons. Croft & Black from the hands of 100 people cultured 29 yeast like organisms from 22 skins, four species of oidiomyces were found, but no pathogenic fungi or *Monilia Albicans* were present.

The healthy skin appears to have a natural self-disinfecting mechanism, there has been an intensive study of the self sterilising power of the skin, (Cornbleet 1932), (Morton & Novy 1932), (Arnold & Bart 1934), (Marchionini 1938) and (Burtenshaw 1945 and 1948) but the mechanism is still debatable. Colebrook (1930) found that haemolytic streptococci were rapidly killed on the normal skin of the hand. On the palmar surface of the clean hand, *B. Coli*, and *Salmonella Typhi* could not be detected after ten minutes, though they persisted longer under the nail tip.

The tough, insensitive and relatively inert horny layer of the skin protects against abrasion, heat, and living organisms. It is very difficult to make out how infectious organisms invade the skin and start an infective process. Sherwood (1935) says that "Micro-organisms are able to enter the body only through mechanical or chemical injury, or as a result of altered physiologic integrity." Injury of any kind thus opens the way for these/

these organisms to enter into a less resistant and a highly suitable environment for their reproduction, though this is not always the case when we are dealing with fungi.

In the group of infective dermatitis that we are dealing with, there are a number of affections in which bacteria or fungi play a part in the production of the dermatitis. In the case of bacteria, a traumatic injury, or an infection deep to the skin usually precedes the infective process e.g. a cut wound over the fingers, or a folliculitis over the backs of the hands may precipitate an infective dermatitis which may involve the whole hand. Infective dermatitis following scabies is a very common condition especially in children. In the case of fungi, injury is not necessary. As we shall see later, fungi are capable of invading the stratum corneum without a previous injury, although rubbing and scratching hastens the process of invasion.

#### BACTERIAL INFECTION

The initial lesion after the injury or the folliculitis, may be an erythema, scaly or crusted plaques, vesiculation or pustulation. A certain amount of oedema and lymphangitis may be present. At first the lesion is localized e.g. around the opening of an abscess, a perionychia, or a traumatic wound, later the infective process creeps over the adjacent skin surface and in certain cases scattered plaques over the arms and face may be seen. The process spreads by peripheral extension and the whole hand may be involved in the infective process. Not uncommonly a sudden outbreak of pustular lesions/

lesions develop over the hands with marked swelling and inflammation. Impetigenisation and crusting may supervene in certain cases. The epidermis at the periphery of the lesion is usually undermined, detached, or split, due to collections of sero-purulent fluid. There is no tendency to central healing, and vesiculation, pustulation or even bulla formation may be seen at the advancing edge. This type of infective dermatitis usually runs a subacute course, and the process could be checked by treating the primary focus. A very common cause of recalcitrancy<sup>e</sup> is too energetic treatment producing a contact type of eczema, e.g. after penicillin and sulphonamide creams or quinolor ointment. Acrodermatitis continua of Hallopeau vel Dermatitis repens of Crocker (Barber & Eyres 1927) is included in this group of infective dermatitis. The initial injury, the involument of the nails and the gradual extension of the lesions are characteristic features of this disease. A distinct strain of staphylococci have<sup>s</sup> been attributed as a probable cause. It is very stubborn and resistant to treatment, and runs a very chronic course. The duration recorded in our cases varied from five weeks to five years. It does not show any sex incidence, the youngest patient was a housewife of 24 and the oldest a man of 68 years of age.

#### MYCOTIC INFECTION.

This is a common affection encountered in this group of infective dermatitis. It takes invariably a circinate type of contour beginning by a red papule, which soon/

soon develops into a vesicle and spreads by a peripheral extension of new crops of vesicles. Mycotic infection of the hands and feet will be dealt with in detail in the second part of this paper.

IN our series of 1364 cases of eczematous dermatoses of the hands 198 cases or 14.5% belonged to this group. There were 117 males and 81 females. Primary fungus infection of the hands constituted 129 cases or 65% of the group. There were seven cases of Dermatitis Repens and the rest were infective dermatitis, post-follicular or post-traumatic. These figures do not include perionychia or onychomycosis. There is a predominance of males in this group probably because they are more exposed to trauma. The common sites for mycotic infection are the backs of the hands and the wrists. Dermatitis repens usually begins over the fingers and spreads to the palms. Post-scabiectic infective dermatitis is commonest in children, it affects the sides of the fingers, palms and wrists and usually misses the back of the hands, while post-follicular type of infective dermatitis affects the backs of the hands and fingers invariably.

#### ENDOGENOUS ECZEMA.

This group embraces those cases of eczematous dermatoses of the hands in which both the predisposing and the exciting factors seem to originate inside the body. It is unsafe to say at present whether these dermatoses are the expression of some allergic reaction of the body or not, and one must exercise caution in attributing them to the gastro-intestinal tract. There is/

is a controversy as to the extent to which food, metabolic products and the nervous system are responsible in a given case and as to the mechanism of interplay of these factors in the production of the different clinical pictures.

Contactants have little or nothing to contribute to the aetiology of these cases. These eruptions affect the hands as well as other parts of the body and their diagnosis is sometimes very difficult.

In the series of 46 cases of this group atopic, psychoneurotic metabolic and other constitutional factors such as the menopause, menstruation, and hyperthyroidism have been encountered. The atopic cases were associated with Besnier's Prurigo. The backs of the hands and wrists as well as other parts of the body were affected. The eruption showed confluent lichenoid papules intensely pruritic forming ill defined plaques, circumscribed in certain cases and giving the skin a characteristic course appearance. The lesions may break down from severe scratching and superimposed infection may result in impetigenisation. These are commonly seen in the first and second decades of life either following infantile eczema or occurring in conjunction with asthma or hay fever. A definite nervous element is encountered in fully developed cases and this has lead many workers to call it Neurodermatitis, Brocq<sup>6</sup>, (Urbach 1946), Becker and Obermeyer.

In such cases an unstable nervous system and over reaction to emotional strain seem to precipitate an attack or exacerbate an already present but fading eruption. Peterkin records a very interesting case of

a soldier who developed an acute vesicular eruption of the hands after he heard the news of his posting to the battle front. Eczematous eruptions on the hands and forearms were met with in five cases, these developed or were made worse by the death of one of the family or an extreme emotional upset.

Metabolic factors play a role in the production of eczematous dermatoses as in:-

1. Deficiency dermatosis e.g. vitamin deficiency.
2. Dermatitis due to endogenous Metabolic products or faulty metabolic functioning of any of the internal organs e.g. liver, Endocrine etc. Diabetes constitutes an underlying cause of recalcitrant eruption.
3. Sensitization to certain foods. The ingestion of or abstinence from certain foods produces occasionally, or alleviates certain skin eruptions.

This relationship is very well marked in certain cases but owing to lack of specificity to these foods it is very difficult to ascribe any sharp relationship.

#### PUSTULAR PSORIASIS.

#### - IDS.

-Ids are more of a reaction than a clinical disease picture. They were first described by J. Jadassohn in 1911.

This reaction has four outstanding characteristics.

1. They are usually associated with a primary lesion but may appear remote from it or only three surrounding it.
2. They are usually free from micro-organisms.
3. They are accompanied by skin hypersensitivity to extracts of the micro-organisms in the primary focus.

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4. They usually disappear on treatment of the primary focus.

It is universally accepted that the -id reaction is a manifestation of a hypersensitive or allergic skin to micro-organisms or their products, carried to the skin by the haematogenous route; and it is believed that owing to the rapid destruction or attenuation of the living agent by the immense forces of the hypersensitive skin, the localised lesions are always free from any micro-organisms. J. Jadassohn (1912).

The primary focus can be either an infective or inflammatory process somewhere in the body, or a trauma or damage resulting in a mechanism of auto-sensitization. Whitfield (1930). Thus we can have a bacterid in a bacterial infection, a dermatophytid in a mycotic infection, and eczematide or dermatid in an inflammatory process.

#### BACTERIDS.

##### PUSTULAR PSORIASIS.

This eruption has been described by (Barber 1936) as a variety of Psoriasis. He considers that focal sepsis particularly that of the tonsils is a causal factor in many cases. He says "a patient can develop a pustular psoriasis of the extremities if he is a potential or actual Psoriatic", but he also admits that he has seen cases unaccompanied by Psoriasis. Only three cases were encountered that accurately conformed to Barber's classical description of the clinical and pathological features of Pustular Psoriasis. Of these cases two were affected by or had suffered from Psoriasis,

psoriasis, and the third gave a family history of psoriasis but had never suffered from it. Septic foci were found in two cases but nothing suggestive in the third case. A description of some of these cases will be included in the second part of the paper.



Fig. No. 9- Extensive Pustular Bacterid of the palms with wide spread vesiculation and desquamation. Note the absence of the eruption on the dorsum of the hand.

#### PUSTULAR BACTERID.

This is another -id eruption described by (Andrews and Mackacek 1935) which they distinguished from pustular Psoriasis by having specific clinical characteristics and histological features, an associated leucocytosis, an allergic state to streptococcal and staphylococcal vaccine and a relation to septic foci. Six cases are included in this series and septic foci were discovered in four cases only.

The clinical picture of both pustular psoriasis, and pustular bacterid changes greatly during their evolution. It is not possible at certain stages and especially/

especially when there is no history of Psoriasis to differentiate between the two pictures. In pustular psoriasis the patches are usually sharply circumscribed, dry and with the smooth rather glazed surface of ordinary psoriasis when the scales are removed. The scales are as a rule silvery and dry. The pustules appear rather deeper than in pustular bacterid. Although vesicles with almost clear contents may in certain phases occur in undoubted pustular psoriasis they are commoner in pustular bacterid. In pustular psoriasis the brownish intra-epidermal crusts are usually deeper in colour and tend to be larger.

According to Barber (1947), pustular psoriasis is like psoriasis histologically but with larger pustules instead of the micro abscesses of Mönro, while pustular bacterid is eczematoid in type and resembles a pustular dermatophytid.

These eruptions are very chronic and persist for a long time. The shortest duration recorded was eighteen months in a female aged 27, and the longest was ten years in a female aged 69.

#### DERMATOPHYTID .

In 1911 J. Jadassohn directed attention to the true nature of the disease he classified as Trichophytid. He stressed the fact that certain specific changes in the reaction of the skin, "an allergy", is a sine qua non for the appearance of a Trichophytid eruption. Von Grafferied was the first to point out that in spite of the apparent superficiality of the foot infections an allergic state was/

was produced and the trichophytin reaction was positive. Williams (1927), Peck (1930) and Weidmann (1937) and others have shown that the trichophytid reaction may take the form of an eczematous or pompholyx like eruption; the primary focus is usually located on the feet but may be elsewhere on the body, Sutton Jr. reported a case where the primary focus was vaginal.

46 cases of Dermatophytid of the hands have been encountered and they will be presented in detail in the second part of the paper.

Four types of Dermatophytid of the hands have been observed.

1. Vesicular type.
2. Squamous or post-scarlatiniform type.
3. Erythema Multiforme type.
4. Exanthematic type.

The palms of the hands, fingers, wrists, the soles of the feet and occasionally the lower forearms are the sites of predilection of these eruptions. The primary fungus infection was present in 43 cases on the feet, in two cases on the hands and one case had Kerion Celsi on the back of the neck.

#### ECZEMATIDE OR DERMATID .

This type of -id reaction affects the hands and forearms as well as other parts of the body and it is believed to be due to absorption of toxic material from the primary focus, or to hypersensitivity to skin products. e.g. reaction around a varicose eczema. Percival (1948) described Eczematide in Chemical Eczema as Papulo-vesicular spots which appeared anywhere over the body when the allergic reaction was well established. MacLachlan and/



and Brown (1934) described a sago-grain vesicular eruption on the hands and feet as an -id manifestation of Scabies and in another case a similar eruption followed a major operation. Lehmann (1930) recorded a symmetrical vesicular eruption which he called "Cheir-opompholyx"; this followed the extraction of a septic tooth with a root abscess.

In this series were encountered three cases of -id eruption on the hands and forearms following varicose eczema, two cases after an infective process on the feet and five cases following a chemical contact eczema.

The lesions usually begin as red itchy spots which develop into papular or a papulo-vesicular lesions, usually discrete but sometimes showing confluent crops. The commonest sites are the back of the hands, the palms and forearms as well as the trunk and limbs. The lesions are itchy and tend to persist for a long time, they develop in crops but usually die down after the primary focus has abated.

## PART II.

We have seen in the first part of this paper that eczematous eruptions of the hands constitute one of the most common affections in dermatological practice. I have endeavoured to show that most of these affections can be graded at least clinically and morphologically, and to a certain extent aetiologically. It would be natural in view of the striking clinical characteristics presented by a number of these dermatoses to classify them according to their aetiology, if it were not that we are ignorant as to why the skin reacts similarly to varying irritants, and differently sometimes to the same agent, and what is the mechanism behind these differences. Thus a careful study of the different factors in each case is the only means of obtaining a reasonable explanation from the objective signs.

In this part of the paper I am presenting a study of 122 cases of eczematous dermatoses of the hands, predominantly vesicular in character, with a special study of the incidence of mycotic infection in dermatoses of this type. These cases were also used to test out the validity of the classification of dermatoses of the hands presented in the first part. It also includes an observation of an Epidemic of Fungus Infection.

The data reported here was specially collected for this study. Each patient was first seen by an honorary or first assistant and was then referred for examination and further investigations at each visit. The cases selected consisted of vesiculo-squamous eruptions of the hands, acute or persistent. Treatment was usually given after the first examination except/

except where it was decided to wait till investigations were completed. Therapy consisted in most cases of  $\frac{1}{2}\%$  silver nitrate soaks in acute vesiculation, gentian violet in localised infected patches, Castellani's paint or Tinct. Iodine when indicated in mycotic lesions, Tar varnish and tar paste in the resolving stage and chronic cases, and 1% Ichthyol paste was used as the routine application whenever needed.

A complete history of the patient and his skin trouble was taken according to table No.1 on page (8). In every case a trichophytin test was made and occasionally an oidiomycin test as well. Patch tests were made whenever indicated.

The demonstration of fungus in the vesicular eruptions of the hands and feet by Sabouraud and Whitfield in 1911 supplanted the previous concepts of the cheiropompholyx and dyshidrosis of Hutchinson and Fox thus stimulating a world wide interest in the study of such vesicular eruptions.

In 1919, Darier suggested dividing these eruptions into parasitic epidermophytotic and non-parasitic dyshidrosis and he expressed the opinion that if occupational dermatitis was excluded, the dyshidrosiform eruptions were probably always mycotic in origin.

Sicoli in 1924, classified dyshidrosiform eruptions of the hands and feet into true dyshidrosis of Tilbury Fox produced by the accumulation of sweat under the thick corneal layer, and pseudo-dyshidrosis which includes parasitic, occupational and other causes.

Williams (1927) - declared "I do not know of any/

any way of telling which vesicles on the hands will be fertile." He meant which positive for fungi, and which sterile. He stated later that "so far as our knowledge goes at present most cases of cheiropompholyx are produced by ringworm infection and the burden of the proof lies on those who attempt to prove that they are not of fungus origin."

Wise & Sulzberger (1930) attributed cheiropompholyx to be due to dissemination of products of micro-organisms from a focus of infection usually a mycotic infection of the feet and nails and rarely other organisms like monilia.

Lehmann (1930) discussing acute vesicular eruptions of the hands and feet attributes the largest group to allergic reactions of mycotic origin, and, excluding dermatitis due to chemical agents, vesicular eruptions whose etiology is unknown he has pigeon-holed in "Pompholyx".

Ragab (1934) classifies dyshidrotic eruptions into 4 groups 1 - True dyshidrosis, 2- Mycotic dyshidrosis, 3- Mycosides, 4- Toxinides. In 52 cases he cultured one fungus, 15 yeasts, 5 staphylococci and streptococci and in 28 cases nothing was found.

Maclachlan & Brown (1934) disapprove of the term dyshidrosis, and though they label their article as "Cheiropompholyx" they warn against the use of the term so loosely. They hold no evidence to support the contention that the disease is either solely due to or connected with sweat gland dysfunction or essentially a fungus infection. They consider cheiropompholyx as a/  
a/



a cutaneous reaction and not a disease "sui generis", frequently due to contact occupational dermatitis or an expression of a true sensitization dermatitis, and the hereditary factor is important and a considerable number of these cases belong to the diathetic group.

Muende (1934) reviewing the findings at St. John's Hospital Laboratory and his own clinical and pathology experience says "No bilateral cheiropompholyx were met with in which fungus could be recovered from different vesicles on both hands. More than 50% of cases resembling clinical Hutchinson's cheiropompholyx take the form of vesicular allergic eruptions and are associated with fungus infection elsewhere, and the feet were affected in 90% of cases.

Davidson (1943) classifies recurring vesicular eruptions of the hands under Exogenous substances, bacteria, fungi and constitutional causes producing a dermatitis either directly or indirectly and attributes cheiropompholyx to constitutional causes acting indirectly only.

Lane et al. (1945) were able to confirm the diagnosis of dermatomycosis, dermatophytid, contact and soap dermatitis in only very few number of cases of dermatoses of the hands. They postulated the fact that owing to the several complicating factors, the exciting factor may be removed but the eruption may persist as infectious eczematoid dermatitis. They also hold pompholyx as a group of cutaneous disturbances on its own but they do not give a definition of it.

Benedek/

Benedek (1946) who attributes Pompholyx to *bacillus endoparasiticus*, describes vesicular, eczematous, hyperkeratotic, erosio interdigitalis, onychial and paronychia forms of pompholyx from which he has cultured the *bacillus endoparasiticus* at certain stages of evolution of the disease.

There is no doubt that a very large number of workers have dealt with the subject of vesicular eruptions of the hands, either as such or under pompholyx or "Id eruptions", and all possible causes on earth have been interpreted to produce these vesicular eruptions.

Fox, Crocker, Santi, Sutton, Macleod, O'Donovan, Becker & Obermeyer, Maclachlan & Brown and Martin agree that some of these patients are of high strung nervous temperament, worried and over worked.

The exogenous theory is held by almost all workers except Benedek whose ideas we shall discuss later. A whole series of substances have been recorded and besides the common ones, Ephedrine, Orange peel belladonna (Brain) Explosives (Sequeira) Lime (O'Donovan 1925) Paraphenylenediamene (Adamson & Macleod) have also been recorded.

Supporters of the endogenous theory are also numerous. Cummings as early as 1846 attributed vesicular eruptions of the hands to gouty disposition. Hutchinson mentions food as one of the possible causes of pompholyx. Lortat-Jacob and Muende each records dyshidrotic lesion provoked by the ingestion of salicylic acid. Rowe (1947) attributes a number of these/

these vesicular eruptions of the hands of unknown origin to food and pollen allergy, but he also states that irritation of the skin from occupation and other avocations helps to activate a potential sensitization to food in the skin.

The Association of cheiropompholyx with endocrine disturbances has been mentioned by some authors. Lehmann recalls a case recurring a few days before each period especially in hot weather. Wile found many cases associated with exophthalmic goitre. Machlachlan & Brown marked that pregnancy, menstruation and the menopause coincided with the attack in 21 of their cases.

Unna (1896) suggested a bacterial etiology and described a bacillus which he found in the vesicle. Benedek describes a circulating endoparasite which he cultured from the blisters of pompholyx. Rajka (1928) and several french writers described cases due to infection with streptococci and staphylococci. Sulzberger (1945) and Stokes (1945) suggested the possibility of a virus infection. Hutchinson recorded a case of vesicular eruption of the hands which resembled the lesions he had described but due to Syphilis. Milian (1922) reported cheiropompholyx in association with syphilis and stated "the eruption receded after anti-luetic treatment".

Darier, Bloch, F. Jadosohn (1930), Peck (1930) Williams, Sicoli, Ragab, Machlachlan & Brown etc. have all isolated at some time a pathogenic fungus from Pompholyx-like lesions on the hands.

Vesicular/

Vesicular eruption of the hands due to focal infection and autosensitization has been reported by many writers. Conditions due to bacterial focus of infection have been described by Barber and Andrews as pustular Psoriasis and Bacterid, as being in most cases due to focal sepsis in the tonsils. Lehmann described a cheiro-pompholyx of hands and feet associated with pyogenic infection of one toe with cellulitis. Machlaclan & Brown noticed in 25 of their cases slight to marked focal sepsis in tonsils or teeth.

Conditions due to mycotic focal infection were first noticed by Sabouraud in 1910 who described vesicular eruptions of the hands as being due to this cause. Jadossohn gave the name -id to suggest the mechanism of their evolution. Later Williams (1930), Delbanco, Martinotti, Bloch, Lehmann, Peck (1929) and Sicoli all reported cases of sterile vesicular lesions of the hands due to a superficial or deep tinea infection mainly on the feet or any other part of the body.

The first account of generalised eruptions occurring in connection with mycotic infections was given by Jadossohn in 1912, who described a spiny lichenoid papular eruption over the trunk occurring in several cases of kerion. Later, cases were reported by other workers; and different forms of these reactions were described. The original site of the infection was always deep seated. Constitutional disturbances of malaise, fever, leucocytosis and lymphadenitis accompanied the development of trichophytid in kerion cases. But it is said that these constitutional symptoms often accompany cases of kerion and are overlooked until the presence/

presence of a generalised eruption draws attention to the probability of a generalised infection Williams (1927).

Several forms of these id eruptions have been observed and it has been noted also that the same patient may present several forms at the same time. The commonest type according to Williams is the lichenoid type and he regards the scarlatiniform type as the early stage of either lichenoid or papular type. The next commoner types <sup>are</sup> the squamous, vesicular and pustular types in frequency of occurrence. Jadassohn & Sutter (1920) has described an eruption on the mucous membrane of the mouth associated with a scarlatiniform type of id eruption. Erythema nodosum type of id eruption have been reported by Bloch (1921) and Bruusgaard. Erythema multiforme and erysipaletoïd type of id reaction to fungi have also been described. Pusey (1925) Seeman & Rajka, Williams (1927) reported Pityriasis Rosea type of id eruption.

The presence of parasites in the blood in the early stages of the id eruption have been demonstrated by some workers. Arzt & Fuhs, and Masia each described a positive finding in generalised id eruption.

It has been noted that patients suffering or having suffered from Tinea infections will react to the inunction or the injection of trichophytin. The commonest reaction besides the local one is the exaggeration of an already existing eruption. Bloch (1921) reported an erythema nodosum like lesion on both legs in a girl of

of eleven after a trichophytin injection and in another case an Erythemato-pustular lesion sterile on culture developing around the area of trichophytin injection. Guth (1913) was the first to report the finding of Mycelia in the lichenoid Dermatophytid, and this was confirmed later by Sutter (1920) Ambrosoli (1922) and Martinotti (1922). They stated that the fungi could be demonstrated in the freshest lesion, those more than a day or two old being invariably negative in spite of repeated examinations. Ayres & Anderson were able to show that from 4 - 8 % of serum from a person with dermatophytid eruption when incorporated in Sabouraud's medium will inhibit the growth of fungi isolated from the primary lesion.

THE FACTS ESTABLISHED ABOUT THE PATHOGENICITY  
OF FUNGI.

Dermatologists throughout the world agree that hyphomycetes isolated from vesicular and intertrigenous eruptions of the feet are the aetiological agents, except for some like Benedek (1941) who believes that they play no role other than a saprophytic one.

In the broad conception of the disease "Dermatophy<sup>+</sup>osis" the lesions that these ringworm fungi produce between the toes, on the feet or on any other parts of the body are in the nature of a local focus wherein the fungi live and multiply. The relationship of the fungus so located, to those lesions over the hands, being the result of the same aetiologic factor as the lesions on the feet, is a problem, and Dermatologists have not all agreed as to the nature in its pathogenicity/.

pathogenicity. The fact that these lesions appear symmetrically and abruptly on both hands made Beck (1929) in association with Jadassohn describe this condition of the hand as toxic lesions caused by haematogenously deposited fungi and/or the associated toxin from lesions on the feet. As a rule they say the lesions are negative bacteriologically, microscopically and culturally, but are accompanied by a positive trichophytin reaction. They concluded from their results that there was a definite relationship between the manifestation of the hands and of the feet, and it was likely that the involvement of the hands were secondary to the primary lesions on the feet.

Kaufmann Wolf, Mitchell and Ormsby (1912), Darier (1924) C. White and A.M. Greenwood and others found and cultivated fungi from the dyshidrotic lesions on the hands and feet. This opposed Peck and Jadassohn's conception and other workers (Scholtz, Bloch, Muende etc.) But it should be pointed out that the above mentioned workers who described dyshidrotic lesions to be positive for fungi have probably examined primary and not secondary eruptions. Among all the investigations performed, only three cases, one reported by Von Granffenried and the other by S. Peck (1930) were observed in which fungi were demonstrated in both hands and feet. Alexander (1927) has also reported a positive finding.

J. Saeves was the first to show that a single intracardial injection of an emulsion of Achorion Quencheanum and Trichophyton gypseum can produce in the guinea/

guinea pig several crops of fungi-containing typical skin lesions. These lesions demonstrated histologically that the fungi could be found mainly in the stratum corneum and hair but not in the living tissues (Bloch (63)). The lesions appear to have a certain predilection to shaved and traumatised sites (Kögoj, 1936). M. Sulzberger showed that no actual mycotic involvement of internal organs can be produced by intracardial injection of *A. Quencheanum* in spite of the presence of fungi in the spleen and other organs.

From the mycotic process of the feet fungi could enter the blood stream. Trauma, inflammation, suppuration and intercurrent infection are likely to have an influence on the mobilisation of microbes from the primary focus. X-ray treatment of a primary mycotic lesion and trichophyton injection have been seen to provoke trichophytid. Bloch, & Jaddosohn (1930) stress the importance of all influences which weaken the systemic resistance. The possibility of a release of bacteria from a silent focus into the blood stream and apparently without any of the known causes must also be considered.

The presence of fungi in the blood in cases of id eruption has been demonstrated by M. Jessner (1924) and Bloch. Peck (1930) found fungi in one of his series of 26 cases. Pellizaro obtained fungi in one out of 700 cases.

