

HILDRICH

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FUNGUS DISEASES

AN

TREATMENT

FUNGUS DISEASES AND THEIR TREATMENT

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FIRST EDITION

AND THEIR TREATMENT

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PREFACE

The role of fungi in diseases of man was until recently considered to be largely confined to superficial infections with their diagnosis and management being the concern of a limited number of physicians. An increasing interest in fungal diseases has revealed a significant number of patients suffering from active systemic fungal disease and a surprisingly high incidence of healthy individuals who show evidence of previous systemic fungal infection. The growing concern with the incidence of mycotic diseases has, in addition, been stimulated by the increasingly important pathogenic role being played by common saprophytic fungi which can cause serious clinical infection under suitable environmental conditions. As a result of the recognition of the significant role being played by fungi in the production of disease, a continuing search for specific chemotherapeutic agents has been made and thus far has provided therapeutically effective antifungal antibiotics for use in treating both topical and systemic infections. The protean clinical picture presented by fungal infections and the availability of effective therapeutic agents have made it important for clinicians to be familiar with the nature of fungal diseases and their treatment.

As a wealth of information on the clinical aspects of fungal diseases and their management is scattered widely throughout the world literature, it seemed appropriate to correlate the pertinent definitive data in a single text for the benefit of practicing physicians concerned with the diagnosis and management of fungal diseases as well as for the benefit of those interested in research. It is our purpose to present the relevant clinical data on the fungal diseases of man as well as to provide information on the means by which they are treated.

The text also outlines the physical, chemical, toxicologic and pharmacologic properties of the commonly utilized antifungal antibiotics so that these unique agents may be used to their best advantage. The morphologic characteristics of fungi mentioned, however, have been deliberately excluded from the text as these data are readily available in adequate texts dealing with microbiology and medical mycology.

We are indebted to many colleagues and associates who have provided critical evaluation and suggestions during the preparation of the book and especially to: Crawford Brown, M.D., M. L. Furcolow, M.D., John Groel, M.D., Gerbert Rebell, M.S., Frank J. Roth, Jr., Ph.D., and W. A. Wynn, M.D. In particular, we acknowledge the assistance of Mrs. Margaret Schenck, Mrs. Barbara Tulare and Mrs. Nancy Fischer in the preparation of the manuscript. We thank those who kindly furnished illustrative material, and have indicated these sources in the appropriate captions. Mr. William Atkinson and the Department of Medical Photography of the University of Miami were of inestimable help in preparing the bulk of the illustrations.

G. H-S.
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PART ONE

MYCOTIC DISEASES AND THEIR MANAGEMENT

SECTION I

Superficial Mycoses and Corynebacterial Infections

TINEA VERSICOLOR (PITYRIASIS VERSICOLOR)

ABSTRACT

Tinea versicolor is a commonly occurring superficial fungus infection characterized by yellow to brown patches or continuous sheets of scaling over the trunk, less frequently on the neck and face. Under Wood's light, the lesions may appear a golden yellow color. The disease is generally symptomless and presents mainly a cosmetic problem.

Genetic susceptibility and high endogenous or administered plasma cortisol levels act as predisposing factors. The disease is due to *Malassezia furfur*, which appears in the scales as short hyphal elements and clusters of spores. Culture of the scales on special media has yielded a growth of *Pityrosporum orbiculare*, which is by some considered to be identical with *M. furfur*.

Numerous preparations have been successfully used in treating this disease, but the condition has a marked tendency to recur. Selenium sulfide shampoo, Whitfield's ointment and Whitfield's alcoholic solution are the preparations in common use.

INCIDENCE

Tinea versicolor is a superficial fungus infection of the skin, seen in all parts of the world. While the disease is extremely common in tropical and subtropical climates and affects a high proportion of the population of Central and South America as well as Africa, southeast Asia and India, it forms only about 5 per cent of the total incidence of fungus infections in more temperate zones (Stein, 1951). The condition