Jaddosohn and Bloch stress the fact that certain specific changes in the reaction of the skin develop in mycotic infections specially in the deep seated ones/



ones, and an allergy of the skin is a "sine qua non" for the appearance of a trichophytid eruption. This allergic phenomenon is further shown by the fact that the entire skin of the patient becomes hypersensitive to fungi and their extracts.

In approaching a case in practice one should have a clear picture of the clinical and morphological appearances of the different types of vesicular eruptions of the hands. It is difficult to make out from the descriptions of cases reported in the literature under pompholyx or any other title whether the vesicular eruptions described tally with Hutchinson's classical Cheiropompholyx, or Fox's dyshidrosis, or some other special features.

Hutchinson (1876) described his lesion as follows: "after a short period of burning and itching on the hands usually between the fingers, there is seen deeply placed small accumulations of clear serum looking like sago grains. These are perfectly transparent and not infrequently resemble vesicles of Scabies. After a few days, in almost all cases, these vesicles dry up and the disease is at an end, although probably a little inconspicuous desquamation of the epidermis will follow leaving quite a sound skin behind. This differentiates it from Eczema of which the indefinite duration, and the tendency to persist and become aggravated, are such marked characteristics. The disease is characterised by rapid and symmetrical development, tendency to spontaneous cure and liability to recur over and over again. The hands/

of these diseases are of highly nervous temper<sup>a</sup>ment or suffering from nervous debility. The former thought that his disease was not connected with any local cause nor was it influenced by local treatment. He found no reason to suspect any articles of diet or any drug administered. The latter thought that his disease was produced by the retention of sweat and the distention of the sweat follicle, occurring mainly in the warm season and did not mention any causative agent.

We are not in a position at present to explain Hutchinson's Cheiropompholyx and Fox's Dysdidrosis in the light of our present knowledge of the causative factors of some of these vesicular lesions of the hands and feet. But there is no doubt since most authors believe that the clinical picture described by both represents a symptom complex "reaction cutanée" rather than a disease entity.

If we compare these two classical descriptions to each other, we find, that though they have some characteristics in common e.g. Sago-grain appearance, depth and location of the lesions and subjective symptoms; the behaviour, the progress and the resolution of these lesions are quite different. When studying on the other hand descriptions of other authors e.g. Barber's Pustular Psoriasis, Andrew's et al Pustular Bacterid, we find a striking resemblance of their descriptions to the dyshidrotic lesions of Fox, White, Williams and Peck's descriptions of trichophytids of the hands bear great resemblance to Hutchinson's Cheiropompholyx.

If we stop here to consider eczematoid eruptions of the hands, especially those that presents marked vesicular/

vesicular and wide spread characters, we find that, all patients give a history of a feeling of heat and itching before the appearance of the lesion. Redness and swelling do not seem to be a common feature among these eruptions except when accompanied by an infective process. The palms of the hands and the sides of the fingers are commonly affected in most cases. Vesicular eruptions commonly show sago-grain appearance and if left unruptured tend to resolve gradually and finally desquamate.

These common characteristics among those lesions of different etiology remind us of a pattern that the skin would present in spite of the different causative agents. But undoubtedly there are some marked features which are likely to appear in certain conditions more than others as we shall see in the description of the Dermatophytid eruptions later.

The general belief among a large number of Dermatologists is that the vesicular eruptions of the hands as they stand are, with certain exceptions, undistinguishable from one another in the large proportion of unselected cases. And attempts to differentiate the vesicular, palmar and plantar dermatoses by means of clinical criteria alone has not been so far successful. Scholtz (1932) expressed the opinion that if more attention was given to the details of clinical changes it might be helpful to arrive at a correct diagnosis. Mitchell (1929) admitted frankly saying "I do not pretend to be able to determine what is mycotic and what is not, and the only way this can be determined is by making strenuous efforts to find out whether they are mycotic.

Relative to this aspect of the subject it could be/

1. Scrapings, tops of vesicles and vesicular fluid were examined microscopically and culturally on Sabouraud's medium and Blood agar.
2. Trichophytin skin test was performed to all cases and Oidiomycin to 35 cases only.
3. Cultures of throat smears from 82 cases and stools for 28 cases on blood agar and Sabouraud's medium.
4. Blood cultures were performed in 51 cases and complement fixation test in 21 cases and Agglutination test in 8 cases.
5. 5 Human inoculations and 42 animal experiments were performed.
6. Patch tests with Trichophytin were made in 10 cases.

Material and Methods.

This study began in October 1946 and continued into the early spring of 1948. In Scotland the wintry season begins in the early autumn and continues into the late spring. About 50% of the patients reporting to the skin department of the Royal Infirmary come from outside Edinburgh and some may need to travel over 60 miles before they reach the outpatient dept. Tab.No.2 shows the number of attendances of new patients of both sexes during the different months of the year. Individuals of different occupations and all ranks attend this department, and are attended to free of charge. Medicaments are supplied by any chemist in the vicinity of the patient.

Hyperhidrosis.

Sweating, especially of the hands and feet is a physiological process present in almost every individual. In some, it is not perceptible while in others it may become/

become excessive especially during the warm weather. Hence, excessive sweating could be functional as well as organic in origin. It has been greatly stressed that vesicular eruptions of the hands and feet mainly of mycotic origin are associated with hyperhidrosis.

From the study of 122 cases, hyperhidrosis was found very marked only in 13 cases, irrespective of time and season. In another 31 cases it was less marked, but perceptible. It is usually present symmetrically, more frequently over the soles than the palms, commonly seen with men and hard labourers more than women.

Hyperhidrosis, mainly of the feet was an apparent feature among the group of Dermatophytosis. It was very marked in 8, and less marked in 17 cases. It did not show any marked appearance among the other groups. It was absent in the group of pustular psoriasis and bacterid.

Hereditary and Constitutional Factors.

This was not a striking feature among the many other different contributory factors. To every patient the question of family and personal history of, Infantile eczema, Asthma and Hay Fever was put and the findings were as follows:-

- Asthma or Hay Fever in patient only - 3
- Asthma or Hay Fever in the Family only 4
- Asthma or Hay Fever in both patient and Family 2
- Infantile Eczema in Patient 2

In the series of 52 cases of Dermatophytosis only one case gave a history of allergic diathesis (Hay/

(Hay Fever). So it could be safely concluded that the allergic manifestations of the id eruption bears little or no relation to any diathetic predisposition.

#### Flat Foot.

Flat foot was not a common feature among the cases of Dermatophytosis of the feet. Liebenthal (1927) in a series of 195 cases of mycotic infection of the feet demonstrated Flat Foot in 90% of the cases. In the series of 52 cases only 3 had very marked flat foot and in another 8 cases slight degree of flat foot was noted.

#### Seasonal Incidence.

Dermatoses of the hands excluding those related to fungus infection shows no seasonal prevalence. The incidence of dermatophytoses of the feet shows a marked increase during the warm weather. This indirectly raises the incidence of dermatoses of the hands in a relative proportion to the incidence of Dermatophytosis of the feet in particular.

	<u>T.Ped.</u>	<u>T.Corp.</u>	<u>T.Cap.</u>	<u>T.Cru.</u>	<u>Kerion</u>	<u>T.Ver.</u>	<u>T.Barb.</u>	<u>Onych.</u>
Jan.	3	15	20	2	3	1	1	-
Feb.	4	27	31	3	3	-	2	-
Mar.	8	34	20	4	3	-	3	-
Apr.	8	21	33	1	1	-	-	-
May	7	24	32	1	2	-	2	1
June	15	25	29	1	1	-	1	1
July	22	15	25	1	1	1	-	-
Aug.	27	20	31	2	1	-	-	3
Sep.	11	12	51	3	1	1	-	1
Oct.	15	16	31	2	-	-	1	2
Nov.	7	21	27	4	-	-	-	-
Dec.	3	23	17	1	2	-	-	2

Table No.7 Showing monthly incidence of Mycotic infections for the years 1946 and 1947.

Apart from the above instance Fungus infections in general show no special occurrence in any part of the year. Table No. 7 shows that T. Corporis and T. Capitis occur fairly irregularly throughout the different months; while dermatophytosis of the feet shows a marked increase between June to October with highest incidence in August. No conclusion as regards incidence was drawn from the study of the 122 cases. Fig. No.10 shows the incidence of the 52 cases of dermatophytoses:

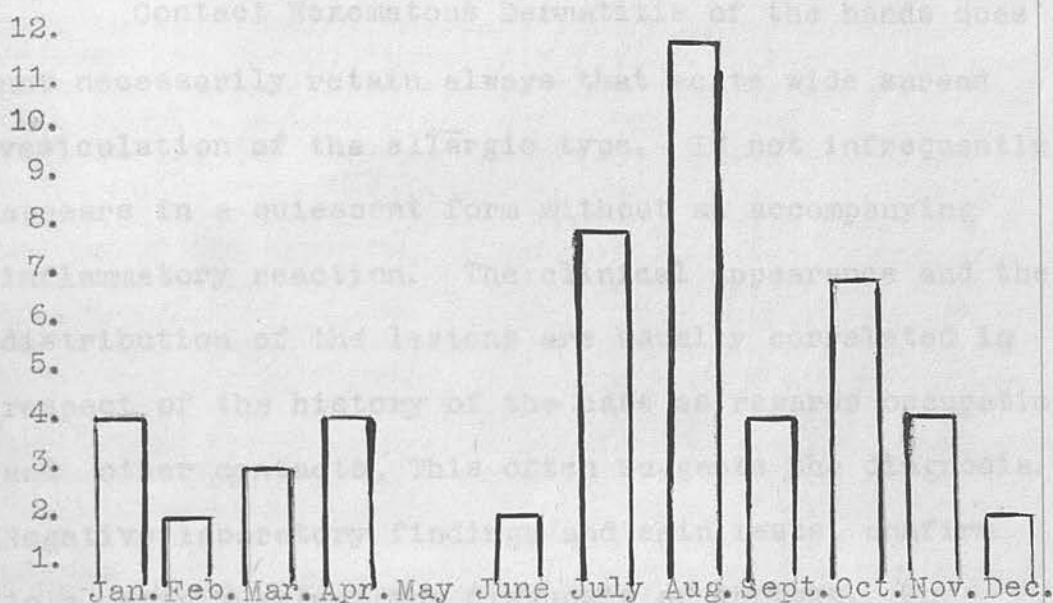


Figure No. 10- Showing the incidence of the 52 cases of Dermatophytoses. (In May no cases were selected).

Some of these cases tend to acquire a chronic course because of the lack of knowledge of the pre-existing factor and secondary associations. The results in many cases in dramatic recovery.

The 122 cases studied in detail fell into the following groups.

Contact	30
Infective	15
Bacterid	9
Undetermined	22
Dermatophytids	<u>46</u>
Total	122

TABLE NO. 8.

Contact Eczematous Dermatitis of the hands does not necessarily retain always that acute wide spread vesiculation of the allergic type. It not infrequently appears in a quiescent form without an accompanying inflammatory reaction. The clinical appearance and the distribution of the lesions are usually correlated in respect of the history of the case as regards occupational and other contacts; This often suggests the diagnosis. Negative laboratory findings and skin tests, confirm to a certain extent the diagnosis of contact. The affection in housewives of the interdigital webs, suggested in many cases Erosio Interdigitalis Blastomycotica, but microscopic and cultural examinations were always negative, and abstinence from wet work and soap, resulted in many cases in dramatic recovery.

Some of these cases tend to acquire a chronic course because of the lack of knowledge of the precipitating factor and secondary eczematization and infection which tend to alter the appearance and behaviour of the lesions which thus becomes misleading. In the 30 cases studied a wide variety of contactants have been/



been encountered including such substances as rubber, dutch tulips, cabbage, paraffin, dyes of the aniline series, Turpentine, Morphine, soap and other alkaline and detergents, /complex organic substances such as British Anti-lewisite.

In some cases vesicular types of lesions were observed on the hands where the patient had been in contact with fumes of irritants to which he is hypersensitive, as it is described in the following case.

Age 30, laboratory worker. After three months work in the Chemical Warfare laboratories developed a Mustard gas vapour dermatitis with swelling of the eyelids and conjunctivitis. At that time he was handling Mustard oil, chloracetone and dichloracetone. Occasionally during the work he had noticed small vesicular eruption between the fingers. June 1st, 1947, developed an acute vesicular eruption over the hands with slight oedema of the eyelids. Substances handled in the previous 24 hours were: BAL. Lead acetate, Cyclohexane, Ether, HCl. Chloroform and CTC. The swelling and the vesicular eruption subsided in twelve days of simple treatment and off-work. One June 14th a severe oedema of eyelids with swelling of the face. Substances handled in the previous 24 hours were: Aniline, Sod. Nitrate, HCl. Arsenious oxide, and phenylarsonic acid. The inflammation subsided in ten days of simple treatment. One June 24th. had another attack of severe oedema and swelling of the eyelids with discharge and the substances handled in the previous 24 hours were: Lead Acetate, NaOH, HNO<sub>3</sub> and perchloric acid. Part of the work was carried out in an atmosphere laden with HNO<sub>3</sub> and HClO<sub>4</sub>. After the acute inflammation had subsided patch tests were made with 1:100,000 Mustard gas gave a negative result; Patch test with 5% BAL in Ethylene Glycol and another with Ethylene Glycol alone gave positive results in both patches. From January to April, 1948, had been working in the same laboratory and worked with BAL. in three occasions without any ill-effect. On April 10th had a very bad cold. On April 13th had an exposure to BAL. as well as other substances for one day. On April 17th. developed an acute swelling of the eyelids with vesicular eruption of the hands very much like an -id eruption.

Comment: There is no doubt that this patient has developed an idiosyncrasy to a large number of chemical irritants. His exposure was mainly to gasses and fumes emanated during the experiments and direct hand contact was specially avoided. Lesions over the hands did not show any special localisation to areas where direct contact could be possible. Though a contact with fumes could be blamed for the lesions over the hands but the localisation to the sides of the fingers and palms suggests an absorption rash.

INFECTIVE DERMATOSES.

Vesiculo-pustular lesions of the hands may be produced by both fungi and infective micro-organisms. A special mention as regards fungi will be dealt with later. Micro-organisms, streptococci and staphylococci were cultured in vesico-pustular lesions over the palms and fingers in eight cases. In two cases, trauma ushered in the infective process. The lesions appear as tiny deep seated vesicles scattered over the palms and palmar surface of the fingers, becoming pustular and eventually breaking down. Eczematisation and impetiginisation may be seen, but the denuded surface usually becomes dry and desquamates while new crops develop in the vicinity. This picture differs from Pustular Psoriasis and Bacterid in that it may remain unilateral, does not tend to alternate in stages of activity and quiescence and shows more inflammatory reaction accompanied by oedema and lymphangitis. Staphylococci could be demonstrated in the early vesicular stage.

Two cases of Dermatitis repens were investigated and staphylococcus aureus was cultured from the intact vesicles.

Trichophytin test was negative in all the eight cases. Throat swabs from these patients showed an unusual increase of micro-organisms with S. Aureus<sup>a</sup> and Streptococcus haemolyticus.

These lesions tend to pursue a chronic course and not uncommonly acute outbreaks of extensive pustular lesions develop over both hands with marked inflammatory reaction and lymphangitis.

BACTERIDS/

BACTERIDS.

Bacterids including pustular psoriasis and pustular bacterids, have already been described on page 48. The following two cases summarise the picture of the two conditions.

J.L. housewife, age 33, attended the skin department on the 21st. Oct. 1947 with deep pustular lesions on both palms and feet.

Her trouble began 22 months ago in India with pustular scaly lesions on both heels spreading gradually to the insteps, but never between the toes. Shortly afterwards, the soles and the right hand showed similar small blisters, and four months later the left palm was also affected. She has never been completely clear of these lesions throughout the whole period inspite of many treatments; her complaint passed through periods of remissions and exacerbations not related to season, food or work. The lesions are extremely itchy and hot especially when new blisters are showing.

There is no history of previous skin disease nor any history of psoriasis in the family. She gives a history of attacks of hay fever in 1937, and on the 16th. may of the same year, a sinus operation was performed and polypi were removed, and since that time she had no attack of hay fever. A history of kidney trouble during pregnancy was obtained. On jan43 she had an attack of influenza followed by dry pleurisy. She is suffering from nervous exhaustion since Feb. 1947. Her periods are normal and she has no gynaecological complaint.



† Fig. No. 11- Pustular Bacterid. Note the vesicular lesions and the intradermal scabs.

Both hands and feet showed marked pustules erupting inside a red cyanosed area of skin, dry in places showing the typical intradermal brownish scabs and at other places desquamating where the pustules have broken down. The eruption seems to affect the arch of the soles mainly and sparing the front and back thirds of the soles and medial side of the feet, affecting the center of the palms mainly. No adenitis was present, and the sides of the fingers and the backs of the hands were clear. See Figs 11,12

She had five of her teeth removed 4 years ago, Xrays of her teeth and sinuses showed - peripheral opacity in the right antrum suggesting mucous membrane thickening, probably due to infection. Dental films show a degree of alveolar absorption particularly in the upper jaw. No evidence of periapical infection.

Examination of scales and tops of vesicles from both hands and feet were negative for fungi. Culture examination of pustules and pustular contents on blood agar and Sabouraud's medium were negative. Throat swab cultures revealed haemolytic streptococci. Trichophytin test was negative, and oidiomycin test gave an insignificant positive reaction. White blood count was 10,000. Biopsy. The skin shows several considerable vesicles in the horny layer, collapsed and containing strands of degenerate parakeratotic epithelium and numerous degenerate polymorphs. One more recent vesicle contains only plasma and occasional polymorphs, the remainder of the epidermis shows no abnormality. The papillary layer of the dermis shows a mild degree of patchy oedema and perivascular lymphocytic infiltration. No bacteria or fungi are seen.

This is case of pustular bacterid showing typical clinical findings with negative laboratory examinations.



Fig. No.12- Pustular Bacterid, feet. Same case as Fig. 11.

J.B. Housewife, age 69, reported to the skin department on Nov. 8th. 1937, for an eruption on the thenar eminance of the left hand and the insteps of both feet, which had been present for over a year. The eruption first began on the palm of the left hand, then the instep of the left foot then the right foot was ultimately affected. In the past ten years she had experienced irregular attacks of acute pustulation followed by a prolonged period of scaling and desquamation which remains without causing symptoms for periods of 2-10 weeks after which fresh crops of vesicles develop again. These attacks do not show any seasonal prevalence; soap, water and housework do not seem to make the lesions worse. No history of sore throats or any infectious conditions was obtained. No history of psoriasis in the family. The patient cannot attribute these attacks to any cause. All teeth have been extracted 30 years ago, and her last menstrual period was six years before the onset of her disease.

The clinical appearance is of a typical pustular psoriasis, both in characters and distribution. Moreover on clinical examination psoriatic patches were observed over the knees and elbows to which the patient attaches no significance, and says that they come and go but recur just before the hands and feet flare up. See Fig. 13.

Repeated clinical examination, <sup>for septic</sup> foci were negative. A history of dyspepsia suggestive of gall-bladder was present. The liver was palpable but no tenderness over the gall-bladder. No history of urinary trouble was present.

Microscopical examinations, and cultural methods were all negative. Trichophytin test was negative.

Xrays, crude tar, and vitamins A and D given seperately affected a temporary relief. 96 grams of Sulphadiazine given last May showed great improvement, but a relapse followed six weeks after.



Fig. No. 13- Pustular Psoriasis. Patient J.B. with a psoriatic patches on the knees.

In these cases neither the history nor the clinical appearance gave any clue as to the possible aetiology. The history was indefinite and the clinical appearance variable. A large number of these cases suggested a bacterid reaction and focal sepsis was also found in some of them, but their clinical features were not related to the classical descriptions of the bacterids. In these cases lesions appear over the palms, mainly on the hypothenar and thenar eminences. The vesicles are transparent and appear like glistening pearls under the stratum corneum of normally coloured skin. They do not tend to raise the surface of the skin, commonly occur in groups but do not tend to join together. They involute by absorption and desquamation and occasionally show brownish tops of dry intracutaneous scabs. Sometimes they break down and show a denuded surface but do not present any tendency to eczematousation or impetiginisation. Both hands may be affected but not necessarily symmetrically. Only in two cases were the feet also involved. Dried lesions clear up and the skin returns to normal while new crops continue to appear. The process may disappear spontaneously and recur after a lapse of time. The duration and behaviour is not as persistent as that of Pustular bacterid or psoriasis.

The longest duration encountered was  $3\frac{1}{2}$  years with irregular attacks unrelated to time, food or contact. The shortest duration was 3 weeks with no attributable cause. Septic teeth, tonsils or sinus infection were found in 8 cases, two of which made a dramatic recovery after extirpation of the septic focus. Nervous factors, food/

food and endocrine disturbances were investigated in these cases and some of them were found to be suggestive, but it is very difficult to explain how far they could be involved aetiologically in the production of these lesions.

Microscopic examination of tops of vesicles and scales <sup>as</sup> were negative and on culture no pathogenic fungi grew. Culture of fluid contents of these vesicles on blood agar was always negative. Non-pathogenic fungi and monilia were grown from scrapings taken from hands or the interdigital spaces of the feet.

In all these cases throat swabs and stool specimens were taken for culture and the following findings were obtained.

	Throat	Stools
Streptococcus Haemolyticus	6	-
Staphylococci and other organisms	17	19
Monilia Albicans	9	-
Other types of Monilia	5	1

There was a strikingly high incidence of Monilia Albicans in the throats of these cases as well as the presence of streptococcus haemolyticus. These established pathogens may well play a part in the recalcitrancy of these eruptions if not contributing to its direct causation.

The history of some of these cases suggested a previous dermatophytosis, but no evidence was found to support this diagnosis.

Trichophytin reaction was positive only in seven of these 23 cases, two of which presented a striking resemblance to dermatophytids of the hands, but fungus was not demonstrated either in the feet or on the hands.

DERMATOPHYTOSIS AND DERMATOPHYTIDS.

There is no essential criterion, in the strict sense, which is present in every case of ringworm infection at all times, in the course of the disease. It cannot be denied that typical cases can be diagnosed on clinical grounds alone, but since experience often teaches one to be less dogmatic, it is only justifiable to consider the diagnosis of a lesion as dermatophytosis when the morphological appearance is confirmed by both microscopic and cultural methods.

PRIMARY DERMATOPHYTOSIS.

Primary on	<u>Intertrigenous.</u>	<u>Vesicular.</u>	<u>Hyperkeratotic.</u>	<u>Total.</u>
Hands	-	3	5	8
Feet	15	27	7	51 49
Neck	Kerion			1

SECONDARY DERMATOPHYTIDS.

	<u>Squamous</u>	<u>Vesicular</u>	<u>Ery. Multiforme</u>	<u>Exanthematic</u>	<u>Total</u>
Hands	3	40	2	1	46
Feet	1	27	-	1	29

Table No. 9

Dermatomycotic lesions may be mimicked by non-mycotic lesions and cases are frequently met with where the clinical appearance is typical of a mycotic lesion, while microscopic and cultural methods do not confirm the diagnosis. However, it is not sound to accept a lesion as mycotic where fungi cannot be demonstrated.



DERMATOPHYTOSIS OF THE HANDS.

Only two types of dermatophytosis of the hands are here described.

1. VESICULAR TYPE.

Widespread vesicular or dyshidrosiform dermatophytosis have not been encountered. The only vesicular variety encountered is the one confined to a circumscribed patch occurring less commonly on the palms than on the backs of the hands, and wrists. It is characterised by a well margined papulo-erythematous plaque, soon becoming vesicular. It forms a round, oval or polycyclic patch which spreads slowly by peripheral extension with a tendency to central healing. Vesicles and pustules appear deeply seated when the palmer surfaces of the hands are involved, while lesions over the wrist or the back of the hand tend to be more inflammatory and eczematous. The hairs and the hair follicles over the back of the hands are commonly involved. The patch is often single but it may extend to cover a large area of the hands and does not ever appear in isolated vesicles symmetrically on the sides of the fingers and palms. The feet are usually clear, and vesicular and squamous -id may follow such a mycotic lesion over both hands and feet. Generalised specific hypersensitivity is demonstrable.

In this series only three cases of primary dermatophytosis of the hands producing an -id eruption are included. One of the cases was experimentally inoculated and will be dealt with later in detail. The next two cases, each presented a circumscribed patch/

patch, one over the hypothenar eminence extending to the anatomical snuff box and the other confined to the wrist.

The details of one case are as follows.

J.A. female, age 15, works in a draper's shop. She developed a tiny red, itchy spot on the left hypothenar eminence, gradually getting larger in size. There was no history of allergic diathesis or any previous skin disease. The lesion was circinate in shape, 8cm. in diameter involving the hypothenar eminence and extending up to the lateral side of the wrist. The edges of the lesion on the hypothenar eminence were undermined with advancing deep pustules, while on the side of the wrist they were eczematous, crusted and showing perifolliculitis. Tiny discrete vesicular lesions scattered over both palms and the sides of the fingers were seen on the 23rd day after the initial lesion. There was no lymphangitis nor adenitis and both feet were clear.

Microscopic examination showed mycelial elements in the hairs and scrapings from the circinate edge, and on culture a growth developed after 10 days which attained the character of "Trichophyton Cerebriformi" was seen. Microscopic and cultural examinations of the discrete vesicular lesion were completely negative. Trichophytin test was strongly positive performed three days after the appearance of the -id eruption. Blood culture was negative for fungi and the complement fixation <sup>test</sup> was also negative.

## 2. HYPERKERATOTIC TYPE.

The initial lesion in the vesicular type is either a papule or a vesicle, but in this type papulation is not seen and vesiculation is not apparent. The skin is thickened, showing irregular desquamation and at certain areas an irregular type of scaling. The palms and the sides of the hands and fingers are usually affected. No inflammatory or eczematous reaction is seen but occasionally localised eczematous patches develop in which mycelial elements are also demonstrated. The feet always show the same picture with more marked hyperkeratosis. The disease tends to pursue a chronic course and onychomycosis of the hands and feet is very often present. Treatment is often difficult and unsuccessful. Mycelial elements are demonstrated in the nails and the desquamating skin of/

of both the hands and the feet. Skin sensitisation to fungus extracts was not demonstrated.

The five cases of hyperkeratotic dermatophytosis were accompanied by the same type of dermatophytosis on the feet, and so it is difficult to state where the infection starts first. Four of the cases were accompanied by onychomycosis of the hands, feet, or hands and feet.

#### DERMATOPHYTOSIS OF THE FEET.

Three types of dermatophytosis of the feet are described:-

##### 1. VESICO-BULLOUS TYPE OR DYSHIDROTIC VARIETY.

This type begins with deep seated vesicles or groups of vesicles over the instep of the feet and soles. These often rupture exposing a smooth denuded surface. New crops of vesicles develop and the process spreads in all directions showing confluent vesicles and bullae. In 65% of cases the process began on one foot and eventually affected the other one usually over the insteps or between the toes.

This vesicular variety may present itself either in confined circumscribed patches which may run together to form a large polycyclic patch, or in discrete vesicles or groups of vesicles scattered over the soles, extending to the toes, sides, and dorsum of the foot. Hyperhidrosis seems to be marked during the acute stage of vesiculation, rendering the skin soft and sodden. Pustulation and eczematization is not an uncommon sequel.

Accompanying these fungus positive blisters, one often encounters groups of smaller sized vesicles of brownish/

brownish tinge developing abruptly, after an elapse of time, on the periphery of the initial lesion, over the soles and sometimes the dorsum of the foot. These vesicles, which are sometimes very difficult to distinguish from the primary lesion, are sterile on culture. A similar eruption is commonly seen over the hands in this variety of dermatophytosis.

This type runs a very acute course initially, but when the primary mycotic vesiculation subsides and desquamation takes place, there is a tendency in some of the cases for it to turn into a subacute stage of desquamation, vesiculation or even eczematization, sterile on culture. The following case cited, illustrates this variety.

No.45- J.H. Male, age 24, fitter, reported to the skin department on 20/8/47 with wide spread vesiculation on both hands and feet. The disease began 18 days previously with two blisters on the sole of the right foot, which he had punctured with a needle. Three days later, a fresh crop of blisters appeared around the two blisters to which he applied calamine lotion to relieve him of the intense itching. Ten days later, the right foot became itchy and showed few tiny vesicles. Two days before he reported he was playing a game of football and on the next morning he noticed that his feet have become worse and his hands were itchy and hot. Physical examination revealed wide spread vesiculation involving the instep of the right foot and the instep and the medial side of the left foot. There were few broken down vesicles showing denuded surfaces. The toes and in between the toes were clear and so also was the whole body surface. Fig 14. Both hands were studded with a vesicular eruption affecting mainly the sides of the fingers and the hypothenar eminence. Tops of vesicles removed from the lesions on the feet were studded with mycelial filaments. On culture *Trichophyton Kaufmann-Wolf* was grown. The vesicle on the hands were negative both microscopically and culturally. Trichophytin test was +++ positive. Blood culture was negative for fungi, and the complement fixation test was positive.



Fig. No. 14- Case No. 45. Vesico-Bullous variety of Dermatophytosis of the Feet. Note the +++ positive Trichophytin Test.



Fig. No. 15 Case No. 81- Vesicular Dermatophytosis of the Feet.

## 2. INTERTRIGENOUS VARIETY.

This is the most common variety of dermatophytosis of the feet but in our series it comes second in the group because it is less frequently accompanied by the -id reaction. It may appear as a fissure or a sodden mass of epidermis at the base or in between any of the toes, affecting most commonly the fourth interspace. It may assume an intertrigenous type of dermatitis with a marginate border studded with crops of vesicles and pustules extending to the sides of the toes and plantar surface of the feet. Trichophytid eruptions may accompany this dermatophytosis over the palms and soles.

This variety runs a subacute or chronic course, and is liable to recurrence and exacerbation especially in the hot weather and after a hard day's work. It responds fairly well to treatment, but as already stated is subject to repeated recurrences.

15 cases in this series presented the intertrigenous variety. In each case, between 1-6 toes and interspaces were affected and in 13 cases the fourth interdigital space was involved. In 9 cases there were bilateral involvement of the feet and the left foot was more commonly affected than the right. The following case illustrates this variety.

No. 56- M.S. female, age 18, clerkess, complaint began by itching between the toes where two blisters were noticed over the plantar surface of the left toes spreading from the fifth toe to the flexor surface and interdigital spaces of the toes. Gentian Violet was applied with no improvement. Ten days later the right instep showed a few itchy blisters. On the 15th day the hands were itchy and crops of tiny blisters appeared on the palms and fingers. A circinate patch over the back of the left foot involving the dorsum of the outer three toes and the flexor surfaces of all the toes. The toes/



Fig. No. 16. Case N. 56. Intertrigenous Dermato-  
phytosis with vesicular variety over the insteps spreading  
to the dorsum of the foot. Note the -id eruption surrounding  
the lesions on the instep.



Fig. No. 17- Case No. 85. Intertrigenous variety  
of Dermatophytosis followed by a secondary infection  
and eczematisation. There was an accompanying vesicular  
-id on the hands.

toes of the right foot were less severely affected. The patches were marked with vesiculation and pustulation especially at the outer edges. The soles of both feet showed vesicular lesions varying in size and depth. There were tiny shotty vesicular lesions over the sides of the fingers and the edge of the palms, varying in size from a pin head to a lentil scattered over both hands without showing any confluence or tendency to run together or break down.

### 3. SQUAMOUS OR HYPERKERATOTIC VARIETY.

This is very much like the hyperkeratotic variety on the hands, characterised by thickening, scaling and absence of apparent vesiculation. The soles, the sides, and the dorsae of the feet may be affected and a marginate edge is often found between the affected hyperkeratotic and normal skin. Desquamation and peeling may take an irregular or a lamellar shape. Onychomycosis and involvement of the hands are commonly seen.

This variety runs a very chronic course. In the seven cases reported the hands were affected in 5, and in 4 cases more than 3 nails were affected. In the remaining 3 cases there was no nail involvement. No skin sensitization was demonstrable in these cases.

One case of hyperkeratotic dermatophytosis of the feet and onychomycosis of the finger and toe nails showed a vesicular type of -id over both hands and feet from which no fungi were demonstrated and his trichophyтин reaction was negative. The case is described below:-

**No. 80-** W.B. male, age 55, school teacher. In 1927, in West Africa, complained of scaling and fissuring between the toes, and ever since recurrences experienced especially during the hot season. The complaint was always confined to the toes and never on the soles. Occasional scaling was noticed over both palms and soles, but not so marked as to require attention. In 1939 the two nails began to show thickening and caking. This gradually affected all the toe nails. In 1944, a vesicular eruption over both hands and feet was seen, which cleared completely after treatment without breaking down, and was followed by extensive /



by extensive desquamation. Three attacks of similar vesiculation developed after the first one. In 1946, the left middle finger nail became thickened and crumbly, as were also three other nails of the left hand.

The hands were dry and thickened, showing sago grain-like brownish spots, which when removed, were shown to be dried vesicles containing no fluid. The finger nails affected were the 1, 3, 4 & 5th. of the left hand, showing thinning of the nail plate at the distal end where the nail had become brittle and broken down, while the proximal end was thickened and showed yellowish spots spreading towards the perionychial end. The feet were dry, hyperkeratotic, and desquamating with sodden skin and fissuring between the toes. Similar yellowish spots were also seen, some of which showed collarette desquamation. All the toe nails were thickened, brittle and fragmented.

Microscopic examination of scrapings from the nails of both hands and feet were positive for fungi. On culture an uncommon trichophyton was grown and was difficult to type. Repeated examination of scrapings of tops of the yellowish brown blisters were all negative microscopically and culturally. The trichophytin test, repeated three times with extracts from different species of fungi were all negative.

No. 50- S.A. Female, age 27, housewife, had suffered from acute vesicular lesions of the feet about ten years ago when she was in India, diagnosed as athlete's foot. She had applied Whitfield's ointment and the lesions disappeared. Five years later, she noticed that one of toe nails had become boggy and tended to break easily and the skin over the soles was peeling. She did not pay any attention to it till a year later when three of toe nails began to show a similar picture. She was given some treatment but without improvement. Five weeks before she reported to the Royal Infirmary, she developed an eczematous patch over the right heel and the back of the left foot, which was not responding to ordinary treatment. She gives a history of bad circulation and chilblains on her legs during the winter months, and scaliness of the hands during the hot weather.

She had eight toes and three finger nails affected, showing marked thickening and caking of the nail plates. The nails affected are:-

	<u>Right</u>	<u>Left</u>
Hands	2nd.	2, 3d.
Feet	1, 2, 3, 4th.	1, 3, 4, 5th.

The skin of the palms showed irregular desquamation. The feet were dry with marked hyperkeratosis and scaling, and fissuring between the toes. There were three semicircular patches varying in size from 2"-4" over the medial side, and dorsum of the right malleolus and the left heel, extending up to the lateral malleolus. The patches were eczematous in character with undermined edges. See Figs 18 and 19

Microscopic/

Microscopic examination of scrapings from the active patches, the nails, and the desquamating skin showed mycelial filaments, which on culture grew *trichophyton rubrum*.

Trichophytin test was doubtful, showing a reaction less than  $\frac{1}{2}$  cm. in diameter.



Fig. No. 18- Case No.50. Onychomycosis with eczematous mycotic patches over the dorsum of the foot positive for fungus microscopically and culturally.



Fig. No. 19. Case No. 50. Showing Hyperkeratotic Dermatophytosis of the hand.



Fig. No. 20- Case 70. Onychomycosis of the hands and feet.



Fig. No 21. Hyperkeratotic Dermatophytosis of the feet. Same case as Fig. 20.

DERMATOPHYTIDS OF THE HANDS AND FEET

A dermatophytid is an eruption accompanying a mycotic focus of infection most commonly located on the feet. Its development depends mainly on two factors:-

- 1- An altered reaction of the skin.
- 2- The dissemination of fungi or their products, or possibly both to the site of the -id eruption

The altered reaction is produced by a previous mycotic infection which is responsible for the initiation of the -id reaction, which is in fact an inflammatory response of the skin to the fungus products. It can also be demonstrated by the intradermal injection of fungous extracts, "the trichophytins".

There is general agreement among most dermatologists, as to the validity of the first factor, but as regard the second factor; the method of dissemination of fungi or their products and the production of the -ids are much debated.

Most observers favour Jadassohn's suggestion of the haematogenous spread, but there are still some workers who accept the idea of exogenous spread i.e. self-inoculation.

Invariably, the development of dermatophytids, pursues a characteristic course of events, which is so frequently typical, that, one is compelled to stand firmly by this clinical conception.

The history begins with a primary focus of mycotic infection, commonly located on the feet and, usually vesicular and inflammatory. After a lapse of 10 - 30 days, /

days, and when usually both feet have been involved, a sudden outbreak of discrete bilateral vesicular lesions over the hands, or feet and hands.

The period between the establishment of the primary focus and the appearance of the secondary rash is very variable. In acute cases, in patients infected for the first time, the duration in those studied varied between 15 - 40 days. In chronic or relapsing cases, the duration was indefinite. The type of fungus as well as other precipitating factors seems to contribute to the production of the -id reaction. In eight cases, patients were quite unaware of any affection of their feet until they were questioned regarding them and then were examined and proved to be affected. In five cases the -id reaction developed on a recurrence of infection and in eighteen cases the infection was complained of for the first time, as far as could be obtained from the patients' histories. In three cases the -id eruption developed after commencing treatment and in another four cases after a trichophytin skin test. Secondary infection and eczematization also provoked the production of dermatophytids. In forty two cases the primary infection was on the feet, in three over the hands and in one case the -id eruption followed a kerion celsi on the back of the neck.

The types of dermatophytids encountered are:-

1- Vesicular	39
2- Squamous	4
3- Erythema multiforme	2
4- Exanthematoid	1

The/

THE VESICULAR TYPE.

This is the most common variety of dermatophytid and appears on the hands as well as on the feet. The vesicles look like tiny shotty elevations of the skin, often easily felt and not seen, occur superficially and are not accompanied by redness or inflammation. They are usually discrete and seldom collect in bunches and so they do not coalesce to form large bullae and do not show any tendency to form circular or polycyclic zones or clusters. They vary in size from a pinhead to that of a lentil. They usually involute by absorption and desquamation but occasionally become pustular or in extensive and large size vesiculation they may break down showing a denuded surface with a tendency to eczematization. Desquamation may be of a simple collarette type or an irregular post-scarlatiniform type. They do not show usually any brownish intradermal scabs nor clear intradermal vesiculation. They appear in successive crops over the sides of the fingers and palms symmetrically on both hands. New crops appear over the thenar and hypothenar eminences and palms, less commonly over the wrists and the backs of the hands.

On the feet dermatophytids appear more or less like the primary mycotic lesions except that they are smaller in size and probably more superficially situated. They tend to occur more in clusters and affect mainly the soles and sometimes the sides of the feet and toes. The vesicles as a rule develop abruptly over both feet and hands at the same time. The feeling of heat, itchiness and tension usually precedes the development of this type of dermatophytids. No constitutional disturbances/

disturbances have been found to accompany the development of these eruptions.

On the hands microscopic examinations have always been negative in cases following the typical course. Over the feet it is very difficult to say which lesion is fertile and which is sterile, but undoubtedly on microscopic examination of many vesicles, one encounters a group usually situated over the instep or between the toes that are positive for fungus while a number of scattered ones are negative.

#### SQUAMOUS VARIETY.

This type of dermatophytid often follows the vesicular variety after absorption of its fluid, or the erythema multiforme type. Sometimes, the vesicular stage is not distinct and only desquamation is to be noticed.

Two types of desquamation are encountered. The collarette variety accompanying the mild and discrete vesiculation, and the post-scarlatiniform type in deeper and severe vesiculation, with an irregularly shaped dry lamellar flakes and large fragments of skin. When the eruption is mild the lesions appear mainly on the sides of the fingers and <sup>are</sup> deep seated. They may be easily overlooked if not specially looked for.

#### ERYTHEMA MULTIFORME VARIETY.

This variety was met with in two cases only with severe tinea infection over the soles of the feet. One, a young man of 28 developed this type of -id after an injection of 0.1 cc. of trichophytin. The palms of the hands, the forearms and the legs were the sites affected.



Fig. 22. Vesicular -id eruption on the hands due to mycotic infection on the feet caused by *T. ast. gypseum*. Case No. 78. Note the distribution of the eruption.



Fig. No. 23. Extensive vesicular dermatophytid on the hands involving the dorsum of the fingers and hand. Case No. 45. Trichophytin test +++, Se Fig. No. 14.



EXANTHEMATOID VARIETY.

- This was encountered in one case only. It appeared very much like a purpuric rash mainly over the palms and soles. The backs of the hands and the dorsae of the feet also showed <sup>a</sup> few scattered spots. The primary lesion on the feet was of the vesicular type.



Fig. No. 24- ERYthema Multiforme variety of of Dermatophytid of the hands. Case No. 82. The eruption developed 3 weeks after the mycotic process on the feet. The Trichophytin Test +++ positive.

LABORATORY METHODS.

Sabouraud's original medium still remains the ideal culture medium for growing fungi. Modifications and substitutions have not proved as efficient especially in producing macroscopic characters and colour production. Carlier (1948) has compounded a medium using 1% oxoid peptone and 10% glucose, and found that the colonies produced parallel those of the standard American control culture and also Sabouraud's pictures.

At the beginning of this work Sabouraud's medium was prepared by using bacteriological peptone (Melville & Hunter) and ordinary maltose, the only products available. Later on Sabouraud's original Brut du Chanut, a product which dates back to 1932 was found in an old store and was employed for the preparation of Sabouraud's medium.

SABOURAUD'S MEDIUM

Peptone	1%
Maltose	4%
Agar	2.3%
Tap Water	100%

SABOURAUD'S BOUILLON

Peptone	1%
Maltose	4%
Tap Water	100%

The mixture is kept in a steam oven till ingredients dissolve. Filtered and sterilized at 15 lbs. for 30 minutes. The final pH. was 5.5.

Sabouraud's medium adjusted to pH. 10.5 was prepared by adding 3.4ccs. of N/10 NaOH to 100 ccs. of Sabouraud's medium. It is necessary that the NaOH should be sterilized separately and added to the medium after sterilization/

sterilization at a temperature not over 45°C. to prevent the medium from caramelising.

For every case, 4 tubes were inoculated, two of ordinary Sabouraud and two SAB. Medium adjusted at pH. 10.5. Scales and scrapings were soaked in 60% alcohol for 2-5 min. before inoculation. At the beginning every tube was smeared with one drop of Penicillin 5,000 units @cc. in order to inhibit the growth of Penicillin sensitive contaminations. This was found to have no adverse effects on the growth of pathogenic fungi, but this procedure was abandoned because of the difficulty of obtaining fresh penicillin whenever needed.

By the above mentioned measures, it was possible to obtain about 85% pure cultures of pathogenic fungi, and when secondary contaminants were encountered early subcultures on to ordinary Sabouraud usually insured pure growth.

Tubes were incubated at 27°C. and were inspected every third day. Subcultures were not made before the fifth day to give time for the non-pathogenic fungi to show their characteristics sporing colouration. Sabourauds medium, plated, was used to give a contaminated inoculum a larger surface area whence suspected colonies could be selected for subculture. Final inspection of colonies was made 20-30 days after inoculation.

Blood culture for fungi was made by using 50c.c bottles containing 25ccs. Sabourauds bouillon with a rubber cap, sterilised and kept ready for inoculation. Between 1-2.5ccs. of blood was used. Vesicular fluid and throat swabs were inoculated on to blood agar plates and Sabouraud's medium at the same time. Stool cultures were/

were made on blood agar plates and a special selective medium.

#### pH. 10.5 ADJUSTED SABOURAUD'S MEDIUM.

This medium was found to have no inhibitory effect on the growth of pathogenic fungi, at least *Trichophyton asteroides gypseum*, and *Epidermophyton Kauffmann - Wolf* grew luxuriantly as well as in the ordinary Sabouraud's medium. Colonies of *Epidermophyton Kauffmann-Wolf* and *Trichophyton asteroides gypseum* on Sabouraud's medium adjusted at 10.5. were found to be more fluffy than that on an adjusted medium and microscopically sporing was not abundant and macroconidia were fewer than on ordinary Sabouraud's medium. *Epidermophyton Floccosum* and *Achorion Quinckeanum* did not show as a luxuriant growth in the adjusted medium as that of the ordinary medium. (See figures No. 29-32).

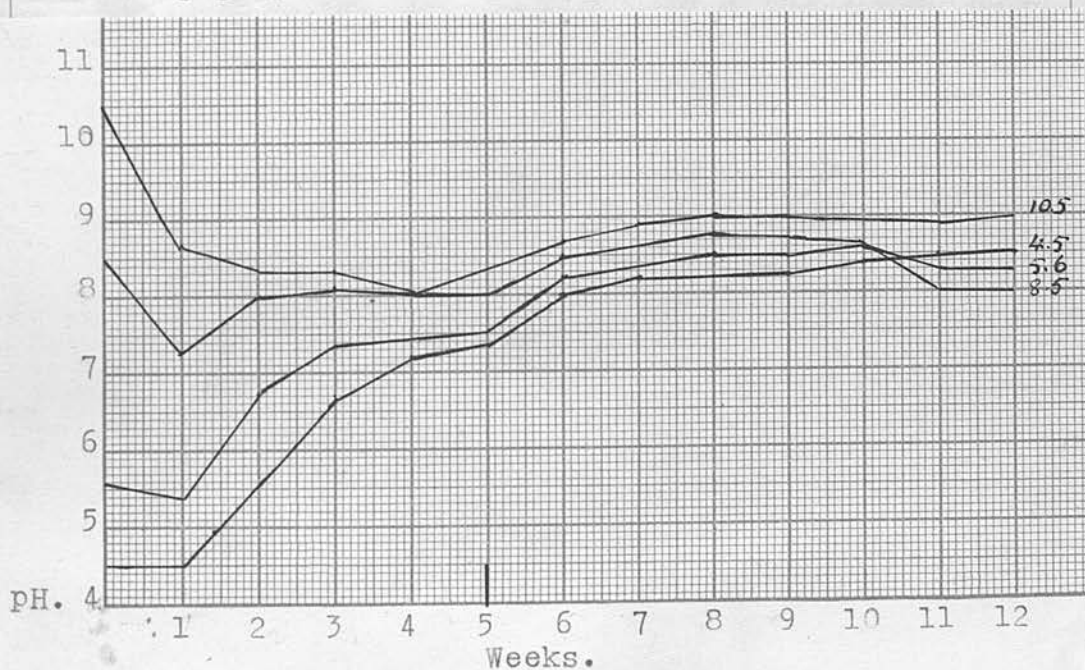
In this medium *Rizopus Nigricans* and some of the other non-pathogenic fungi were completely inhibited. *Penicillium* and *Aspergilli* showed marked inhibition as compared to the normal Sabouraud's medium, and it was found that if the tubes were incubated at 27°C. for 24-48 hours only, and then removed and left at room temperature the inhibition was very striking and pathogenic fungi could easily be selected for subculture.

#### THE EFFECT OF pH. ON FUNGUS GROWTH.

An observation was made when studying the growth of fungi in culture media which deserves mention. It was noticed that when a Sabouraud's Bouillon at an initial pH. of 5.6 was inoculated with a fungus and left for/

for three months, the size of the growth mass varied directly with the surface area of the medium, and when rubber stoppers were used, the growth was much less than when cotton plugs were used as stoppers. The facts which would require further study by control experiments, nevertheless suggest that a large surface area and free oxygen are both factors encouraging the growth of fungi. Culture media, after a lapse of time, when growth has become abundant, tend to become darker in colour, and the pH. at the end of three months was found to vary between 8.5 and 9.5. The greater the growth, the more alkaline the medium becomes.

A study of this change of pH. was made, and bottles of Sabouraud's bouillon adjusted at pHs. 4.5, 5.6, 8.5, and 10.5 were prepared and were inoculated with 1 species of fungus, and the pH. was tested every seven days. For the first few weeks the bottles were kept upright in the incubator, but after the fifth week they were laid flat to give the medium a larger surface area. The pH. estimation was continued till the twelfth week. The following graph shows the range of change of pH.



It was noticed at the beginning that the fungus growth was abundant in bottles of pH. 8.5, and very much less in bottles pH. 4.5, but later all the bottles attained fairly equal amounts of growth. *Epidermophyton Kauffmann-Wolf* and *trichophyton asteroides gypseum* both grew fairly well in all the bottles in contrast to *epidermophyton floccosum* which showed a poor growth with no surface layer at pH. 4.5 even after three months incubation with a final pH. of 6.4.

In the series of the 51 cases of dermatophytosis of the feet, the growth of pathogenic fungi was obtained in 49 cases only. In two of the cases which showed no growth except for some bacterial contaminants in the four tubes inoculated, when after one month of incubation an examination was made in liquor potassae of the pieces of skin used for the original inoculation, it was found that the fungi still retained their filamentous character but had degenerated showing vacuolation and tiny scattered granules. In the third case no filaments were recovered from any of the tubes.

Identification of fungi was made according to the descriptions of Sabouraud (1910), and Macleod and Muende (1946). A few specimens were sent to the school of Tropical Medicine and Hygiene, London, for confirmation of the type of the fungus growth. The following fungi were encountered in the series of the 52 cases of dermatophytosis with -id eruptions.

<i>Trichophyton Asteroides Gypseum</i>	13
<i>Epidermophyton Kaufmann-Wolf</i>	28
<i>Trichophyton Rubrum</i>	3
<i>Trichophyton Cerebriforme</i>	2
Unidentified	3

No/

No attempts were made to identify saprophytic fungi, only group typing were made and these were:- Penicillia, Aspergillae, Phizopodes, Torulae etc. Nor was any identification of bacteria made except in throat cultures and vesicular fluid cultures where the presence of haemolytic streptococci and staphylococcus aureus were to be excluded. Monilial growths were identified according to their sugar reactions.

Most of the saprophytic growths, begin with moist, whitish fluffy colonies, which soon begin to show a highly coloured appearance. For example, the familiar green colour of Penicillium, the black or brown colour of aspergillus etc. Very few of the pathogenic fungi are coloured, and in cases where colouring is apparent, it is only a light uniform one. Pathogenic fungi grow slowly, and do not tend to spread quickly or show fluffy aerial growth. The most rapid grower is the *Trichophyton asteroides gypseum* which produces a colony of half to one centimeter in four days.

So discarding the moist, rapid, and fluffy growth, which may show as wide a range of high colouration as non-pathogenic fungi, the probable pathogens are those which make their appearance in three to seven days and grow slowly with a powdery appearance or slight aerial growth, and remain whitish or take a yellowish or purplish red colour. Moreover, microscopic examination confirms the differentiation between pathogenic and non-pathogenic fungi, by demonstrating the different types of mycelial filaments and macroconidia .

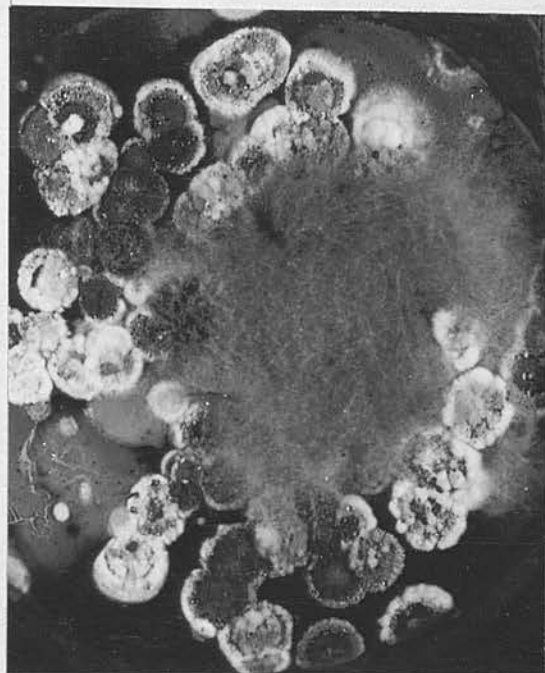


Fig. No. 25- Normal Sabouraud's Medium after five days incubation at 27C.

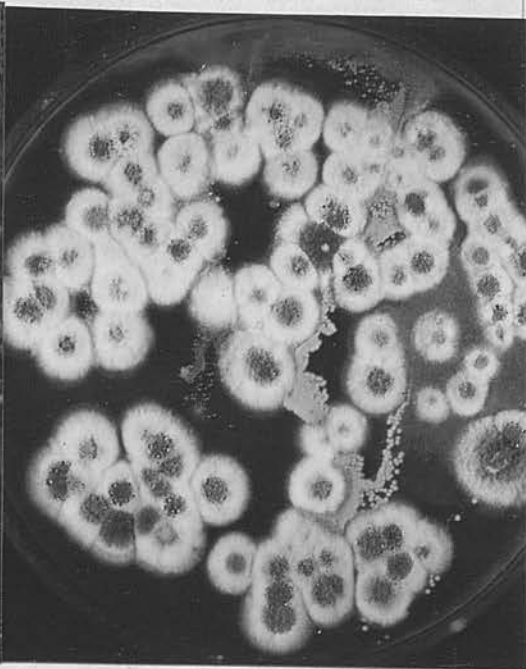


Fig. No. 26- Sabouraud's medium adjusted to pH.10.5 after five days incubation at 27 C.

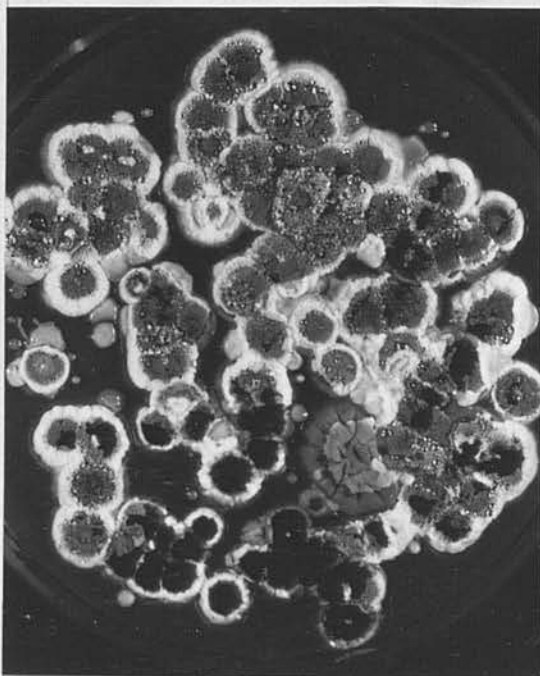


Fig.No.27- Normal Sabouraud's Medium incubated at 27 C for 24 hrs. and kept at room temperature for four days.

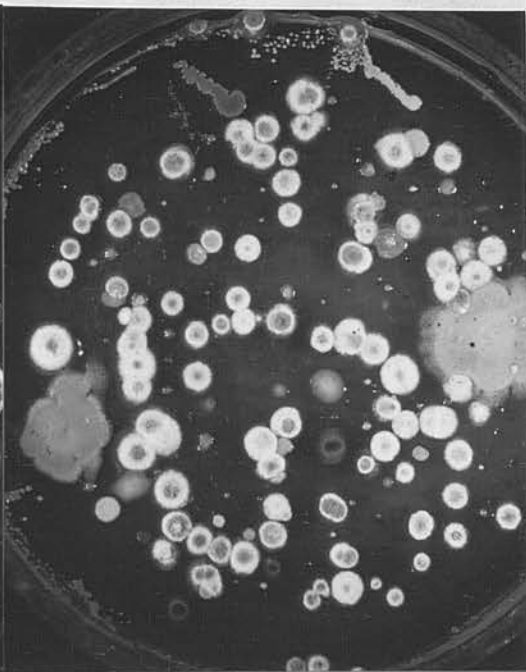


Fig. No. 28 Sabouraud's medium adjusted to pH.10.5 incubated at 27 C. for 24 hrs. and kept at room temperature for four days.

These growths of organisms were obtained from the air inside an inpatient ward by the Sieve Air Sampler.



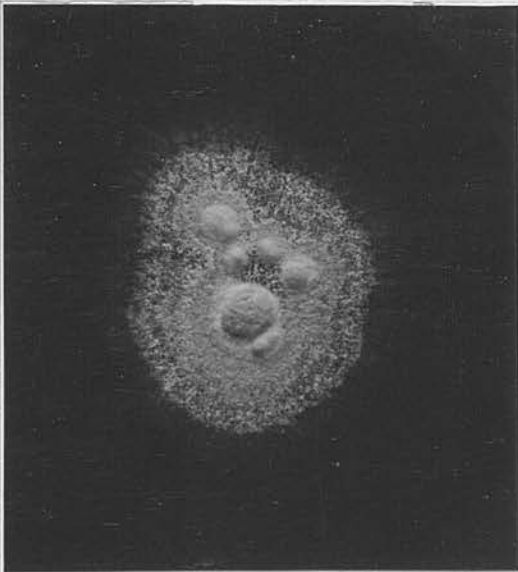


Fig. No. 29 A colony of *Trichophyton Asteroides Gypseum*, 20 days old on ordinary Sabouraud's medium, incubated at 27 C. for 48 hrs. and left at room temperature.

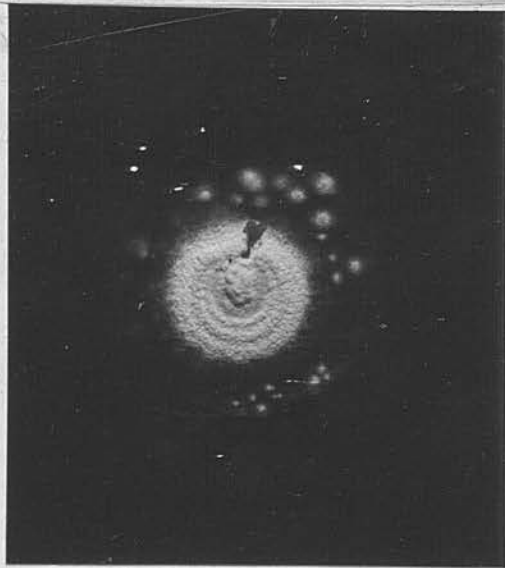


Fig.No. 30 A colony of *Trichophyton Asteroides Gypseum*, 20 days old on Sabouraud's medium adjusted to pH.10.5, incubated at 27 C. for 48 hrs. and then left at room temperature.

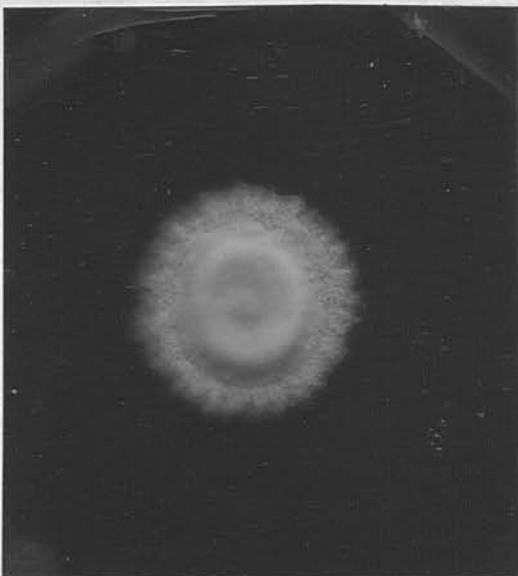


Fig. 31- A colony of *Trichophyton Kaufmann-Wolf*, 20 days old, on ordinary Sabouraud's medium incubated at 27 C. for 48 hrs. and then left at room temperature.

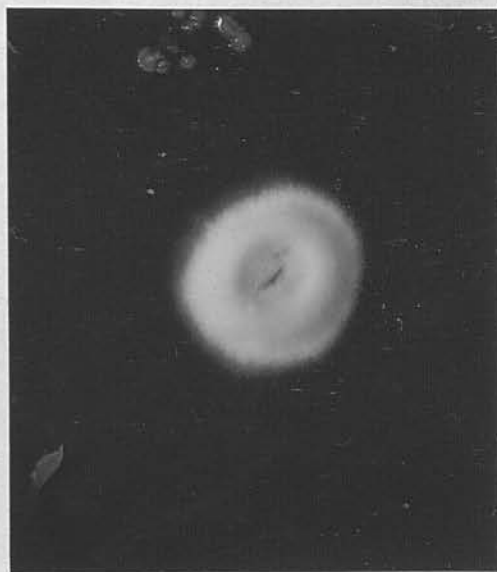


Fig. No.32- A colony of *Trichophyton Kaufmann-Wolf*, 20 days old, on Sabouraud's medium adjusted at pH.10.5, incubated at 27 C. for 48 hrs. and then left at room temperature.

MYCOLOGICAL TECHNIC.

Scrapings or tops of vesicles are mounted in 30% KOH with the inner surface facing the cover slip. Little heat is necessary to facilitate the clearing of the cells, boiling destroys the preparation and crystallises the KOH on the piece of skin. It is advisable also, to allow the preparation to stand for five minutes and if time is available, examination after 30-60 minutes ensures complete clearing, and in this way no mycelia or spores are likely to be missed. It is essential to spread the piece of skin by applying pressure over the cover slip to insure flattening of the <sup>layers of</sup> cells and clear visibility throughout.

Examination is done at first under the low power of the microscope in a subdued light, by using the convex mirror and lowering the condenser. This helps to demonstrate clearly the mycelial threads between the cellular network. Confirmation of suspected threads is made by examination under the high power. See Figure No.

The fungus appears as distinct branching threads between the irregular and nondescript appearance of the epidermal cells. Under high power, these threads are seen to be made up of closely set cuboidal cells lying side by side and traversing the epidermal cells.

In spite of the fact that fungi are present in the roof, the fluid, and the floor of vesicles, they are not often seen in broken down vesicles, probably because of oozing and secondary contamination. At least half the time devoted to confirming the clinical diagnosis of mycotic infection should be allotted to the selection of the area from which the specimen is to be taken/

taken. Cleaning the lesion with alcohol or ether before removing the material for examination is very important, and in cases of ulcerated or crusted lesions, care should be taken to select the area at the invading active edge of the lesion.

The inability of non-pathogenic fungi to invade and grow in the epidermis, renders microscopic examination of greater importance than cultural methods. It is occasionally the case that, positive scrapings do not show any growth in culture, especially in treated cases and scrapings from affected nails, or when non-pathogenic growths over-run the pathogenic ones, thus obscuring the diagnosis. Therefore, a primary microscopic examination is necessary for diagnosis.

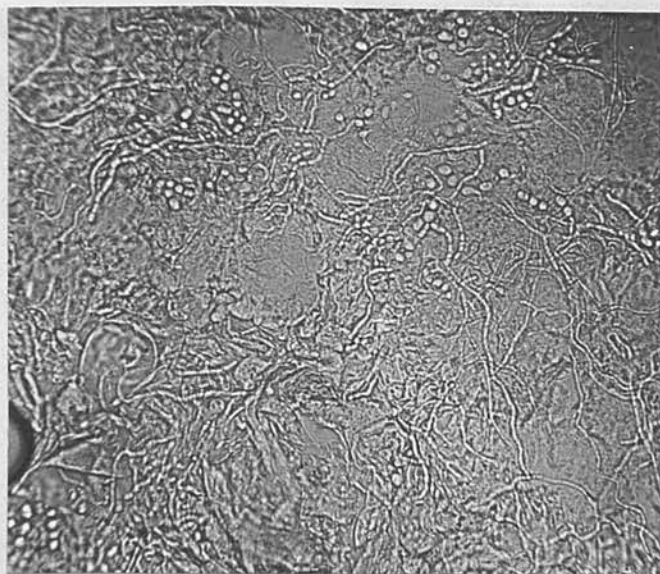


Fig. 33- Fresh preparation of a roof of a vesicle in Liqueur Potassae, showing mycelial filaments and arthrospore formation.

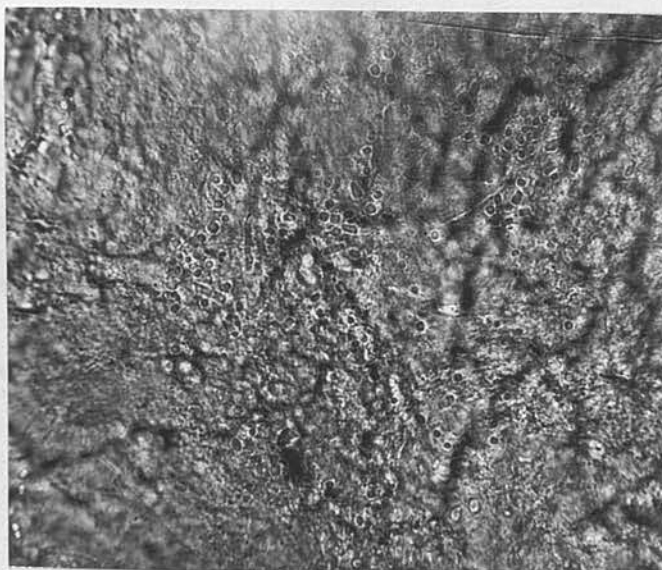


Fig. No. 34- Fresh preparation of scrapings of a mycotic lesion on the feet in Liqueur Potassae, showing abundance of arthrospores with very few mycelial filaments.

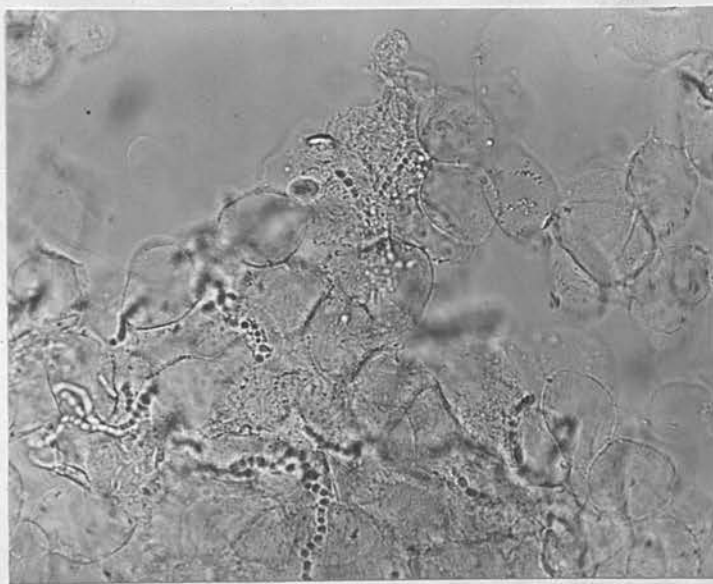


Fig. No. 35- Fresh preparation of superficial scrapings of a desquamating mycotic lesion in Liqueur Potassae, showing mycelial hyphae, arthrospores and a clamydospore.

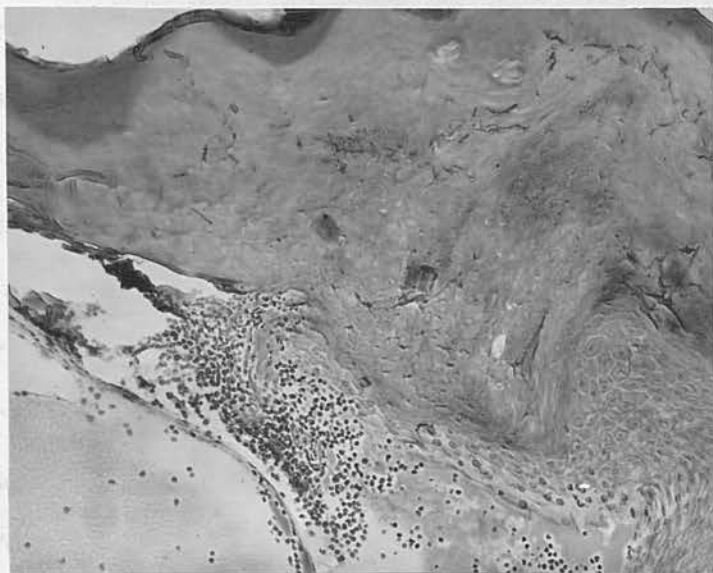


Fig. No. 36- Histopathological section of a mycotic lesion on the foot. Note the vesicle formation, the cellular infiltrate, and the mycelial filaments in the roof of the vesicle.

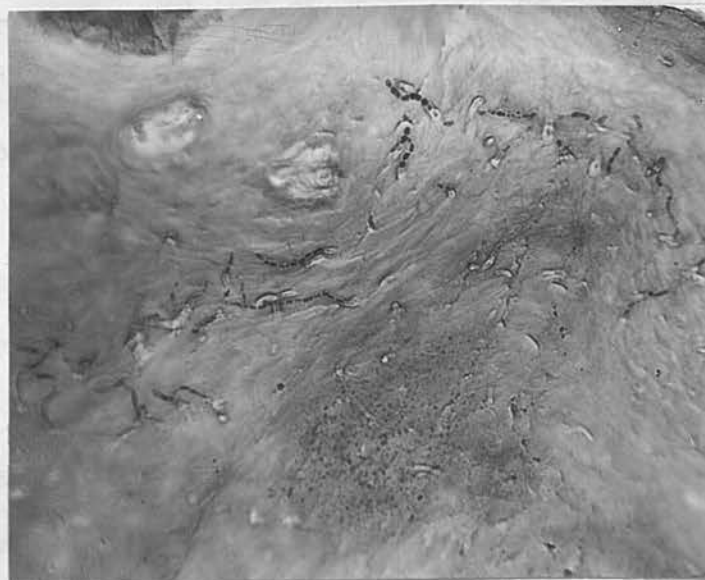


Fig. No. 37- Histopathological section of skin showing mycelial filaments in the horny and upper layers of the epidermis. No vesicle formation were seen.

"MOSAIC FUNGUS".

This is an irregular branched filamentous structure that appears in certain scales of the epidermis, especially those of the hands when treated with KOH. It tends to occur in small bunches and never shows long filamentous threads like fungus hyphae. It is made up of an irregular cell-like structure of a mosaic pattern, following the outline of the epidermal cell.

The exact nature of this structure is unknown. It was first described by Weidmann (1927). Downing and Orr (1936) although they were unsuccessful in growing the mosaic fungus nevertheless concluded that it is of fungus origin, on the evidence that mosaic segments have been observed in tissues with trichophyton gypseum hyphae joined end to end, and that during the healing of lesions of the patient suffering from tinea infection, the mosaic fungus is increased and the pathogenic fungus is decreased in number. Further studies were made by Davidson and Gregory (1925) who suggested that the mosaic fungus is made up of cholesterol crystals which are soluble in xylene. Cornbleet et al. (1943) support the belief that mosaic fungus is not a true fungus, nor does it develop from a true fungus and they obtained evidence by examination in polarized light with fluorescent dyes and staining of the presence of cholesterol compounds at the site occupied by the mosaic fungus.

It has been noted during this study that mosaic fungus is recovered only in KOH preparations and scales obtained from parts other than the palms and soles have also shown this type of structure. Moreover, roofs of vesicles taken from/

from an acute contact eczema of the hand have in one case shown this mosaic structure.

It was further observed that if a skin KOH preparation warmed over a flame and left for ten to thirty minutes, is spread widely by applying pressure over the cover slip, all the mosaic structure disappears, and if a preparation showing a mosaic structure is displaced to another slide it also loses this mosaic structure.

#### BLOOD CULTURES.

The possibility of the entrance of fungi from a focus of infection into the blood stream has been studied by many workers. The first reported cases of the recovery of ringworm fungus in the blood stream of a patient suffering from epidermophytosis of the feet with -id on the hands were those of Peck (1930), who found it only in one case in a series of twenty six cases. Pellizaro obtained it only in one of seven hundred cases of dermatophytosis. Sulzberger(1928) found that following the cutaneous infection of guinea pigs with *Achorion Quincheanum*, fungi could be cultured from the blood. In the first positive phase, fungi were demonstrable in the blood stream from one to two hours after cutaneous infection. This was followed by a negative phase varying in duration from three to nine days, then came the second positive phase ten to eleven days after infection in which fungi were also demonstrated in the blood stream. This he states corresponds to the time of the acute stage of the primary lesions at which allergy is at its maximum.

1-2 ccs. of blood was taken from every patient suffering/

suffering from dermatophytosis of the feet with -id on the hands and was inoculated into SAB. broth. bottles and incubated at 27°C. Most patients were examined during the acme of their -id eruption at which time they tended to report for advice. Forty seven blood cultures were made with no positive finding in any case.

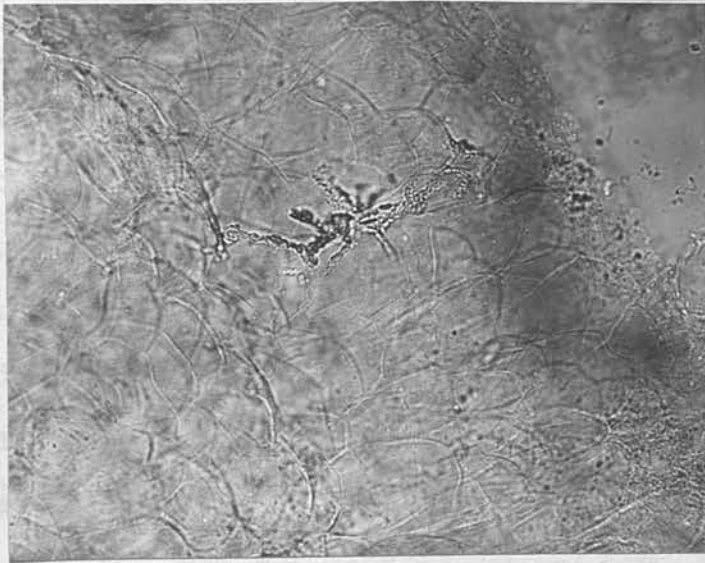


Fig. No. 38- Fresh preparation of scales from the author's palm showing "The Mosaic Fungus". Note the nondescript character.

#### TRICHOPHYTIN AND REACTION TO TRICHOPHYTIN.

Trichophytin is an extract of fungus growth, first prepared in 1902 by Plato and Neisser.

Since that time it has been established by many investigators that a positive reaction following an intracutaneous injection of trichophytin, is due to a specific sensitivity resulting from a mycotic infection of the skin.

Trichophytins prepared from different groups of fungi; Trichophytans, Achorions etc. contain a common sensitising/



sensitising factor, so that a patient infected with a *Trichophyton* in whom a state of sensitivity has developed will react to trichophytins prepared from any other group. According to Jadassohn, Schaff and Wohler (1937) Fungi contain both a common group antigen and a species specific antigen characteristic of the individual fungus. Trichophytin, as commercially available is a complex substance whose potency is dependent to a great extent on the method of its preparation, and this militates against an adequate method of standardization.

Bloch(1924) prepared his trichophytin from a four months culture of *T. Interdigitale* in Sabouraud's bouillon. The growth was collected and washed with sterile water, and the washings were combined with the broth and evaporated down to 5 cc. This solution was poured with stirring, into 30 cc. of Methyl alcohol and a precipitate obtained. This was filtered and the filtrate labeled 3-A and recovered after the methyl alcohol had been removed by evaporation. The residue small in amount is washed repeatedly with methyl alcohol, then is dissolved in 10 cc. of sterile water and labeled 3-C. The fungus recovered was mixed with Fuller's earth, ground and then frozen and thawed repeatedly by means of dry ice. This was taken up with a minimum amount of sterile water and filtered. The residue discarded and the filtrate labelled 3-B. No precipitate was obtained when adding 3-B to 100% Methyl alcohol up to 40% of the original volume.

Da Fonesca and his collaborators (1931) prepared what they called the clasovaccine from over 300 strains of/

of fungi. This was a protein free extract and it was said to be efficacious for treatment only, and that it did not contain the skin reaction-eliciting substance. While Sulzberger, Lewis & Wise (1937) tested this class-ovaccine and were able to show that it contained the skin test principle.

Lederle Laboratories prepare their Trichophytin from a three months culture incubated at 32-34°C. The growth is collected and 0.5% phenol added to it and is placed in a shaker for 24 hours. It is then put in the incubator for 24 hours and again shaken for another 24 hours. This shaken mass and broth is filtered and filtrate is passed through a sterile Mandler Filter. For cutaneous tests 1:30 dilution is used.

There are many other methods used for the preparation of Trichophytin. Krueger & Templeton (1934), Miller et al. (1941) Undenatured Trichophytin, Peck-Glick (1941) etc.

All of these preparations lack a method standardisation. Some preparations are standardised by comparing the antigenic strength at different dilutions of known preparation Goodman & Marks (1935). Traub & Tolmach (1935), Miller et al. standardise their Trichophytins according to its nitrogen content.

Bloch, Laboucher & Schaaf in 1935 isolated from ordinary trichophytin a starch-like, protein-free, polysaccharide containing nitrogen which elicits positive reaction in patients sensitive to ordinary trichophytin, and is capable of producing specific cutaneous reaction in guinea pigs infected by fungi and elicited the Schultz-Dale reaction in the isolated uterus of sensitized guinea pigs.

EXPERIMENTS.

Different methods of preparation of Trichophytin for testing skin sensitization were used. Also every preparation was employed as an antigen for testing complement fixing bodies in the blood of affected patients and animals. At first each preparation was compared with the proprietary preparation of Lederle 1:30 Trichophytin. Later, one concentration of a fixed preparation was used, as described below.

Numerous 500 ccs. bottles each containing 200 ccs. of Sabouraud's Bouillon were inoculated, each with one of the following fungus growths 20-30 days old:- Trichophyton Asteroides Gypseum, Epidermophyton Kaufmann-Wolf and Achorion Quinckeanum. These were incubated at 27-30°C. for 3-4 months. Bottles were observed once a week and after the third week they were laid flat to provide a larger surface of broth for the fungus to float. At the end of the period the massive growth which had covered the surface of the fluid was collected and washed thoroughly in distilled water, and was treated in different ways. The original fluid medium was preserved for later use.

1. The fungus growth was desiccated in a vacuum desiccator which reduced the massive growth to a dry fluffy mass. 10 ccs. each of saline, alkaline buffer and the preserved inoculated bouillon were added to separate amounts of 0.5 grams of the desiccated fungus, and ground thoroughly in a mortar. These mixtures were allowed to stand overnight at laboratory temperature, filtered by Seitz Filter and made into different dilutions for/

for testing.

2. One gram of fungus growth was ground thoroughly in a mortar with sterile sand and saline, and a similar amount treated with alkaline buffer and inoculated bouillon separately in other mortars. The mixtures were allowed to stand overnight at laboratory temperature, and then the supernatant fluid was removed, and the heavy mass at the bottom of the mortar was ground again with fresh fluids. The fluids were collected together and filtered through a Seitz filter and made into different dilutions for testing.

3. The fungus growth was put into bijou bottles in which ballotini grade 9 glass beads were added with a few ccs. of saline. These were placed in a shaking machine for 12 hours, and were allowed to stand for 12-24 hours after which the supernatant fluid was collected and fresh saline was added, and this was placed for another 12 hours in the shaking machine. The mixtures were collected, the residue and ballatini were washed with saline and the fluid wash was added to the fluids previously collected and were allowed to stand in the refrigerator for three days. The fluid was then placed in a centrifuge at 1500 rev. @ min. until the fluid ~~it~~ became almost clear of any cellular material. The supernatant fluid was treated with 5 times its volume of 100% Methyl alcohol, giving a whitish milky precipitate. This was allowed to stand 24-48 hours, in the refrigerator to allow the precipitate to settle to the bottom. If the precipitate did not settle, 2-4 drops of glacial acetic acid was added, and this assured complete precipitation.

The /

The supernatant alcohol was discarded and the precipitate was dissolved in water. If the watery solution was not clear, another precipitation with methyl alcohol was made until a clear whitish fluid was obtained. This fluid extract was desiccated in a vacuum desiccator which turned it into a solid mass. This was dissolved in diluant fluid, and dilutions made with certain percentages for both skin tests and complement fixation tests.

4. The preserved broth in which the fungus was grown, was brought to boiling point under a vacuum and left to evaporate to 20 ccs, to which 5 times its volume of Methyl alcohol 100% was added. The precipitate was dissolved in water, and the process was repeated again with alcohol until a clear solution was obtained. This watery solution was desiccated under a vacuum and dilution made according to weight/volume.

These extracts which could now be called Trichophytins, were employed for skin tests, at first to sensitised guinea pigs then compared with Lederle 1:30 trichophytin. Skin tests in Human beings were then started.

The great difficulty encountered with the first two methods was to establish a safe dilution for use in human beings, and there was a great difference of reaction to the different extracts when prepared again by the same method. Positive reactions were obtained to much the same degree as with that of Lederle, and there was no difference in reaction between the saline extract, the Buffer extract, or the Sabouraud's fluid extract. The third method was found to be the most satisfactory with good and constant results. A degree of standardization was found to be possible by preparing a constant dilution of the solid extract/

extract in the diluting fluid.

The diluting fluid contains the following ingredients:-

0.036%	$\text{KH}_2\text{PO}_4$
0.134%	$\text{Na}_2\text{HPO}_4 - 12 \text{H}_2\text{O}$
0.5%	$\text{NaCl}$ .
0.5%	Phenol.
100.0	Water.

#### GENERAL PROPERTIES.

The active principle of Trichophytin appears to be a polysaccharide, soluble in water, non albuminous with a negative Biuret reaction, dializable and precipitated by methyl alcohol from the crushed fungus growth. It gives a positive reaction to the Molisch test. It is not destroyed by boiling, or desiccation "in vacuum". One cc. of a 1% solution contains 0.134 mg. of nitrogen.

In dilutions of 1/8000 it produces an inflammatory reaction in the skin of hypersensitive individuals or animals. This reaction is characteristic. It is a delayed tuberculin-like reaction, varying in intensity from a red macule of the size of less than  $\frac{1}{2}$  cm. to a large indurated papule surrounded by a red areola of the size of 3 cms. in diameter or more, accompanied sometimes by an ascending Lymphangitis and adenitis. It takes between 12-48 hours for the reaction to reach its highest level, although in two cases, this was delayed for 3 to 5 days. After this, the reaction involutes gradually, and after the tenth day it begins to desquamate, and disappears completely in 10-15 days, leaving slight pigmentation which may remain for a few months.

In two cases an immediate wheal reaction was noticed/

noticed in 3-5 mins. In one case, a red papule was seen 24 hours later. The second did not turn up in time but there was no evidence of positive reaction four days after test.

An eczematous reaction to the intradermal injection of the Trichophytin was met with in two cases. One of these also developed an eczematous reaction on patch test with Trychophytin.



Fig. No. 39. Trichophytin Reaction ( the author ) 24 hrs. after injection. Note the surrounding inflammatory reaction.

The reaction to the intracutaneous injection of Trichophytin has been thoroughly studied by many workers. Sulzberger, Lewis & Wise (1937), Goodman & Marks (1935), Lewis et al. (1938), and all the evidences presented shows that the reaction to the trichophytin test is genus specific.

The trichophytin test in this study was performed on 315 patients. 10 cases of whom had a trichophytin patch test as well. 0.1 cc. of a 1/8000 dilution of Trichophytin by intracutaneous injection, and 0.1 cc. of the/

the diluent fluid was used as control.

These cases could be classified in two groups.

1. Patients suffering from apparent mycotic lesion positive for fungus totaling 103 cases.
2. Patients with or without skin trouble, totalling 209.

In the first group of 106 cases, there were 71 cases suffering from Tinea pedis, 46 had dermatophytids over the hands, and the rest of the cases were affected with tinea of the glabrous skin. There were 2 children below one year of age and 3 below 10 years of age, the rest varied between 10-65.

	(+++)	(++)	(+)	(±)	(-)	Total
T. Pedis with -id.	11	23	10	1	1	46
T. Pedis without -id.	4	12	6	2	4	28
T. Corporis	5	12	7	3	5	32

- (-) Showing no reaction.
- (±) Showing a reaction less than  $\frac{1}{2}$  cm.
- (+) Showing a reaction  $\frac{1}{2}$ -1 cm.
- (++) Showing a reaction 1-2 cms.
- (+++) Showing a reaction 2-3 cms.

Table No.10.

The two children with multiple lesions of Tinea corporis showed a positive reaction and of the two children under 10 years of age one showed a ++ positive and the other a negative reaction. In the group of Dermatophytosis with -id eruption, the trichophytin test was positive in 98% of the cases but the number of +++ strong positive reactors was 24%, not as great as expected. In contradistinction dermatophytosis without the -id eruption only 75% were positive reactors 15% of which were +++ positive reactors.

The second group of 209 cases, consisted of 128 patients suffering from Pulmonary Tuberculosis including 5 cases of TB. Cutis, and the rest were patients with various/



various skin diseases other than mycotic. Only 27 cases or 13% were positive reactors and their histories did not convey much information as regards previous mycotic infections.

21 cases from the first group were retested about 4-6 months after the first test. They were completely symptomless except for two with onychomycosis. 16 cases showed same degree of positive reaction, 2 showed an increase from + positive to +++ positive and the rest remained negative including the two cases with onychomycosis.

8 cases were retested for the third time after 8-12 months, only one showed a slight decrease in the degree of positive reaction.

Oidiomycin was injected intracutaneously in 134 cases from both groups together with the trichophytin. A strong positive reaction was obtained in 97% of the cases irrespective of their complaint but none showed any lesion suggestive of monilial infection.

Patch tests with undiluted trichophytin was performed on 10 cases with an eczematous eruption, which had already presented a positive intracutaneous trichophytin test. A piece of filter paper cut in the shape of a crescent and soaked in 1% Trichophytin and was applied over the upper arm. The patch was removed 48 hours after application and readings were made 10 mins. later.

Only 3 cases showed a positive reaction, and one, whose intracutaneous trichophytin produced an eczematous reaction, reacted with the patch test in an eczematous reaction as well. The rest of the positive patch tests only showed a slightly indurated reaction the size of 1cm.

Secondary reactions or manifestations following the intracutaneous injection of Trichophytin have been noticed in some of the cases. An accentuation of the primary lesion and an aggravation of the existing trichophytid eruption was marked in 5 cases. In 3 other cases the trichophytin test precipitated an -id reaction, one an erythema multiforme type and two the vesicular type of dermatophytid. Sulzberger & Kerr(1930), Wise & Sulzberger (1930), and Ramirez (1932) have shown that secondary manifestations may take the form of Urticaria, Asthma, Hay Fever, or a Febrile state. None of these complications were met with among our cases, nor any unpleasant reaction encountered.

#### INTERPRETATION OF RESULTS OF TRICHOPHYTIN TESTS.

A positive trichophytin test denotes that the skin is sensitized to the dermatophytes, and if a pathogenic fungus is isolated from an active lesion at the same time, the positive reaction adds evidence that the secondary "-id eruptions" at a remote point are also of fungous origin. But a positive reaction has no significance as regards a given lesion unless the development of that lesion follows the common course mentioned in the development of the -id eruptions.

The value of the trichophytin test as regards its specificity is unquestionable, as well as its diagnostic value in children and young adults.

A negative trichophytin test in some cases is of even/

even greater value than a positive one, especially in cases with inflammatory lesions. One can safely accept a lesion as non-mycotic if the microscopic examination and skin tests are negative, in spite of the clinical appearance being very suggestive of dermatophytosis. In other words, a vesicular eruption on the hands resembling dermatophytids with negative trichophytin and negative laboratory findings can be safely accepted as non mycotic. But, a fungus negative lesion with a trichophytin positive reaction can be accepted as mycotic only if the lesion is accepted as an -id following a primary lesion elsewhere.

Negative reactions in patients with fungus positive lesions may be explained in the following way:-

1. The test may have been undertaken before sensitisation had developed.
2. Lesions may have been of the scaly superficial type.
3. The fungus involved may be of low sensitising capacity e.g. T. Rubrum.
4. The presence of the fungus in the skin for a prolonged period may have produced a state of Hypoergy or Anergy.

Observations were made as to whether the administration of Penicillin would excite a positive Trichophytin reaction in patients who had not suffered from mycotic infection. Six individuals who had penicillin injections 1-10 months previously, and who were not suffering from any skin disease, were skin tested with trichophytin. Only one positive reaction was seen, and that was in an individual who had penicillin injections nine weeks before the skin test, with no history of mycotic infection.

ANIMAL INOCULATION.

Animal inoculation was performed for the study of immunity and sensitization in fungus disease. Guinea-pigs, rabbits and cats were used. The procedure was as follows:-

1. Inoculation of living fungi into the skin of guinea-pigs, rabbits and cats to establish sensitisation and to test for:-

- a. The action of prepared trichophytin.
- b. Antibodies by complement fixation method and PK method.
- c. Presence of fungi by blood cultures.

2. Subcutaneous injections of Trichophytins.

3. Intravenous injection of living fungi to study:-

- a. The fate of fungus in the blood.
- b. The production of fungus lesions in sensitized and non-sensitized animals.

4. Repeated skin inoculation of living fungi to study:-

- a. The development of different lesions.
- b. The development of immunity.
- c. Immunity to different species of fungi.

Trichophyton Asteroides Gypseum was the fungus used in most of the inoculations in guinea pigs and rabbits unless otherwise stated. The cats were inoculated with Cat Favus (*Achorion Quinckeanum*) obtained from a scutulum in an infected cat with the idea of studying the behaviour of fungus in its normal host.

METHOD OF INOCULATION.

Inoculation was performed on the ventral surface of the animal on a circular area 2" in diameter after shaving or depilation by means of a powder containing Barium Sulphide. The area was cross-hatched with a hypodermic needle, six scratches being applied in each direction/

direction just sufficiently deep to avoid drawing blood.

The fungus culture was applied by means of a platinum loop, sufficient enough to cover the entire scarified area.

#### INOCULATIONS IN CATS.

Two cats were inoculated with *A. Quinckeanum* on a skin area 2" in diameter on either side of the trunk. The hair was depilated by a depilating powder and the skin was scarified by a needle and a fungus growth 3 weeks old was smeared over the scarified area. Two other cats were given intracardial injections of one cc. of a thick emulsion of *A. Quinckeanum* and in both cats an area of about 3" square was depilated and scarified.

In spite of a successful take and a formation of scutulae in the first two cats, no skin reactions were demonstrated. Blood taken at varying intervals did not show the presence of any antibodies either by complement fixation or by PK reaction. In the next two cats inoculated intracardially no skin lesions were produced and no sensitization was demonstrated, and so experiments in cats were abandoned.

#### GUINEA PIG INOCULATIONS.

All guinea pigs were skin tested with trichophytin before inoculation. The ventral surface of the animal was the site used. The hair was usually shaved and the skin scarified by a needle before inoculation. All guinea pigs were weighed before the experiment and 15 days after/

after. Males and females were used, white and fawn for preference.

#### EXPERIMENTS GROUP A.

13 guinea pigs were shaved, scarified and inoculated with the following fungi:-

	Guinea pig No.
Trichophyton Asteroides Gypseum	5, 7, 13, 19, 25
Achiorian Quinckeanum	6, 11
Epidermophyton Kaufmann Wolf	8, 20, 24
Epidermophyton Floccosum	9, 12

Inoculations of sensitized guinea pigs pursued a more or less regular course of events summarised as follows:-

#### 1. INCUBATION PERIOD.

The first two days after the inoculation, the scarified area is usually quite normal except for the places where the needle has traumatised the skin. There were in addition a few blood crusts and scratch marks made by the animal itself. The first apparent reaction is usually seen between 5-8th day, though it may be more delayed in E. Kaufmann Wolf and E. Floccosum 7-12 days.

#### 2. THE PERIOD OF INVASION.

The skin along the lines of scarification becomes red, inflamed and scaly and scratch marks are very commonly seen. Animals inoculated with A. Quinckeanum and E. Floccosum show discrete papulo-erythematous primary lesions with scaling along the lines of scarification.

Scaling and redness becomes more generalised covering the whole area of the abdomen and extending beyond the area of scarification. No apparent vesiculation is seen in any of the lesions.

### 3. THE CLIMAX.

This starts 12-15 days after inoculation. The whole area is inflamed, indurated and very tender, covered with brownish crusts which when removed show a raw oozing surface. The inflammatory process progresses gradually and involves a considerable area beyond the site of scarification. Guinea pigs left in one cage contracted an infection from each other and lesions were seen over the nose, ears and head showing different fungus on culture than the one used in their inoculation. Guinea pig NO.8 died on the 16th day, and No. 5 on the 18th day of inoculation while the inflammatory reaction was at its peak. Guinea pig No.19 died on the 20th day 15 hours after a trichophytin injection. Post-mortem did not show any mycotic involvement of internal organs, but there was marked enlargement of the kidneys in the two animals, and kidneys and liver in the third animal.

### 4. THE PERIOD OF RESOLUTION.

After the 20th day the inflammatory process begins to subside spontaneously. Crusts peel off and repeated stages of desquamation takes place resulting in complete recovery in 35-50 days. The area remains bare and pigmented, especially in colored animals, for a considerable time and hair eventually develops about a month after complete recovery.

Exceptions to this rule were Guinea pig No.:7 inoculated with T.Ast. Gypseum and No.9 infected with E. Floccosum which contracted lesions over the nose and face while staying in the same cage as No.7 which showed T.Ast. Gypseum on culture. The first one suffered from/

from the infection very severely involving almost all the body surface, and when the animal died on the 53rd day active crusted lesions were seen on the face, arms and sides. Eight days before its death it weighed 545 gms. while its weight before inoculation was 375 gms. P.M. showed greatly enlarged liver and kidneys, but nothing abnormal was found in other organs. Guinea pig No.9 which contracted infection from No.7 showed persistent lesions which lasted over 60 days from the time of its inoculation.

There could hardly be seen any difference between lesion produced by the different types of fungi especially after the second stage. Scutalae were not seen in *A. quinckeanum* infection in the Guinea pigs.

Loss of weight was a striking feature in all the Guinea pigs inoculated. It varied from 85-330 gms. depending on the size of the animal. Even the Guinea pigs sensitized by *Trichophytin* injection showed some loss of weight. The *Trichophytin* test was positive in almost all the animals of this series. The intensity of the reaction was variable and slightly higher concentrations were needed to demonstrate the hypersensitiveness in the Guinea pigs than in the rabbits.

Two of the Guinea pigs in this group were scarified and inoculated two months after complete healing of the first inoculation. The whole course of events was completed in twenty days. One of these animals and two from the same group previously inoculated were inoculated 6 months after the first inoculation. The inflammatory reaction in the different stages was almost similar to that in non-sensitized animals. No difference in intensity of/



of trichophytin reaction was noticed in animals inoculated once or more.

Guinea pigs No. 3 and 4 previously sensitized by trichophytin injections were shaved, scarified and inoculated with T. Ast. Gypseum 30 days after the course of injections. Lesions produced followed the common course pursued by the non-sensitized animals.

#### EXPERIMENTS: GROUP B.

Four Guinea pigs, Nos. 22, 23 and 16, 17 were inoculated with T. Ast. Gypseum and E. Kaufmann Wolf respectively in the following manner.

The ventral surface of the animal was divided into six areas as shown in the diagram

Area No. 1 was shaved, scarified and inoculated with a fungus growth 3 weeks old. On the 3rd day area No. 2 was treated similarly and so on till all the

2	1
4	3
6	5

areas were treated. Guinea pigs No. 22 and 16 were inoculated every 3rd day and No. 17 and 23 were inoculated every 5th day.

In the first two inoculations of every 3rd day, areas No. 1, 2 and 3 took in the ordinary manner described before in inoculations of non-sensitized animals. No. 4 required a short incubation of three days to show redness and scaling. Area No. 4 showed a less marked reaction on the 3rd day. On the 15th day of the first inoculation i.e. 6 days after the 5th inoculation areas No. 5 and to lesser extent No. 4 had almost cleared up without going into the stage of exudation and crusting, while areas No. 1, 2 and 3 were still in the exudative and crusting stage. Area No. 6/

No. 6 on each of the two animals was inoculated with *A. Quinckeanum*. A greater reaction was seen than those in areas 4 and 5 the incubation period was 3 days, followed by redness, scaling and slight crusting, thus following the ordinary course in an abortive manner.

In the second two inoculations of every 5th day the course of events runs as follows:-

1st day - Area No. 1 inoculated.

5th day - No. 1 shows no reaction. No. 2 inoculated.

9th day - No. 1 shows redness, scaling and induration.

No. 2 showing slight redness and scaling. No. 3 inoculated.

14th day - No. 1 and 2 are in the 3rd stage of exudation and crusting. No. 3 with a short incubation period of 3 days has developed redness and scaling and on its 5th day there is slight crusting. Area No. 4 inoculated.

19th day - Areas No. 1 and 2 desquamating. No. 3 showing slight exudation and crusting. No. 4 showing redness and scaling. No. 5 inoculated.

24th day - Areas No. 1, 2 and 3 are almost in the same stage of desquamation and clearing. No. 4 and 5 are almost clear. No. 6 is inoculated with *A. Quinckeanum*.

29th day - Areas No. 1, 2, 3, 4 and 5 are completely clear except for a slight follicular scaling and redness scattered at different areas. Area No. 6 is showing slight redness and scaling.

34th day - All the areas are alike in appearance, with a slight shade of redness.

39th day - All areas clear. No. 1 and 2 showing marked pigmentation, less marked in areas No. 3 and 4 and no change in areas No. 5 and 6.

of the Guinea pigs No. 2,3,4,10,14 and 15 were injected subcutaneously with different types of preparation of trichophytin by three methods.

1. Daily injection for 3 days with increasing doses of trichophytin 0.4, 0.8 and 1.6 cc.

2. Five injections every other day with increasing doses. 0.2, 0.4, 0.6, 0.8, 1.0 cc.

3. Two weekly injections of 0.5 cc. each for 4 weeks.

After a lapse of 15 - 31 days after the last injection, Trichophytin tests were made with the same Trichophytin preparation used for sensitization and other trichophytins of different species.

Results show that sensitization by method No. 2 gave better skin reaction but not before 15 days of the last injection. Methods No. 1 and 3 showed a lesser degree of sensitization demonstrated by skin tests.

EXPERIMENTS: SERIES D.

Guinea pigs No. 1, 18 and 21 were inoculated intracardially with a suspension of T. Ast. Gypseum and No. 26 and 27 with a suspension of A. Quinckeanum. Animals Number 1, and 26 were shaved and scarified over an area of  $1\frac{1}{2}$  "sq." over the abdominal wall when the animal was still under the anaesthetic after the intracardial injection. Number 18 was left unshaved while number 21 and 27 were shaved 46 hours after the intracardial injection. 1cc. of blood was removed from every animal 24 hours after inoculation and was cultured on Sabouraud's <sup>fluid</sup> medium.

The two animals scarified just after the intracardial injection showed the stage of invasion after 7 and 9 days of/

of inoculation respectively. The lesions pursued the ordinary course of events mentioned before but after a slightly longer period. Hypersensitiveness was also demonstrated by skin tests.

The Guinea pig left without scarification and the two guinea pigs scarified 48 hours after inoculation did not show any skin lesion in the first two weeks. One of these animals developed two patches over the face on the 16th day after inoculation and fungus was cultured from these patches.

#### FUNGUS CULTURES FROM GUINEA PIGS.

In spite of the great difficulty in obtaining growths of pathogenic fungi from scales and crusts of mycotic lesions because of the swarming secondary contaminants, this was largely overcome by the use of pH. 10.5 adjusted medium incubated only for 24 hours at 27° C. and then left at room temperature, and subcultures are made from suspicious colonies on to normal Sabouraud's medium. All primary mycotic lesions examined for fungus presented a growth typical of that from which the inoculation was taken. No pleomorphism was seen. It was not possible to grow fungus from every lesion in the animals inoculated repeatedly. Areas No. 1,2,3 in all animals of series B showed typical growth while some of the remaining areas showed growth in some animals and not in others.

#### COURSE OF THE DISEASE IN RABBITS.

Two rabbits were depilated, scarified and inoculated with T. Ast. Gypseum over an area the size of 2" square on the side of the animal.

After/

After an incubation period of 5-6 days whitish scales were seen in the areas of scarification from which fungi were isolated. Scaling became widespread on the whole area and was followed by a generalised redness and swelling on the 12-14th day; the lesion was covered with a yellowish crust which was cracked and clear serum was oozing out. The 3rd stage of exudation and crusting appeared to be much longer than that of the guinea pigs. Also the disease spread far beyond the scarified area in both animals and shedding of hair followed the process. The fourth stage of resolution was also prolonged and it took about 4 months for the disease to clear up.

Two rabbits were also injected intracardially with an emulsion of T.Ast. Gypseum. An area of 2" sq. was depilated/<sup>and</sup> scarified at the same time. 2cc. of blood was removed from each animal for culture/<sup>in</sup> two hourly periods for 12 hours.

Isolated patches of scaling were noticed in the scarified area 12 and 15 days after the injection. Scales removed revealed fungi and on culture T.Ast. Gypseum was grown. The patches increased in number and eventually were noticed beyond the area of scarification. Crusting and exudation were seen in solitary patches without any tendency to become generalised. New patches continued to show for 3½ months after the first inoculation, in new areas while the old spots were clearing gradually.

Skin tests were positive on the 12th day of the appearance of the first skin lesion. Complement fixation test was negative but the P.K. reaction was strikingly positive.

Cultures/

Cultures of the specimens of blood removed two hourly after inoculation were positive for fungi in the first two specimens only.

OBSERVATIONS AND CONCLUSION IN ANIMAL EXPERIMENTATIONS.

1. Inoculation of cats with *Achorion Quinckeanum*, a normal inhabitant, was found to be different from what was expected. Hypersensitivity could not be demonstrated and skin tests were negative in spite of a successful "take".

2. Rabbits were found to show lesions produced by fungi very much like those of guinea pigs, but the course of the disease is very much longer and tends to spread to a much wider area of the body of the animal. Sensitization was very striking and a very strong reaction was obtained from skin tests with 1/8000 *Trichophytin*. Complement fixing antibodies were not demonstrated but the P.K. reaction was positive.

3. Guinea pigs acquire the infection the first time they are inoculated and show a fairly constant course of events after such inoculation.

a. The different stages the infective process follows seems to be very much the same in all different types of fungi, although variation as to degree of inflammatory reaction and duration of the disease were noticed not only between different species but also between different cultures of the same species.

b. The infective process is accompanied by a generalised toxaemia which is evidenced by the loss of weight and death in some of the animals.

c./

c- Skin sensitisation could be demonstrated after the production of the skin lesion and injections of Trichophytins.

d- The presence of sensitisation alters the animal to subsequent inoculation after 10 - 14 days of the first inoculation.

e- Complete immunity has not been demonstrated.

f- Hypersensitisation gradually diminishes over a period of 5 - 8 months, when the skin test is lost or diminished and the altered response to infection disappears.

g- Intracardial injection of suspensions of spores and mycelia produce local skin lesions only in areas previously shaved and scarified at the same time of inoculation. Animals shaved and scarified 48 hrs. after the intracardial injection did not show any lesion. The one guinea pig which developed a lesion on his face 16 days after injection, may have contracted the disease from his neighbour in the same cage.

h-A Antibodies were demonstrated in the blood of sensitised guinea pigs by the passive transfer method (P-K).<sup>X</sup>

i- Serum of sensitised animals incorporated in different percentages in Sabouraud's medium did not inhibit the growth of fungi.

j- Complement fixing antibodies and agglutinins were not demonstrated in the blood of these animals.

k- An -id reaction could not be induced experimentally at any time during the disease.

X . Prausnitz-Kuestner method.



Fig.No.40- Mycotic lesion in a guinea pig inoculated in experiments group:A. Note the spread of the lesion from cross-hatched scarification.



Fig. No. 41- Mycotic lesion in a rabbit developing in the scarified area on the abdomen 15 days after intracardial inoculation of a suspension of T.Ast. Gypseum.



Fig. No.42. Left- Guinea pig No. 7 inoculated with T.Ast.Gypseum, showing lesions on the face which grew the same fungus on culture. Right- Guinea No. 9 inoculated with Ep. Floccosum showing lesions on the nose and face which grew T.Ast. Gypseum on culture.



HUMAN INOCULATIONS.

The object of human inoculation was to apply Koch's postulate and to study the role of immunity and sensitisation evidenced by these fungi. Four patients volunteered for these experiments, and included also are investigations carried out on myself, described below in details.

The methods of inoculation were as follows:- Scarification where employed was produced by cross-hatching with a hypodermic needle a circular area of skin some 2cms. in diameter just sufficiently deep to avoid drawing blood. The fungus culture was applied by means of a small piece of lint which had been charged by means of a platinum loop from a fungus culture. The patch of lint was left in contact with the area for a period of 24 hrs. by adhesive plaster.

By the term "inoculation without scarification" it is implied that a patch of lint 2 cms. in diameter was applied to the intact skin for 24 hrs. in a similar fashion.

Before inoculation every volunteer was skin tested by trichophytin. On the second day, the left soles of the four volunteers were scratched and a loopful of culture of *Epidermophyton Kaufmann-Wolf* 30 days old, on a moist piece of white lint was applied over the scratched area. At the same time a dessicated growth of *Epidermophyton Kaufmann-Wolf* was applied similarly over the right soles without previous scratching. The patches were fixed with an elastoplast and then covered with a bandage and were left in situ for 24 hrs. giving an ample time for the fungi/

fungi to establish themselves. The growths used for inoculation were subcultured and found to be viable.

1. A.L. Male, age 30, confined to bed for some other disease, with Trichophytin test ++ positive. On the 5th day of inoculation a pin head brownish coloured vesicle appeared on the area of the patch on the left foot. The right foot was clear. On the 9th day, the left foot showed five vesicles collected together without any accompanying signs of inflammation. The right foot showed a sodden whitish skin tending to desquamate at the site of the patch. The patient complained only of a slight irritation. On the twelfth day there was no change. On the fifteenth day, the vesicles on the left foot had dried up and were removed for bacteriological examination. The right foot continued to show that sodden scaly appearance, and scrapings were also taken for culture. On the twentieth day the lesions were completely dry with desquamated edges, and treatment was started with Tincture of Iodine. Culture of specimens from both feet showed typical colonies of *Epidermophyton Kaufmann-Wolf*.

2. D.P. male, age 22, confined to bed. Trichophytin test was negative. Continuous observation for twenty days did not show any evidence of any lesion on either foot. The Trichophytin test was repeated on 31st day and it was also negative. Another inoculation was attempted with *Trichophyton Asteroides Gypseum* culture 22 days old. Continuous follow up failed to detect any evidence of a lesion. Scrapings were taken repeatedly and they were all found to be negative.

3. D.N. male, age 32, carpet weaver, well built. Trichophytin test ++ positive. The two patches applied over the soles slipped off in bed during sleep, on the first night of application. On the second day the bed sheets and pyjama were sent to the laundry. On the 8th day, red scaly patches were noticed over the neck and waist. Microscopic examination revealed mycelial filaments which on culture grew *Epidermophyton Kaufmann-Wolf*.

4. P.D. male, age 34, unemployed. Trichophytin test negative. On the seventh day of inoculation he developed itchiness over the left foot, and on the eighth day two blisters the size of a lentil each appeared over the area of the left patch. The patient was asked to continue with his usual activities. On the eleventh day 5 vesicles were showing over the left sole and on the right sole appeared a few tiny vesicles. On the 15th day the lesion on the left sole increased in size and the vesicles became more confluent and the whole area was red, sore and inflamed. The lesion on the right sole was showing more vesicles and spreading gradually. On the 20th day the left sole was very sore and the right showed a wide area of vesiculation. The trichophytin test performed over the left thigh and the right forearm were ++ positive. The patient at this time insisted on treatment and he was given  $\frac{1}{2}\%$  Silver Nitrate soaks. All and every new blister removed from both/

both feet and were found studded with mycelial elements. During this period the hands were closely observed for any -id eruption. Seven days after the silver nitrate the acute symptoms abated and after the use of a fungicide both feet cleared completely and no trace of an -id eruption neither on the hands nor on the feet was seen. On the day treatment was started a specimen of blood was taken for culture and it was negative. Complement fixation and agglutination were also negative.

G.R. male age 28, (The Author).

31/7/47. An Intracutaneous injection of trichophytin and oidiomycin (Lederle) were made. The trichophytin reaction was ++ positive the oidiomycin was +++ positive.

4/8/47 at 9 a.m. an intradermal injection of 0.1 cc. of a suspension of Epidermophyton Kaufmann-Wolf obtained from a 22 days primary culture from case No. 24 was made into the sole of the left foot. 1-2 ccs. of blood were drawn for culture every three hours for the following 15 hours.

Fine woollen socks were worn as usual and an average walking of two miles a day was continued.

No reaction was noticed except for a slight feeling of itchiness at the site of the injection. Scrapings were taken after a month for culture and no fungus was grown. All blood specimens were negative for fungi.

10/9/47. Another inoculation was made over the same site of injection in the same way described before in the inoculation of the four volunteers. The patch was removed 24 hours later and everything was continued as usual.

17/9/47. There was slight itchiness and the site of the patch appeared to be slightly sodden with slight scaling. Scrapings were removed for culture and Epidermophyton Kaufmann-Wolf was obtained. The patch was left untreated and after two weeks the skin appeared to be normal. The area was scraped again and it also yielded positive results on culture. No other reaction was noticed for twenty days later and Tinct. Iodi fort. was applied 5 times after which the skin was perfectly normal.

24/10/47. A third inoculation was made over the inner side of the right little finger with the same procedure described before, with Trichophyton Asteroides Gypseum after previous scratching of the skin.

30/10/47. The area was very itchy and two vesicles appeared on the second day which were covered with elastoplast.

6/11/47. The vesicles had increased in number occupying an area of 1 cm. in diameter. One of the vesicles was removed for examination and the area was covered again with a dry dressing. The lesion increased in size by peripheral extension and when the back of the little finger was involved, hairs were found to have become infected.

1/12/47. The lesion was about the size of half a crown clear in the centre with overlapping skin tags at the edges/

edges and no fresh vesiculation. All hairs were removed and found to be affected.

12/12/47. The area was almost clear except for that of the back of the finger where occasional follicular pustulation was seen. At this stage scales from the edges of the lesion were apparently negative but the hair and the follicular pustules were positive for fungi. Occasional itching followed by tiny blisters at the edges of the lesion were seen which were also positive for fungi.

15/12/47. Treatment with Tinct. Iodi Fortis was begun and Trichophytin test was +++ positive.

17/12/47. Another inoculation was made over the medial side of the left palm with culture of Trichophyton Asteroides Gypseum obtained from scrapings of the right hand, in the same method described before.

2/1/48. Two blisters were seen over the area of inoculation accompanied by severe itching.

6/1/48. The vesicles increased in number and occupied an area of about sixpence and showed fungus filaments on microscopic examination.

13/1/48. The lesion was the size of a shilling, with a clear centre and deep seated vesicles at the margin. Six attempts to ~~the~~ culture the contents of intact vesicles were made and only twice was there a fungus growth. No secondary organism was grown in spite of the tendency for some of the vesicles to pustulate. The area on the right little finger was completely healed except for some redness over the back of the finger.

20/1/48. Treatment with Tict. Iodi Fortis was begun. Fresh vesicles continued to appear for five more days in spite of treatment.

26/1/48. There was a feeling of slight tightness over both hands with marked itchiness over the old healed area. Treatment continued.

27/1/48. Tiny spots hardly perceptible were seen over the sides of the fingers and palms of both hands. Six of these spots which were found to be vesicular were removed for culture and 10 ccs. of blood was taken for culture and tested for antibodies. The old healed lesion over the right little finger became scaly and the redness became intense. Scales were removed but were found negative on culture. At this time a 5th inoculation was made in the same procedure over the left index finger with the same fungus but without previous traumatization of the skin.

28/1/48. New crops of vesicles appeared on the palms and another six were removed for culture with 2 ccs. of blood for another culture. None of the vesicles removed for culture showed any growth, and the two specimens of blood were also negative for fungi. By chance it was noted that there were three discrete vesicles on the left foot, one, the size of a lentil over the site of the old sodden area and the rest scattered over the instep./

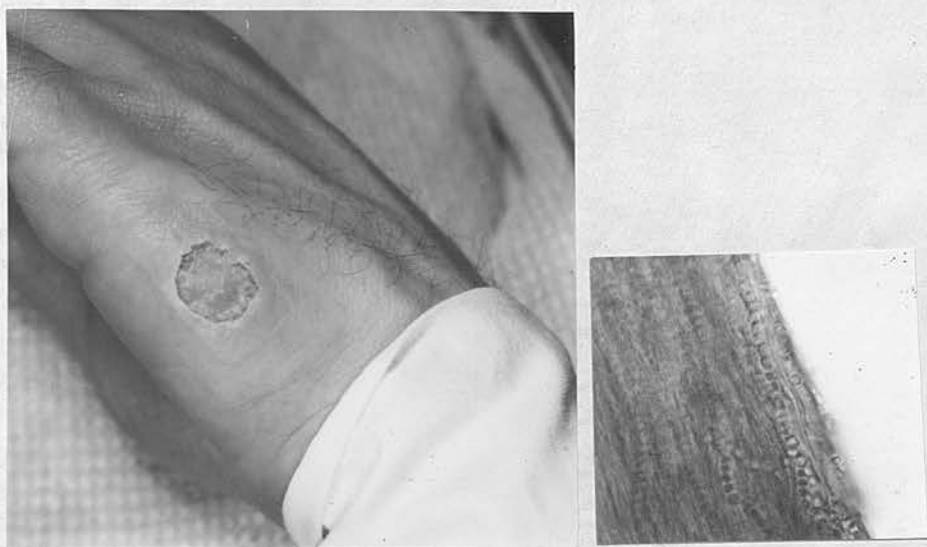


Fig. No. 43- Vesicular Dermatomyiasis of the Hand (author's 3d. experiment) 26 days after inoculation. The side photograph shows affected hair from the vicinity of the lesion.



Fig. No. 44- Vesicular Dermatomyiasis (author) showing areas of collar-like desquamation seven days after the acute eruption.

instep. The right sole showed one tiny vesicle only. All these vesicles were removed completely and cultured. Only the vesicle from the old sodden patch showed Epidermophyton Kaufmann-Wolf, while the rest of the vesicles did not show any growth.

The vesicles on the hands did not get any larger than a pin's head, and showed no tendency for conglomeration. They did not breakdown, become pustular, nor showed any brownish scabs.

2/2/48. The mycotic lesion on the medial side of the left palm abated with no fresh vesiculation, and there were no more fresh crops of vesicles on the palms. The fifth inoculation did not show any activity.

11/2/48. The vesicular rash over the hands began to desquamate showing collarette scaling followed by an irregular peeling.

10/3/47. Both hands were completely clear. The 5th inoculation did not take. A sixth inoculation was attempted with the same fungus and procedure of inoculation over the healed area on the medial side of the left palm.

12/3/48. There was a deep seated vesicular reaction in the whole area where the patch was applied, which eventually cleared up spontaneously. Scrapings removed when the lesion was desquamating were positive on culture.

3/4/48. Three other inoculations were made, one over the right hand and the other over the left forearm in the same procedure described before with the same fungus. The 3rd inoculation was made by applying the fungus culture over an area on the right forearm but without previous scarification. On the third day of inoculation itching and tiny vesicles were noticed in both areas, with positive scrapings. The lesions were left covered but without treatment for ten days. There was no tendency for spreading nor any increase in severity; the lesions remained localised to the areas of scarification. Old areas of previous inoculations were clear except for some scaling over the left sole which was positive on culture. Treatment with Tinct. Iodine was then started and both inoculations cleared without any reaction as in the fourth inoculation. The 3rd area inoculated did not show any changes.

26/4/48. Intracutaneous injection 1/8000 trichophytin and patch test with trichophytin 1/100 were made.

The trichophytin test was +++ positive but less severe than the previous test and faded away completely in eight days. The trichophytin patch test was negative.

#### OBSERVATIONS AND CONCLUSIONS.

These experiments provide some information as regards hypersensitization and local reaction of the skin to the dermatophytes in spite of their limited scope/

scope and other experimental difficulties. They show clearly that different individuals react differently to the same exposure to infection and that certain conditions may influence greatly the course of these reactions.

All attempts to produce any reaction in case No. 2 failed in spite of the absence of demonstrable sensitivity in the skin. Similarly the first two attempts at inoculation in the author's case failed to produce any inflammatory lesion on the feet, whereas an inflammatory lesion developed in the third inoculation in the hand.

The fourth inoculation in the author's experiment produced another deep inflammatory lesion which excited an already present state of hypersensitiveness but this time to the stage of developing the -id reaction. This new state of hypersensitiveness which could be regarded merely as greater in degree than the previous one, excited an active phase of an allergic nature in the already existing state of sensitivity. In other words it induced a flare up of the allergic reaction by the last exposure.

Blood cultures taken at different periods did not reveal the presence of fungi in the blood, nor did the earliest examinations and cultures of the -id eruption reveal the presence of any fungi.

#### IMMUNOLOGICAL STUDIES.

Considerable investigation has been carried out with regard to the demonstration of Toxins in Pathogenic fungi, but it is largely contradictory and inconclusive Henrici (1947). No exotoxin has ever been definitely established and the occurrence of Endotoxin is considered only of theoretical interest. Neither killed culture  
of/

of fungi nor the products they release possess any real toxicity to intact human beings or animals. Plato's first extract and the trichophytin of today produce only in a patient suffering from mycotic infection an inflammatory reaction at the site of the injection, but this does not necessarily indicate a toxic reaction.

So far, the only active product extracted from fungi ever to show any reaction is the polysaccharide of Bloch, Laboucher & Schaaf, and the product described previously in this paper. These extracts seem to act like a hapten which is capable of producing some antibodies though in variable amounts, which are common to species of pathogenic fungi infecting human skin.

Information available as regards immunity reactions to fungi are inconclusive. Bloch, Sutter, Piccori, Carroll, Blumental and Haupt & Nathan, have shown that at least in deep-seated mycotic infections in human beings the immunity processes are not dependent exclusively on the formation of a skin allergy and immunity, but that antibody formation in the blood serum also plays a part. Complement fixing antibodies and agglutinins have been demonstrated by these workers, though only in a small number of cases. In addition to this Jessner & Hoffmann (1924), Ayres & Anderson (1934) demonstrated that the blood serum of hypersensitive human beings contains <sup>certain</sup> substances which inhibit the growth of fungi in culture. But this finding was not confirmed in our series. Sulzberger & Kerr (1930) and Marcussen demonstrated the presence of circulating antibodies by the passive transfer reaction.

Complement/



COMPLEMENT FIXATION TESTS.

For the demonstration of the complement fixing antibodies in the blood serum of patients infected with the dermatophytes, the Wassermann Technique was employed. The amount of antigen and patient's serum were kept constant while varying amounts of complement depending on the Minimum Haemolytic Dose (M.H.D.) were used.

It has been pointed out previously that the difficulty in demonstrating complement fixing antibodies in mycotic infections is twofold, because there are two unknowns to be explored, namely the Antigen and the Antibody. As an antigen, different preparations were tried, Alcoholic extracts, water extracts at different pHs. crushed fungus emulsions and alcohol precipitated extracts.

Sera from 22 patients suffering from Dermatophytosis of the feet with dermatophytids over the hands were tested for the presence of complement fixing antibodies. Each serum was tried with the different antigen preparations.

Positive results were obtained repeatedly in 6 cases with more than one type of antigen preparation. The degree of positive reaction varied from one positive i.e. non-haemolysis with two M.H.D. of complement to three positive or eight M.H.D. complement. In another 8 cases results varied every time the test was repeated. Anti-complementary findings due to ageing of the sera and secondary contaminants militated against accurate and conclusive results.

These positive results obtained are suggestive but there is at present no other independent method available/

available of confirming them on an immunological basis. However, the absence of demonstrable antibodies in the rest of the cases throws some doubt on the specificity of the results and must render these findings for the time being inconclusive. Owing to the lack of proper antigen available for the complement fixation test, accurate finding could not be obtained as to the development, duration and specificity of these antibodies, and if there were any such specific antibodies formed accompanying this allergic reaction there should be no reason why complement fixing antibodies should not be demonstrated in most of these cases.

#### AGGLUTINATION TESTS.

Dreyer's Standard agglutination method was employed and the suspension was prepared by shaking up fungus spores with glass beads to break down all mycelia. Only ten cases were tested for agglutinins. Agglutination was obtained in 4 cases with a varying titre between 60-100, and the remaining also showed some agglutination at a lower titre. Slide agglutination was also employed, but only one case showed a definite agglutination.

#### P. K. REACTION. (PRAUSNITZ-KUESTNER).

For the demonstration of circulating antibodies by passive transfer, animals and human beings were used as media for the reaction. The rabbit was found most useful for the performance of this reaction. Trichophytin prepared by alcoholic precipitation was employed in all the cases. A control for both trichophytin and serum was included in every test.

Fourteen sera including the author's were tested for circulating antibodies. The serum was injected intradermally at two areas, a test area and a control. After 24 hours trichophytin was injected into the test area and a third area as a control. Any changes were observed for the following thirty minutes. In ten cases an urticarial wheal developed in 5 - 10 mins after the trichophytin injection. In the remaining four cases no wheal was noticed, but a red patch developed and persisted even longer than the wheal in the previous ten cases.

#### EXPERIMENTS.

Case No. 45 and 52 with an extensive vesicobullous type of dermatophytosis of the feet with an exceptionally severe dermatophytid on the hands, and a +++ strong positive trichophytin were selected for this experiment.

An attempt to collect the vesicular contents of the dermatophytids was made by aspirating the fluid from each vesicle by a syringe. The fluid aspirated was clear, mucoid, alkaline in reaction and sterile on culture. It was diluted 1 : 2 saline and was tested for the presence of antibodies by the passive transfer method.

A rabbit was prepared and the diluted fluid was injected intradermally, and the same technique of the PK reaction described above was followed. A strong reaction of a wheal surrounded by an areola of erythema was obtained in the test areas. The fluid of both cases gave similar reactions.

This experiment shows clearly that in the dermatophytid reaction the skin manifests another phase of its immuno-

immuno-biological processes by producing certain reagins demonstrable by the passive transfer method to whose presence we cannot attach any conclusion.

Another experiment was made to demonstrate the presence of immunological reagins probably identical to those demonstrated in the previously mentioned experiment.

AS we have seen previously in the study of experimentally induced mycotic infection in animals, after the inflammatory process reaches its peak, desquamation and spontaneous healing follows in 20-30 days. Taking this into consideration an experiment was performed in an animal to demonstrate the presence of antibodies which have taken part in the inflammatory process of the lesion. Guinea pig No.8 was employed for this experiment and the mycotic lesion was produced by the trichophyton *asteroides gypseum*.

On the 30th day of inoculation, and the acute inflammatory process had abated, and desquamation had started, an area of 1" square of the affected skin only was excised excluding the subcutaneous structures. This piece of skin was cut into small pieces and put into small bijou tubes with a few ccs. of saline and ballotini glass beads, put in a shaking machine till all the skin fragments were thoroughly broken down. A watery solution thus extracted was tested for the presence of antibodies by the P.K. method. The same procedure was followed and a positive reaction was obtained, thus demonstrating the transfer of antibodies from the affected area of the guinea pig to a localised one in the rabbit. Similarly blood serum taken from the same animal produced a positive P.K. reaction.

Unfortunately/

Unfortunately circumstances precluded the exercise of controls to confirm the validity of these experiments. Fluid from a cantheridine induced blister, or an ordinary burn, and extracts from the skin of unsensitized guinea pigs should be used for control. Moreover it would be interesting to find out whether fluid from a primary mycotic vesiculation and extracts of normal skin of sensitized guinea pigs would show any similar reactions.

These two experiments lead one to wonder whether skin sensitization in mycotic infections becomes general by absorption of antigens from the primary lesion into the blood stream or by cutaneous dissemination spreading centrifugally from the primary lesion. It has been frequently noted that the trichophytin test in a guinea pig performed on an area which has been previously infected, shows a stronger reaction than on any other site on the body of the animal. Bloch has also noted that a trichophytin test performed near a primary mycotic lesion in humans, shows a stronger positive reaction than one performed distantly.

To contribute some further evidence as to the mechanism and route of spread of the sensitization in mycotic infection, Straus & Coca's experiment of hypersensitization in Rhesus monkey was employed using guinea pigs and rabbits.

A circular incision into the skin of each animal was made separating the skin on the proximal half of the body from that on the distal half by a gutter filled with an antiseptic dressing all round the body, thus interrupting the continuity of skin between the two halves of the body/

NO.	NAME	SEX	AGE	OCCUPATION	DURATION	DATE	DISEASE.	FUN. CULTURED.	TRICHOPHYTIN.	C.FIX.	AGG.	P-K
1-	E.H.	F.	24	Clerkess	4 wks.	22/6	Ves. D. feet with ves. -id on hands	E. K-W.	+++	-	.	.
2-	G.H.	M.	23	Barber	3 wks.	29/6	Ves. D. feet with ves. -id on hands	E. K-W.	++	.	.	.
4-	J.N.	M.	21	Fitter	6 wks.	2/7	Ves. D. feet with ves. -id on hands	E. K-W.	+	-	.	.
5--	L.M.	F.	24	Housewife	4 wks.	2/7	Ves. D. feet with ves. -id on hands	E. K-W.	+++	.	.	.
8-	L.N.	M.	28	Vet. Stud.	2 wks.	8/7	Ves. D. lt. hand with ves. -id on hands	T. A. G.	++	.	.	.
12-	D.S.	M.	32	Doctor	7 years	8/7	Ves. D. feet with ves. -id on hands	E. K-W	+	+	.	+
17-	W.M.	M.	36	Postman	6 yrs. 3wk.	9/7	Interdigit. D. with ves. -id on hands	E. K-W	++	±	.	-
21-	A.N.	M.	36	Weaver	8 wks.	10/7	Ves. D. feet with ves. -id on hands	T. A. G.	++	.	.	.
24-	J.A.	F.	15	Shop Asst.	3 wks.	23/7	Ves. D. lt. hand with ves. -id on hands	T. Rubrum	+	.	.	.
29-	J.L.	M.	46	Miner	9 mts. 2wk.	26/7	Inter D. feet with ves. -id on hands	E. K-W.	++	-	.	-
30-	R.M.	M.	45	Miner	2 months	5/8	Ves. D. feet with scaly -id on hands	E. K-W	++	-	.	.
31-	J.S.	M.	31	Foreman	6 months	5/8	Ves. D. feet with Ery. Multi. on hands	E. K-W.	+++	.	.	.
33-	H.C.	M.	33	Fitter	4 months	11/8	Hyperkeratotic D. hands and feet	T. Rubrum	±	.	.	.
35-	R.C.	F.	30	Housewife	3 months	11/8	Vesicular D. on feet with ves-id on hands	T. A. G.	++	±	+	+
36-	G.R.	M.	26	Fitter	5 wks.	12/8	Ves. D. on feet with ves-id on hands	T. A. G.	±±	.	.	.
37-	A.D.	F.	32	Maid	5 months	12/8	Ves. D. on feet with ves-id on hands	E. K-W.	+	.	.	.
40-	J.H.	F.	20	Nurse	3 wks.	14/8	Interdigital D. with -id on hands	E. K-W.	++	.	.	.
44-	P.A.	F.	30	Housewife	5 years	18/8	Interdigital D. on feet with-id on hands	T. A. G.	+	.	.	.
45-	J.H.	M.	24.	Fitter	4 wks.	20/8	Ves. D. on feet with -id on hands	E. K-W.	+++	++	-	+
48-	A.M.	F.	40	Housewife	7 wks.	22/8	Ves. D. feet with ves. -id on hands	T. A. G.	+	.	.	.
50-	S.A.	F.	27	Housewife	10 years	23/8	Onychomycosis with eczematous D. on feet	T. Rubrum	±	.	.	.
52-	J.S.	M.	20	Miner	7 months	28/8	Ves. D. feet with ves-id on hands	E. K-W.	+++	±	.	.
56-	M.S.	F.	18	Clerkess	3 wks.	5/9	Ves. & inter. D. feet with ves. id on hands	T. A. G.	+++	++	-	+
59-	H.S.	F.	40	Housewife	3 wks.	7/9	Inter. D. feet with ves. -id on hands	E. K-W.	+++	.	.	.
63-	T.W.	M.	24	Civil Ser.	4 wks.	20/9	Ves. D. feet with ves. -id on hands	E. K-W.	++	.	.	.
65-	J.C.	F.	32	Housewife	4 wks.	29/9	Ves. D. feet with -id on hands	E. K-W.	++	-	.	.
68-	L.M.	M.	21	Labourer	5 wks.	5/10	Ves. & inter. D. feet with ves. -id on hands	E. K-W.	++	-	+	.
70-	B.D.	F.	25	Housewife	4 years	12/10	Onychomycosis & Hyper. D. on hands and feet	no growth	-	.	.	.
71-	G.A.	M.	34	Clerk	4 wks.	15/10	Ves. D. feet with ves. -id on hands	E. K-W.	+++	+++	+	+
74-	T.M.	M.	20	Student	5 wks.	20/10	Inter. D. with ves. -id on hands	E. K-W.	+	.	.	.
75-	K.B.	M.	22	Med. Stud.	4 wks.	20/10	Inter. D. with Scaly -id on hands	T. Cerebriforme	+++	.	.	.
78-	D.S.	M.	30	Labourer	2 months	27/10	Ves. D. feet with ves. -id on hands	T. A. G.	++	.	.	.
79-	C.D.	F.	32	Housewife	4 wks.	30/10	Interdigital D. with ves. -id on hands	E. K-W.	++	-	.	.
80-	W.B.	M.	55	Teacher	9 years	1/11	Onychomycosis & Hyper. D. with ves. -id on hands and feet	Unidentified	-	-	-	-
81-	J.S.	M.	36	Painter	5 wks.	7/11	Ves. D. feet with ves. -id on hands	T. A. G.	+	.	.	.
82-	W.A.	M.	34	Shop Asst.	3 wks.	15/11	Ves. D. feet with Ery. Multi. -id on hands	E. K-W.	+++	++	.	.
83-	S.T.	M.	27	Farmer	3 wks.	22/11	Kerion celci neck with ves. -id on hands	T. A. G.	+++	±	-	+
84-	J.D.	M.	30	Civil Ser.	4 wks.	10/12	Ves. D. feet with ves. -id on hands	E. K-W.	+	.	.	.
85-	T.P.	M.	26	Miner	3 months	18/12	Inter. D. with ves. -id on hands	E. K-W.	++	.	.	.
87-	J.H.	M.	27	Painter	3 wks.	14/1	Ves. D. feet with ves. -id on hands	E. K-W.	++	-	.	+
88-	R.I.	M.	26	Brick Layer	5 wks.	16/1	Ves. D. feet with scaly -id on hands	T. A. G.	+	.	.	.
89-	W.V.	M.	25	Med. Stud.	3 wks.	22/1	Ves. D. feet with exanthematic -id on hands	unidentified	+++	±	-	.
93-	P.T.	F.	32	Housewife	3 years	2/2	Hyperkeratotic D. on hands and feet	T. Cerebriforme	±	±	.	+
98-	W.T.	M.	22	Student	4 wks.	20/2	Inter. D. with ves. -id on hands	E. K-W.	+	.	.	.
100	A.R.	M.	18	Fitter	5 wks.	5/3	Ves. D. feet with ves. -id on hands	no growth	++	.	.	.
102	S.S.	F.	21	Student	4 wks.	6/3	Interdigital D. with scaly-id on hands	E. K-W.	-	.	.	.
107	W.C.	M.	30	Joiner	2 wks.	15/3	Ves. D. feet with ves. -id on hands	E. K-W.	+	.	.	.
108	A.G.	M.	21	Labourer	4 wks.	2/4	Ves. D. feet with ves. -id on hands	T. A. G.	++	±	-	+
109	A.D.	M.	39	Clerk	3 yrs.	10/4	Hyper. D. feet and hands	no growth	-	.	.	.
110	B.H.	F.	19	Student	4 wks.	28/4	Interdigital D. feet with ves. -id on hands	E. K-W.	+++	.	.	.
120	G.P.	F.	43	Housewife	7 years	30/4	Onychomycosis & Hyper. D. on hands and feet	unidentified	-	.	.	.
122	G.R.	M.	29	Author	-	27/1	Ves. D. lt. hand with ves. -id on hands	T. A. G.	++	±	-	+

TABLE NO. 11 - Summary of the findings of the 52 cases studied in details.

body of the animal. These animals were then inoculated by one of the fungi on either half of the body. After the lesion at the site of the inoculation had attained its peak in 10-15 days trichophytin tests were made on both halves to test the presence of sensitization.

At present results and conclusions are not ready to be submitted until a sufficient number of these experiments have been done taking adequate precautions and careful observations.

#### HYPERSENSITIVITY AND IMMUNITY IN MYCOTIC INFECTIONS.

Bloch was the first to report that first infection induced by superficial inoculation produced a complete immunity in guinea pigs, but when the fungus is injected subcutaneously or intraperitoneally no immune changes were produced.

Since Bloch's original paper, many investigators have shown that the cutaneous allergy developed in guinea pigs varies in degree and that a second inoculation may result in fungus positive lesions with a shorter course of disease.

Greenbaum (1924) and others, believe that immunity produced is purely local residing in the site of the cured lesion, while Bloch and others consider the whole skin surface to be involved. Sutter presents evidence that in human beings sensitization decreases as the distance from the primary focus increases. Reports conflicting with this observation are also to be found.

Skin reactions of hypersensitive guinea pigs to trichophytin extracts have been studied by many workers, recently by E. D. DeLamater (1938. & 1941).

All these findings in animal inoculations have been observed in varying degree in the course of this present work. But these could not be correlated to the findings observed in hypersensitivity and immunity in human beings. In literature, only few references are to be seen dealing with the study of hypersensitivity and immunity to the dermatophytes in human beings. Most of the work done covers mainly animal experimentation, no doubt because of the inherent difficulty in <sup>the</sup> systematic study of human beings.

It is a well known fact that fungi have an inherent invasive power, and that they are able to spread only after some change has occurred in the fungi themselves or their environment. Fungi recovered from active lesions do not show any increased virulence than when primarily introduced, so it seems probable that the host tissue is altered (Henrici 1946)

It is uncertain whether the changes in the host are the result of endotoxin from the killed parasite altering the tissue susceptibility so that the seeming pathogens are able to grow and extend the local lesion, or the assumed toxin creates a local cellular hypersensitivity, the host exhibiting varying degrees of hypersensitivity.

It is apparent that natural immunity to certain types of fungi exists without a previous or accompanying reactions of allergic sensitivity. The immunity of adults to *Microsporon Audouini*, the spontaneous healing of tinea capitis at puberty are examples of this immunity. Moreover, it has been frequently noted that when a group of individuals are equally exposed to fungus infection, only/



only a certain number develop apparent disease. In the series of human inoculation mentioned previously, it was not possible to induce any reaction in one of the volunteers after two attempts inspite of the negative skin tests.

According to Jadassohn and Lewandowsky, mycotic infections which tend to develop strong trichophytin reactions, have a greater tendency to spontaneous healing, and favourable response to therapy. According to Bloch, mycotic infections accompanied by trichophytids are followed by immunity. Epstein and Grenmandel (1930) showed that centrifugal extension of the zone of sensitivity not only leaves behind it a central zone of increased resistance but even creates a peripheral margin of increased resistance ahead of and beyond the advancing border of the lesion. Jadassohn's view competes with that of Epstein and Grenmandel in that the central healing in mycotic infection is due to loss of keratin structure and not previously formed immunity.

Sulzberger, accepts Epstein and Grenmandel's phenomena as the only adequate explanation of the fact that lesions produced by infectious agents after a certain time, cease spontaneously in their peripheral extension. The advancing borders reach, and are arrested by the area of specific resistance which they themselves have created. (1940).

From the study of 52 cases of Dermatophytosis with dermatophytids on the hands, and a large number of tinea of the glabrous skin, it has been observed with ample evidence that the presence of specific sensitisation does/

does not protect against subsequent infection. Scores of patients have been with frequent recurrences of mycotic lesions and demonstrable skin sensitivity even after treatment. The author succeeded in infecting himself 54 days after the healing of the third inoculation with the culture of the same fungus from the previous lesion with the only difference that the incubation period was 5 days longer than the first inoculation.

When a fungus material is applied to the intact skin of an individual who has been proved to be hypersensitive as evidenced by the production of the -id reaction; no apparent lesion is produced. This would seem, to my way of thinking, to indicate that an intact stratum corneum serves as a barrier to the invasion and establishment of the dermatophytes. When however, a fungus is applied to a scarified area in the same hypersensitive individual, <sup>it</sup> can be demonstrated to have established <sup>itself</sup> very quickly and the incubation period is much shorter than it would be had the fungus been applied to a scarified area in an individual who is not hypersensitive. These facts would seem to indicate that the tissue changes postulated which favour the growth of dermatophytes in the skin had already taken place in the hypersensitive individual, and that the mechanical removal of the stratum corneum facilitates the establishment of the fungi.

Comparing mycotic lesions of the hands and the feet to mycotic lesions on other parts of the body one finds that <sup>in</sup> the case of the former, the mycotic process not infrequently tends to pursue a chronic course with irregular recurrences in spite of energetic treatment, and/

and we know that some cases are very resistant to treatment. It is possible that the thickness of the stratum corneum contributes to this chronicity and spontaneous cure seldom occurs; no immunity seems to be developed. While on the other hand, when comparing this with mycotic infection of the body, the response to treatment seems to be rapid and satisfactory and relapses are rare though reinfection could possibly occur.

With regard to cases with accompanying dermatophytids our observations do not extend over a period sufficiently long to judge the extent of development of specific resistance to the dermatophytes. It has been observed that almost 65% of the cases with -id eruptions do not give any history of similar previous complaint, and that all cases treated and cured have not shown any reinfection in a period varying from 8-14 months.

As we have seen in the author's experiment; mycotic lesions were induced in the area of a previously healed mycotic lesion, at the site of a previous -id eruption and on other parts of the body not previously affected, in spite of the allergic reaction and strong positive trichophytin test. A point which should be taken into account is that these inoculations were induced following traumatisation of the skin, with an inoculum many times greater than would be expected in naturally acquired lesions.

This brings us to a point of fundamental importance in fungus infections. It has previously been demonstrated beyond doubt that pathogenic fungi are capable of multiplying and extending only in the substance of the stratum/

stratum corneum. The experiments outlined above would seem to suggest that where the stratum corneum is absent or incomplete as when an area is in the process of infection or healing, what would appear to be a local area of resistance to fungous infection is not an area where the stratum corneum is entirely normal, but it is one where it is either absent, incomplete, or abnormal in some respect.

It could therefore be concluded that there is hardly any immunity in the real sense of the word or local resistance produced in a previously infected area, and Jadassohn's view of loss of keratin structure seems more suggestive than an accompanying immunity.

The morphological character of individual lesions varies greatly in different cases. The individual usually presents one type of lesion but in different stages of evolution. The variation in character is not related either to the severity or the extension of the primary lesion. Various types of lesions have been described by S. Kaufmann, and the type of lesion which he has called "vesicular" is characterized by the presence of a clear, colorless fluid which may become purulent. The pH. of this fluid is about 7.0.

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OBSERVATIONS ON THE DERMATOPHYTIDS.

The -id eruption provoked by mycotic infection presents certain variations as regards frequency, type and severity. Not all patients developing dermatophytosis present the -id eruption, in spite of the fact that they show positive skin tests. It would be expected, since the -id eruption is an allergic manifestation, that the subject would show a marked degree of hypersensitivity demonstrable by skin tests. But the trichophytin reactions in these cases were all positive, though they did not show a marked degree of reaction denoting a state of extreme hypersensitivity.

The degree of positive skin reaction does not seem to vary according to the type and severity of the -id reaction. A mild squamous type of -id was found accompanied by +++ positive reaction, while an extensive vesicular type showed + positive reaction. The erythema multiforme and the exanthematoid types of -id were accompanied by +++ reactions.

The morphological character of individual -id lesions varies greatly in different cases. The same individual usually presents one type of -id lesion but in different stages of evolution. The variation in character is not related either to the severity nor the extension of the primary lesion. Primary lesions caused by *E. Kaufmann-Wolf* appeared to show a severe type of -id eruption which was sometimes bullous in character.

The vesicular -id is usually filled with a clear mucoid fluid which may contain few cells, but rarely become purulent. The pH. of this fluid is always on the/

the alkaline side, capable of changing red litmus blue.

Dermatophytids, vesicular or otherwise, have been found to be always fungus negative on microscopic and cultural examination, even in eruptions examined 3-12 hours after their development.

As a rule the -id eruption dies down spontaneously when the primary mycotic lesion has abated after treatment. But sometimes vesicular -ids may persist or even recur after the primary lesion has disappeared. These persistent lesions are always sterile and show a more eczematous character than the primary -id. The squamous, the erythema multiforme, and the exanthematoid varieties of -ids were found to disappear completely after treatment of the primary mycotic lesion, without showing any recurrences.

-Id eruptions on the feet present similar characters to those on the hands, except that they are usually larger in size with a tendency to eczematization and pyodermic changes.

Histologically the vesicular -id is very much like an eczema vesicle with no specific characteristic showing acanthosis and spongiosis of the prickle cells with dilatation of the papillae, oedema, and cellular infiltration in the corium. The squamous variety shows an abortive type of eczema vesicle with marked acanthosis, hyperkeratosis and focal parakeratosis. Changes in the dermis are very slight. Histologically no fungi are demonstrable.

#### OBSERVATIONS ON THE DERMATOPHYTES.

The most obvious clinical feature of the dermatophytes, both in man and animals, is the capability of/

of invading the epidermis and hair without a necessary previous injury. Whether the production of an inflammatory lesion, evidenced by the eczema reaction after the entry of the fungus, is a pathological characteristic of the particular fungus or a result of the biological response of the host to the invader, still remains to be seen. Fungi, undoubtedly, are ubiquitous. They are capable of withstanding natural conditions and of retaining their parasitic ability and of flourishing saprophytically. Their ability to grow in the epidermis for a long time without actually causing lesions of clinical importance, and their transmission from one person to another indicates a high degree of adaptability to the parasitic habit.

Some of these dermatophytes show a considerable degree of host specificity. Some of them are predominantly pathogens of man, others are predominantly pathogenic to animals. The species causing dermatophytosis of the hands shows a high degree of adaptation to its host in many cases, and as we have seen the *Trichophyton asteroides gypseum* and the *Epidermophyton Kaufmann-Wolf* are the most common pathogens encountered in dermatophytosis of the feet. In many cases fungi reside in the epidermis and the nails of the feet and the reactivation of a quiescent process is probably a more important factor in the frequent recurrence of dermatophytosis of the feet than reinfection from an exogenous source.

Although fungi will grow upon various sterilized natural media, such as horse-dung, straw, grains of cereals (Brocq-Rousseu, Urbain and Barotte (1925)), and even occasionally grow as saprophytes under natural conditions in farms and stables, (Muende & Webb (1937)) they/

they cannot survive long enough or flourish on these substrata under natural conditions which involve competition with other organisms. Dermatophytes in the saprophytic or dormant state under natural conditions are in an advantageous position relative to other organisms. They are completely protected inside the desquamated cells of the epidermis or hair and so have the advantage of freedom from competition since they are harboured in the keratin substance which no organism will attack in such a dry and dessicated state. But they have acquired the saprophytic characteristic of changing into sporing cells which are capable of growing and invading the human body if brought in contact with a suitable environment. As we have seen for a dermatophyte to produce a lesion it requires certain changes either in the epidermis of the host or in itself. The epidermis or even the keratin is important because dermatophytes do not flourish in the living tissues of the body. More so, they cannot establish themselves either in a parasitic state or in a saprophytic one if they are in an unfavourable position in competition with active pyogenic and other organisms. So it can be concluded that there is very little chance of fungi establishing a mycotic process in an already eczematized or infected wound. When observing mycotic lesions one often finds that after a lapse of time and especially if eczematization or infection has taken place; fungi cannot be demonstrated in lesions that were originally mycotic. Secondary micro-organisms now prevail while the fungi have disappeared. It is not likely therefore that when a lesion due to micro-organisms is already present that a fungous infection will/



will become superimposed.

It has been shown in vitro that *B. Subtilis* inhibits the growth of *Trichophyton Gypseum* and *T. Purpureum* Lewis et al. (1946).

During the parasitic phase of growth in the epidermis, fungi grow by the formation of immense numbers of thalospores which invade the keratin layers of the epidermis. While growing saprophytically for example on culture media they produce most of the mycelial and spore forms. According to Sabouraud "Jamais, dans leur forme parasitaire ces etre ne montrent aucun organe de reproduction c'est toujours un article mycellen, ordinairement un article globuleux, qui essaimera d'une lesion pour en faire une autre, non comme une grain, mais comme une bouture." It is difficult to make out what Sabouraud meant by "organe de reproduction"; fungi in their parasitic phase can produce arthrospores and in certain specimens of dried lesions aleuriospores and clamidospores have been seen. In one case of tinea capitis due to *Microsporon Audouini*, fusiform macroconidia was seen. These show that fungi can grow saprophytically on the human skin.

It has been noticed that during the parasitic phase of growth fungi do not seem to change the character of their lesions when passed from animal to animal or from man to man; though they might show different cultural characters. As regards *Epidermophyton Kaufmann-Wolf*, inoculated into the author's feet; three different types of colonies were observed on culture of scrapings removed ten months after inoculation and treatment. 1. A white milky and fluffy growth with a round surface, 2. A yellowish/

2- A yellowish brown colony with a lamellar spread and cerebriform central area, less fluffy than the previous growth. 3- A whitish fluffy growth which acquired a reddish tinge. All inoculations were made on the same medium and all growths showed similar microscopic findings:- Spiral hyphae, clamydospores, aleuriospores, and cylindrical macroconidia were seen among the extensive mycelial growth.

#### EPIDEMIOLOGY AND VIABILITY OF FUNGI.

It has been shown that fungi can survive for a long time on natural media and inanimate objects, such as silk, linen, wool, leather, sweepings etc. (Kadish 1933). Williams (1934) has cultured *Trichophyton interdigitale* and *epidermophyton inguinale* from floor scrapings, mats, and gymnastic apparatus at a school. The mode of existence of these fungi on the various materials is probably purely vegetative, or in a dormant state. Growth of *Epidermophyton cruris* has been secured in material removed from the groin for 432 days (Farley 1921), and *Trichophyton interdigitale* for 300 days (Mitchell 1922).

The existence of the dermatophytes on the human skin in a vegetative or nonpathogenic state is an important question when studying the role human beings play in the dissemination of fungus infection. It is believed that the direct spread of infection from one individual to another is not possible without intermediate fomites. Downing et al (1937) studying the bacterial flora of the skin were able to demonstrate the presence of one *Trichophyton* and one *Epidermophyton* among the skins of 100 individuals./

individuals. Bruhns considers it certain that ringworm fungi do not vegetate saprophytically on the healthy human skin. A patient therefore, cannot become a carrier without suffering from the actual disease, but he could harbour the fungi in his clothes or socks or other fomites which are in turn contagious.

Observations made during an epidemic of ringworm infection caused by the trichophyton asteroides gypseum show that this particular fungus could survive in a saprophytic or vegetative state on an exceedingly large number of articles in variable conditions.

It has been observed that fungi were demonstrated in a large variety of lesions which would be easily missed were it not for the routine examination of every case which showed a lesion of any kind no matter how minor on any part of the body. Lesions noted in the first twelve hours were examined microscopically and fungus was invariably demonstrated in all cases.

It is very interesting how the same fungus recovered in all the cases produced such a large variety of primary lesions. A large number of the cases began as a tiny red papule which gradually became larger in size with fine scales on the surface. In three cases the primary lesion began as one vesicle the size of a pin head, which rapidly increased in number and eventually acquired a circinate appearance. In a few cases, the initial lesion was a small patch the size of  $\frac{1}{2}$ -1cm. the same colour as the skin, covered with branny scales that were studded with spores and mycelia. Other cases showed small patches of small papular lesions collected together in a circular or circinate plaques with central scaling. The commonest areas/

areas of predilection were the wrists and the distal half of the forearm, the hands, mainly the fingers, and occasionally the elbows and face.

Patients undergoing ward treatment for other skin diseases showed lesions different to those just described. The lesions were widespread all over the body, even on areas which were constantly covered with strips of Ichthyol, or tar paste. Acute inflammatory lesions of circinate vesicular or pustular plaques, papular or papulo-erosive and even eczematous lesions were also encountered. Papulo-squamous lesions as well as multiple kerions were met with in some cases. From all these lesions *Trichophyton mentagrophytes asteroides gypseum* was demonstrated and cultured.

This epidemic of ringworm due to *Trichophyton mentagrophytes asteroides gypseum* has been observed in an institution for the last two years at the time of writing. In spite of strict precautions to prevent the spread through the medium of the nursing staff, cases continued to occur, even though the incidence of these was reduced. The original source of infection and the exact mode of spread of this fungus is still a mystery.

The place of antiseptics and disinfectants in the control of such an epidemic was studied in a series of experiments employing fresh and old-standing cultures, and by this means some idea of the resistance and viability of the fungus was obtained. A thin suspension of fungus culture in saline was used, passed through cotton wool to remove clumped mycelial elements and to insure equal exposure of the fungus cells in the different/

different experiments. A culture control of every suspension prepared was made to insure the viability of the fungus used. It was also found that saline does no harm to the fungi.

I should point out, that fungi do not occur in nature in such a state, they are usually protected by layers of corneal cells, and under these conditions they are more resistant than in pure cultures.

Boiling killed the *Trichophyton asteroides gypseum* in suspension instantaneously. The fungus in suspension heated to 80°C for five minutes did not show any growth when inoculated in Sabouraud's medium, heating to 70°C for one minute did not kill the fungus. *Epidermophyton Kaufmann-Wolf* withstood higher degrees of temperature than the *Trichophyton gypseum*. It was subcultured after heating to 80°C for one minute, but did not survive at boiling point. Fungus cultures left at -5°C for one month grew on subculture in Sabouraud's medium.

Dessication under vacuum did not influence the viability of the fungus, but strangely enough subcultures made from old standing cultures whose media had gone dry did not show any growth. Dust and cloth inoculated with *Trichophyton asteroides gypseum* and left at room temperature for one month did not show any fungus growth.

Soap was found to have no fungicidal effect whatsoever. Fungi left in soap emulsions at different strengths for seven days, grew again on subculture. Sodium hydroxide incorporated in Sabouraud's medium at different dilutions and inoculated with 0.1 cc. of the fungus suspension showed inhibition only in the following tubes. See table No.12/

	1/50	1/100	1/150	1/200	1/300	1/400	1/5000
After 5 days incubation	-	-	-	+	++	++	++
After 9 days incubation	-	-	-	+	++	++	+++
After 14 days incubation	-	-	-	++	++	+++	+++

Table No. 12, Showing the inhibitory effect of NaOH on the growth of fungi in Sabouraud's bouillon.

To test the disinfectant and fungicidal power of the different disinfectants and antiseptics, the following procedure was followed:-

1- A thin suspension of *Trichophyton asteroides* gypseum was prepared in sterile water.

2- Six tubes containing 2 ccs. of each of the following:- Phenol, Lysol, Antiseptol, and Sodium hydroxide, in varying dilutions of 1/50-1/400, prepared with the fungus suspension.

3- Twenty four hours later 0.2 cc. of fluid from each tube was removed for culture in Sabouraud's bouillon. Similar inoculations from the same tubes were made three days and seven days after. Readings were made after ten days incubation. The results were as follows.

Table No. 13

1/50 1/100 1/150 1/200 1/300 1/400

Phenol

1 day after inoculation	-	-	++	++	+++	+++
3 days "	-	-	++	++	++	++
7 days "	-	-	+	+	++	++

Lysol

1 day after inoculation	-	-	+	++	++	+++
3 days "	-	-	+	++	+	++
7 days "	-	-	±	+	+	++

Antiseptol

1 day after inoculation	+	++	++	+++	+++	+++
3 days "	-	+	++	++	+++	+++
7 days "	-	+	+	++	++	++

NaOH

1 day after inoculation	+	++	++	+++	+++	+++
3 days after "	+	++	++	++	+++	+++
7 days "	+	++	++	++	+++	+++

The same procedure was repeated with different dilutions on the following:- Phenol, Lysol, Dettol, Antiseptol, Soap, Iodine, and Alcohol. Inoculations onto Sabouraud's bouillon was made 48 hrs. later, or otherwise the time is mentioned.

	1/100	1/125	1/150	1/175	1/200	1/225
<u>Phenol</u>						
After 48 hrs.	-	-	++	++	++	++
<u>Lysol</u>						
After 48 hrs.	-	-	-	++	++	++
<u>Dettol</u>						
After 48 hrs.	-	+	++	++	++	+++
<u>Soap</u>						
After 48 hrs.	++	++	+++	+++	+++	+++
	1/20	1/30	1/40	1/50	1/60	1/70
<u>Antiseptol</u>						
After 48 hrs.	-	-	-	+	+	+
	1/100	1/500	1/1000	1/1500	1/2000	1/2500
<u>Tinct. Iodi.Fort.</u>						
After 10 mins.	-	-	-	+	+	+
After 30 mins.	-	-	-	-	+	+
After 24 hrs.	-	-	-	-	+	+
	100%	90%	80%	70%	60%	50%
<u>Alcohol</u>						
After 30 mins.	-	-	-	-	±	+
After 24 hrs.	-	-	-	-	-	-

Table No. 14 Showing the effect of dilution of different disinfectants and fungicides in common use.

To exclude the possible spread of the epidemic by the pastes used for treatment, samples of ichthyol and tar pastes were inoculated with a living growth of trichophyton asteroides gypseum and after twenty four hours the paste was spread on pieces of lint and used for testing.

Six volunteers were tested, three with the tar paste and three with the ichthyol paste. The patches were left on the skin for thirty six hours. No fungus positive/

positive lesion was elicited in any of the volunteers.

The possibility of the presence of fungi in the air or dust where the epidemic was spreading was considered as a possible source of infection. In investigations carried out to support or discredit this hypothesis air sampling by a sieve sampler was undertaken. Approximately 20 cubic feet of air @ minute were passed over culture plates by means of the above mentioned apparatus.

Several plates were used and sampling was performed about 20-30 minutes after sweeping and dusting the floor. Sabouraud's culture medium adjusted to pH. 10.5 was used and plates were incubated for 24 hours and then left at room temperature. (See Figures No 25-28).

Whitish granular colonies very suggestive of *Trichophyton gypseum* colonies were picked up and subcultured on ordinary Sabouraud's medium. Microscopic examination of these colonies failed to show findings suggestive of *Trichophyton*s. Animal inoculations for testing the pathogenicity of these growths were made but no lesion was produced.

Considering these findings, one can conclude that soaps and antiseptics in the dilutions commonly used are not fungicidal enough. Contaminated clothes and bed sheets require boiling or steaming to insure thorough disinfection. Bath tubs, instruments etc. should be covered with antiseptics such as lysol, or dettol not in higher dilutions than 1:50 and in such cases twelve hours are necessary to insure thorough sterilisation. Tincture Iodi Mitis is sufficient to insure sterilisation of the skin. Soap may help in cleansing a contaminated area of skin by its detergent action, but it is not sufficient to kill the fungus.



DISCUSSION.

There are many ways in which a substance can affect the cells of the human skin. By far the most common is by the direct chemical action. There are certain substances which affect the organism in virtue of their physical properties as well as by their chemical action. Some, extract essential ingredients or disturb the normal nutrition of the tissues, and so, either excite a reaction or pave the way for external contacts or micro-organisms which are otherwise unable to produce noxious effects.

In the present state of our knowledge it can be said that the activity of drugs depends on a large variety of factors, involving at least two separate processes, namely a chemical action and a biological response to this reaction. According to Cushny (1947) this complex chemical reaction takes place between the drug and certain receptors in or on the surface of the cell, therefore if the action of a drug is due to chemical combination between it and the tissues, then substances of similar chemical structure will have similar action.

When a chemically active substance comes in contact with the skin a biological response takes place varying with the pharmacological properties of the substance as well as the physiological state of the tissues. Keeping these factors as constant as possible, individuals tend to show marked variability in their biological response to a given stimulus. A given concentration of a substance which will induce a given reaction in the majority/

majority of individuals will thus produce a more striking action in a few more sensitive individuals, and fail to act in some who are resistant. These biological variations in apparently normal individuals may be acquired or natural characteristics and are subject to wide fluctuations.

We can then take the majority of individuals as being normal reactors to the pharmacological action of the substance at a given concentration. Of the remaining minority, some are sensitive or idiosyncratic in that they react to a low concentration of the substance; the remainder are resistant or tolerant in that they show no reaction to the same substance. Idiosyncrasy and tolerance to these substances therefore depend greatly upon the nature of the substance, the concentration, and the physiological state of the tissues during the period of contact.

Percival (1933) tested a large number of individuals with eczematogenous substances and was able to produce the same type of eczema reaction with all the different substances and concluded that its intensity was to some extent proportional to the concentrations employed. He found that these substances fell into two groups. Group I, included Mercury salts and chrysarobine, and Group II, included picric acid, iodoform, and paraphenylenediamine.

Substances in group I in very low concentrations produced a visible reaction in only a small percentage of individuals, while in adequate concentrations they produced a reaction in 100% of individuals. The reactions produced by the low concentrations in the most intolerant individuals were identical with the reactions finally obtained in the most tolerant by merely increasing the concentration/

concentration of the substance applied. This showed therefore, that idiosyncrasy is only a relative term depending not only on the nature of the substance but also on its concentration.

Substances in group II while giving the same type of reaction as group I differed in that, by increasing the concentration, only a very slight increase in the number of positive reactors was obtained. Idiosyncrasy was therefore more obvious.

When chemical substances were first used by human beings it was soon recognised that some were stronger than others, and by trial and error and animal experiments the usual concentration and dosages now used were arrived at.

Idiosyncrasy seems to develop more readily towards certain substances than to others; the reason that not all people show this intolerance is because such toxic chemicals are not commonly handled, certainly not in high concentrations. Individuals presenting this type of reaction do so in virtue of their biological peculiarities.

The skins of children and of old people are less able to tolerate noxious substances than those of young adults. The female skin is said to be less resistant than that of the male, but even this is variable during pregnancy and menstruation. A dermographic individual is more susceptible to trauma, and an ichthyotic skin is less resistant to chemicals than that of a normal individual (Stokes). Moreover even in the same individual the resistance varies in different body areas, and a traumatised area reacts more readily to irritants than a sound area.

On this basis we can conclude that idiosyncrasy and tolerance are merely individual biological variations in cutaneous responses; and in this way we can explain why all housewives do not develop a reaction to soap, and why one particular housewife develops a reaction, or suffers an exacerbation of an established one following excessive use of alkaline detergents.

Critical interpretation of patch tests in such reactions without an allergic basis is necessary. A nurse might develop a toxic type of reaction on the hands from prolonged use of the usually harmless 0.1% solution of hydrarg. perchlor, and patch tests with 0.1% concentrations on her arm or back will fail to show a positive reaction; this fact will make us conclude that her trouble is not due to the perchloride lotion, whereas it is in fact responsible, by reason of its cumulative chemical action and not in virtue of its potential sensitising properties.

I myself when working in my private clinic made the following rather interesting observation. I developed a scaly fissure on the palmar surface of my left thumb. This had persisted for about five weeks before I began to pay much attention to it and to look for a possible cause. The localization and the shape of the lesion made me suspect an external contact irritant. Observing everything touched only with my left thumb I eventually found that every time I prepared a solution of Potassium Permanganate from a concentrated stock solution, I held the glass stopper with the ball of my thumb resting on the base, thus covering it with the solution. After that I always held the stopper between my right thumb and forefinger/

forefinger and avoided contact with the liquid as much as possible. In about 15 days my left thumb cleared up completely; in about three months, however, I noticed that my right thumb had started to fissure and show a similar appearance to that previously on my left thumb.

Let us not forget that the skin, like other bodily tissues, may have a tendency to accumulate certain chemicals and that a chemical in a non-toxic concentration applied repeatedly may produce a summation of effect, resulting in an apparent toxic response.

So far we have been dealing with the normal responses of the human skin to the various substances at different concentrations. I say the normal responses because it is apparent that such biological responses depend mainly on the degree of damage the substance has inflicted on the living cell. They are only abnormal in the sense that one individual reacts differently to the majority we accept as normals, and even these normal individuals may react abnormally by the mere increase in the concentration of the substance. This may also be the mechanism behind a large number of these toxic type of reactions which develop after prolonged and repeated contact, reactions which are not allergic in nature as shown by negative patch tests.

A study of the suspected chemicals in a group of individuals equally exposed helps greatly to exclude such a possibility especially when a new substance has recently been introduced in their work.

Prolonged and continuous friction and mild irritation also results in a type of toxic dermatitis showing/

showing scaling, fissuring and thickening of the skin. The superficial horny layer is dry and breaks down easily due to defective keratinisation. This picture is commonly encountered in housewives, labourers, and individuals with ichthyotic predisposition. Housewives are commonly seen with dry, scaly and fissured palms, labourers have dry rough hands with areas of hyperkeratosis. More localised affections are met with in a specialised group of workers who use some parts of their fingers or some part of their hand very constantly during work. For example, a worker who handles a screwdriver very frequently may develop a localised patch of imperfect keratinisation in the centre of his palm.

When the allergic state sets in, an altogether different course of events ensues. There is not only a different type of reaction (Von Pirquet) but also a specific change in the degree of sensitiveness towards a definite substance or a physical stimulus on the part of an individual or one or more of his tissues (Goldsmith 1936). This specific change and the altered capacity to react does not depend on the concentration of the substance as is the case with idiosyncrasy. The first contact or all the previous contacts, are all tolerated with impunity, but when the allergic state sets in, the lowest concentration or minute amounts are capable of demonstrating this intricate state of altered reaction.

In the present state of our knowledge we do not know how the allergic state commences nor the mechanism of the allergic phenomena. At the present time a great number of reactions are being indiscriminately attributed to/  
Results/

to the allergic state, and if we are to label every eczema or dermatitis as allergic we are no nearer to a solution of our problem.

First we should differentiate between allergy - an altered degree of sensitiveness, and idiosyncrasy - an individual variation in tolerance to certain substances. In the former a primary exposure to the substance or allied substances is necessary to produce the altered state. In the latter one school of thought requires the presence of a primary exposure, while another excludes the presence of primary exposure and attributes the state to some inborn biological peculiarity.

An idiosyncratic individual is not necessarily allergic, but an allergic individual is always idiosyncratic. A normal skin can be made intolerant to certain substances on different occasions and in different circumstances, and still does not present an altered reaction. For example, in a factory with a large number of workers handling morphine and allied products, there were only three cases suffering from an allergic contact of the eczematous type with positive patch tests. Twenty four other workers suffered from occasional lesions over the hands and face especially after prolonged exposure; patch tests were negative. This clearly shows that the first three cases had developed an alteration and increase in the degree of sensitivity to the morphine, and the 24 individuals had only developed an idiosyncrasy to the alkaloid. The rest of the employees numbering 230 with more or less similar risks of exposure were clear from any lesion throughout that period.

Despite/

Despite the fact that allergic reactions may show many different manifestations, the skin exhibits only a limited number of responses to a variety of stimuli. Thus, on one occasion almost any form of reaction may be produced by a given allergen upon an allergic tissue, while <sup>on</sup> another occasion the same type of tissue response may be elicited by stimuli not quite unrelated to specific sensitization. The best example of this, is the eczematous dermatitis showing similar tissue changes, but being on one occasion allergic, on another clearly nonallergic.

Certain conditions must be satisfied before we are justified in labelling a condition allergic. That eczema is in many instances allergic in the proper sense of the word i.e. due to acquired specific sensitization, is beyond dispute. There are, however, many other similar types of dermatitis which may resemble eczema but which do not fulfil the conditions of acquired specific alteration in the capacity to react.

A manifestation may be accepted as allergic when it can be conclusively demonstrated to be the result of a given agent or substance acting on a skin which has been specifically sensitised, and when it can be shown that the alteration in the capacity to react is the result of a previous exposure to the same, or to a closely related substance. In other words it is necessary to show that the causal agent:

1. was encountered at some previous time.
2. that the response at the subsequent reaction-eliciting encounter was different from that encountered at the first exposure.
3. that the demonstrated alteration was the result of a recent previous encounter.

The/



The incubation period between the first contact and the appearance of the altered state varies greatly in certain experimentally induced cases. This time falls between 6-20 days with wide variation in both directions. It can be concluded that the incubation period in these allergic contact cases, as well as that in many infectious diseases is in the main, if not entirely, due to the time required for the production of a specific alteration in the tissues of the host. This might hold true in some cases where sensitization is markedly demonstrated, and during the incubation period the altered reaction is established all over the skin surface. But how can we explain those cases in which the altered reaction becomes apparent 10-20 years after the first contact? Such cases are common in industry where workers may handle with impunity materials for periods up to twenty years before showing specific sensitisation. Certainly it cannot be presumed that twenty years is needed in certain cases to establish their sensitization.

In many cases it is extremely difficult or even impossible to determine whether the alteration in the capacity to react is the result of previous contacts or due to some adventitious factors and circumstances. Not uncommonly one encounters workers handling dyes, rubber or fur for many years without ill effect; suddenly on returning to work after a sore throat, rheumatic fever, malaria or accident they present an intolerance.

The specificity of the allergic state is widely accepted, and the allergic skin can distinguish very clearly the substance to which it is allergic even after/

after a lapse of many years.

At this point it is convenient to consider the relationship of allergic to non allergic eczema. It has already been mentioned that a skin sensitised to one substance appears to be specially prone to develop multiple sensitivities to others, which may be quite unrelated to the original. A further observation is that made by innumerable clinicians - that a specifically sensitised skin is more liable to develop nonspecific idiosyncrasy as typified by the toxic types of dermatitis.

Allergic contact type of dermatitis usually clears up completely after the removal of the exciting allergen. In certain cases one finds that abstinence and treatment is not enough to affect a cure and one begins to doubt the diagnosis. I think in such cases the epidermal cells have suffered extensive damage, by the previous contact, which delays greatly the normal regenerative power of the skin and in certain cases even the most bland applications become intolerable.

#### PATCH TESTS.

The patch test is a simple procedure. It aims at exposing the allergic skin to the suspected substance with a view to demonstrating an altered reaction. It is a well known fact that individuals allergic to Primula for example, would develop a rash after touching the primula leaves; and reactions may be obtained simply by rubbing the suspected allergen on a sound area of skin. Both of these methods are accepted as perfect examples of exposures demonstrating a hypersensitivity. On the other hand we still accept certain reactions as positive/

positive which require 24-48 hours exposure to the test substance.

We could easily interpret the results of these two methods by describing the skin as highly allergic or hypersensitive in the former and less sensitive or hypoallergic in the latter; but we cannot differentiate by this test an idiocyncratic individual who might also develop an eruption by the latter method. Patch tests, then, are only useful when they reproduce the exact conditions obtaining at the place of exposure. - The site of application of the test is also important in certain cases because the skin may not be equally sensitive to the same substance in every area at a given time, and so when employing patch tests in occupational dermatitis, the sites of previous eruptions must be tested before a substance can be exculpated.

In spite of the useful information provided by patch tests they are sometimes misleading, giving positive results in many cases with polyvalent sensitisation and negative results in cases in which the patch test does not reproduce the manifold conditions operative during the clinical exposure e.g. in cases where repeated exposures over long periods are necessary to produce the allergic reaction or other predisposing factors, such as sweat, friction and trauma, are operative.

We can conclude therefore that patch tests are of no value in dermatoses with no allergic background. They do not provide any evidence in toxic types of dermatitis, and unless they are employed in a manner which approximates to the natural exposure, their results/

results may be misleading.

#### POST-TRAUMATIC INFECTIVE ECZEMA.

In post-traumatic infective eczema we have two outstanding features "the trauma, and the infection". It is widely accepted that micro-organisms cannot establish a skin infection without a previous portal of entry incurred by trauma of any type.

Experimental inoculation with organisms recovered from these lesions often fails to reproduce exactly the mechanism which may have been operative in the production of the clinical disease. In contradistinction, these experiments differ greatly from those performed with non living allergens. In the case of the living organisms the causal organism however, brings about its effect when it continues to multiply, invade and disseminate its toxic products into the neighbouring structures. The results may also depend on the virulence, the rate of multiplication and the local defensive powers of the skin. These lesions tend to spread by an exogenous or endogenous process of autoinoculation, scratching undoubtedly subserves this autoinoculation.

Such autoinoculation and recurrence suggests an infectious process in a suitably differentiated skin. The lesions behave in a manner closely analagous to certain established pathological entities such as those of mycotic infections; but the break in chain of proofs that they are produced by certain micro-organisms lies in the failure to reproduce the lesions experimentally. Thus any definite conclusion as to the nature and mechanism of development is impossible.

Considering/

Considering nummular eczema - circumscribed coin-shaped papulo-vesicular plaques, growing by peripheral extension mainly over the extensor surfaces of the hands and forearms, with a tendency to exacerbations and chronicity - many causal factors have been postulated. Some authors regard it as a distinct and separate entity as no special cause has been conclusively demonstrated. A number of observers believe that it is based on some as yet unelucidated form of skin allergy possibly related to herpes i.e. a virus, or a fixed "-id" eruption Sulzberger (1940). Others attribute the condition to focal sepsis, nervous instability, food allergy, vitamin deficiency, and even to excess of salt. (1947) Van Studdiford et al./associate it with diminished gonadal function which precipitates a hyperactive personality resulting in a minor skin disturbance which directs the attention of the personality to the skin.

It is worth noting with interest that most of these workers observed that trauma, or exposure to irritating substances preceded the lesions. Some noted also that the condition followed other forms of eczema and various unrelated skin diseases. Moreover I do not think that anyone doubts that an indistinct patch of eczema, irrespective of its primary cause, can become transformed into a marginate plaque. Furthermore an eczematous condition characterised by sharp borders may be associated with any dermatitis. Micro-organisms of the normal skin flora or from the outside are capable of producing an inflammatory process whenever conditions are suitable.

In such nummular lesions staphylococci and other organisms/

organisms may be found in abundance on culture and by direct examination. There is no reason for refusing to accept the rôle of organisms in the production of the lesions. To consider them entirely unrelated because they are also found among the resident flora of the normal unbroken skin is illogical. After all we always accept an inflammatory lesion as mycotic whenever we succeed in demonstrating fungi in it.

All victims of this affection are not irritable with hyperkinetic nervous system. Some individuals are of the neurasthenic type. In some cases reported, focal sepsis was demonstrated, in others exacerbations followed attacks of influenza, or sorethroat. It is not clear how these factors precipitate such localized stubborn lesions. It may well be that nervous instability, septic foci or any constitutional disturbance influence the course and behaviour of an established nummular eczema just as they <sup>may</sup> influence any other skin disturbance. I find it difficult to accept such fanciful explanations as those of the psychosomatists who invoke the skin as a safety valve through which the high tension personality seeks relief from its excess of nervous energy.

#### ENDOGENOUS ECZEMA.

Considerable difference of opinion exists relative to the mechanism of production of the various lesions which have a metabolic and constitutional background, and few undisputed facts are available. These cases are difficult to recognise even after long experience, and efforts to establish organic lesions as the cause of their various manifestations have been unavailing.

Stokes/

Stokes and Pillsbury suggested that the gastrointestinal tract may be the source of a histamine-like substance that in turn could be the cause of the urticaria. Becker mentions a neurogenic dyshidrosis and describes these patients as born with a nervous system different from their neighbours and points out that that they have more than the normal share of ambition. Although allergy to food has been suspected in certain of my cases, like any other functional mechanism it is a complicated response which may vary from time to time, depending on very many factors extrinsic or intrinsic. New sensitivities may also develop and complicate the original picture. There is much to criticise in reports Rowe (1947), which mention cases of vesicular eruptions of the fingers and palms claiming that as long as pork, bread cheese, chocolates and lemonade are eliminated completely from the diet the condition remains quiescent. If these isolated lesions are attributed to proteins or carbohydrates in the food or to some of their by-products, there seems to be no good reason why the involvement is not more generalised. Carbohydrate in diet and water intake influence greatly the course of certain eczematous lesions but it cannot be maintained that they are essential factors in causation. I am inclined to believe that a local factor is much more important than the ingestion of pork or any other food in these patients.

It is a frequent occurrence that established eczematous eruptions e.g. after a traumatic injury, a contact or an infective process, undergo remissions and exacerbations following psychical or emotional instability/

instability, especially among highly-strung and temperamental individuals. Neurogenic and psychogenic factors can assist in maintaining an allergic background, as in neurodermitic phase of the diathetic state or affections affecting the skin associated with infection allergies. Great care must be exercised before attributing eczema lesions to food allergies or nervous factors. The inconvenience and expense suffered in attempts to rectify such factors is unjustifiable until other more common causes have been eliminated.

- Applying Koch's postulates we find that:-
1. Fungi have been constantly recovered from such lesions on the feet.
  2. They have been grown on culture media.
  3. The same clinical picture has been reproduced in human beings following inoculation with the fungus.

These facts permit us to accept the "Dermatophytes" as pathogens and, as the direct causative agents of at least some of the vesicular eruptions of the feet from which they have been isolated repeatedly.

Accepting these facts, the next problem requiring explanation is: "Does the eruption of the hands bear any relation to the mycotic infection of the feet?" That it does so is still doubted by some dermatologists, and before I consider the question in detail I would like to discuss Strickland's conception of the dermatophytes (1911). I do not intend to criticize here Strickland's concept of the aetiology of "Tinea"; not because it has/



DERMATOPHYTIDS.

The feet and hands are frequently affected with a vesicular type of eruption while the rest of the body surface is perfectly clear. Leaving classical terminology aside and accepting these eruptions as merely "vesicular eruptions of the hands and feet"; the question arises "Can Dermatophytes produce a condition which could be described as a discrete vesicular or dyshidrosiform eruption on the hands and feet?" The answer is in the affirmative. This answer is not based only on the mere recovery of fungi from these vesicles but also on experimental findings..

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has met with the disapproval of most dermatologists, but because if I can prove that the dermatophytes can produce such vesicular manifestations I have indirectly refuted Benedek's whole theory.

I agree with Benedek that no one, including Bloch and his pupils, has so far proved that these fungi circulate in the blood at the time of the sudden appearance of the -id eruption, nor that the fungi themselves produce these lesions; despite the fact that a few positive findings have been recorded. That fungi produce the primary lesions on the feet is however, a well established fact.

It is not a matter of sheer coincidence that forty-six cases of vesicular eruptions of the hands were encountered among a series of 51 cases of Dermato-phytosis of the feet. Moreover, the striking similarity of these cases as regards the primary infection, the eruptive character of the -ids, their distribution and prevalence, and response to treatment of the primary focus, constitutes a disease entity of its own.

In most of the cases the primary lesion begins on one foot and not infrequently spreads to the other foot later. After an interval an acute vesicular eruption appears on both hands simultaneously, being mostly obvious over the sides of the fingers and palms and evolving as successive crops. In some cases this -id eruption develops after a trichophytin injection, or on commencing treatment of the primary lesion. In some cases secondary infection of the primary lesion precipitates the -id reaction. In every case fungi were demonstrated in the vesicular lesion on the feet.

Severe dermatophytosis of the feet is almost invariably accompanied by the development of -id eruption on the hands, but the severity and the character of the eruption do not depend on the severity of the primary lesion. The -id reaction is an expression of an internal process initiated by the mycotic infection. It is always accompanied by a state of hypersensitivity demonstrable by the intracutaneous trichophytin test.

In uncomplicated cases the -id eruption disappears spontaneously after treatment of the primary lesion; recurrences do not occur if the primary lesion has been thoroughly checked. Sometimes one finds that eczematization or infection of the primary lesion modify the character of the -id eruption which become more eczematous and recurrent. It is occasionally found that dermatophytosis with hypersensitive reactions ushers in a state of intolerance to other substances that were without ill effect before the mycotic process; affected areas show an increased non-specific reaction to external contacts. It should be pointed out that these secondary complications are not of mycotic origin, and appear totally different from the dermatophytid reaction. These eruptions, especially when appearing over the feet mimic the characters and distribution of mycotic lesions with which they are often confused. Distinction depends on failure to demonstrate fungi in the lesions.

The few but convincing human experiments reported in the text establish, without doubt, that fungi are the causative organisms of these eruptions and are capable of producing similar lesions when applied experimentally. Moreover, the production of the -id reaction/

reaction in the author's experiment provides convincing evidence of the relationship between mycotic infections and -id reactions.

The demonstration in the fluid of the vesicular -id eruption of antibodies, by the passive transfer method, establishes another proof that the -id eruption on the hands bears a relation to the mycotic process on the feet.

Having established the relationship between the -id eruption on the hands and the primary mycotic process on the feet, the next point to consider is the mechanism of production and the peculiar localisation of the reaction which is limited to the hands and feet.

The repeated negative findings in the examinations of these eruptions, though conflicting with the findings of many authors, confirm the belief that this reaction is the expression of an internal process. The suddenness of onset, the bilateral involvement and the peculiar distribution rule out the possibility that the -id eruption is produced by direct autoinoculation. It is unlikely that fungi could grow so uniformly and in so many widely separated lesions. The abrupt appearance of these lesions on both hands, and their rapid involution (20-30 days) in the absence of local treatment renders such a possibility even more unlikely.

Certain dermatologists believe that the -id eruption on the hands is due to direct contact with the primary lesion. Patients, they say, frequently touch the feet with their hands and owing to the presence of generalised hypersensitivity of the skin such an exposure acts as an external contact irritant and excites an/

an allergic inflammatory reaction. This is hardly possible because of the uniformity and distribution of the -id eruption. Moreover, patients report on account of the eruptions of the hands without any previous complaint regarding the feet; frequently the primary lesion does not show any denuded surface. If fungi from these lesions are as ubiquitous as is commonly believed, there is no reason why such lesions should not develop elsewhere on body areas which are equally hypersensitive.

From the primary infection on the feet toxic products produced by the fungi in the inflammatory process may gain entrance to the circulation. The chances of fungi themselves gaining access to the circulation is not beyond possibility, though this has not been confirmed by our blood cultures, and only three cases of positive findings have been recorded in the literature. Moreover, animal experiments have shown that after four hours, fungi were not demonstrable in the blood of animals injected with 1cc. of a heavy suspension of fungus culture. Blood is not a good medium for the growth of fungi, as it has been found to possess a fungicidal or phagocytic action in vitro.<sup>‡</sup> Thus there is a very limited opportunity for the fungi to survive in the blood stream.

Supporters of the theory that the -id eruption is produced by the deposition of fungi in the different sites of the lesions claim that fungi have an affinity for the skin of the hands and feet, and owing to the great/

‡ Studies are in progress to test the fungustatic power of blood.

great hypersensitivity of the skin these organisms are quickly destroyed. This they state explains the negative findings of the -id eruptions.

In considering this theory all attempts to isolate fungi from the very earliest lesions were unsuccessful, as were the blood cultures taken at the very early stage of the eruption. It could be presumed then that if fungi are ever able to gain access into the blood stream they do so only in the form of arthrospores which are carried away by the osmotic properties of the vascular lymphatic channels; stray mycelial hyphae are not easily detached from the parent element. Even if some were to gain access to the systemic circulation, their survival-time would be strictly limited. (See above). For a number of spores then, to get into the circulation and settle in the hands in such a bilateral and discrete manner they would require to traverse the capillaries of the skin in order to reach the epidermis and to excite such a vesicular eruption. It is hard to understand how these fungi could produce such a reaction without invading and multiplying in the epidermal layers. Even if they could do so, why should all the -id eruptions reported be negative for fungi both microscopically and culturally? How could we explain the action of a trichophytin injection in producing an -id eruption in twenty four hours, or an -id reaction developing soon after treatment of the primary lesion is commenced? It follows that an -id reaction could not develop in superficially situated mycotic lesions, where there is no ready access to the bloodstream.

It would therefore appear that fungus products  
or/

or products of inflammation are absorbed into the circulation from the primary lesion and are brought via the blood stream to the hands and feet. This strict localisation to these parts of the body reminds us of a combined peculiarity of the hands and feet to which these products show an affinity. The characteristic peculiarity common to both palms and soles is the abundance of sweat glands in a comparatively thick stratum corneum. These products of inflammation in common with other toxic substances and chemicals could be easily excreted by the sweat apparatus. Normally the body endeavours to excrete the byproducts of internal metabolism in this way. When passing through a hypersensitive skin an allergic reaction might well be excited.

It could very well be that chemical irritants, foods, or endogenous products absorbed into the circulation are excreted through the sweat apparatus thus exciting the same pattern of reaction. Possibly most of the cases grouped under "Undetermined Cases" are produced by the same mechanism i.e. an -id reaction of a sensitised skin to toxic products excreted in the sweat.

Histologically all of these vesicular lesions present similar findings. See figures . . . . .  
No pathological changes in the sweat glands or ducts are to be expected because this anomaly is not related in any way to the sweat apparatus.

While the above theory is not yet susceptible of direct proof, it would appear to be a more satisfactory explanation of the established facts than many of these propounded in the literature.

SUMMARY.

1- 1364 cases of Eczematoid dermatoses of the hands have been studied and classified under six groups  
1-Post-traumatic Infective Eczema, 2- Toxic Contact Dermatitis, 3- Allergic Contact Eczema, 4- Infective Eczema, 5- Endogenous Eczema, 6- -Id. eruptions.

2- Toxic Contact Dermatitis of housewives, Mechanical workers, and individuals in contact with chemicals have been studied.

3- The role of the different factors in the production of the eczematoid dermatoses have been considered, and the mechanism of the development of the different types of dermatoses have been presented.

4- 122 cases of Vesicular Eruption of the Hands have been studied in detail, including 52 cases of Dermatophytosis and 46 cases of Dermatophytids of the hands.

5- 5 Human inoculations and 42 animal experiments were performed for the study of immunity and sensitisation of the dermatophytes.

6- Observations presented on the production and characters of the Dermatophytids.

7-Observations presented on the laboratory methods and cultures of Dermatophytes.

8- A new method for the preparation of Trichophytin is presented.

9- The immunological reactions to the dermatophytes were studied.

10- The study of Immunity and Sensitisation to the Dermatophytes in animals and human beings.



11- The epidemiology and viability of dermatophytes including observations on an epidemic of fungus infection caused by the " Trichophyton Asteroides Gypseum ".

12- The establishment of the relationship between the dermatophytids on the hands and the primary dermatophytosis on some other parts of the body.

13- The mechanism of production of the -id reaction have been postulated.

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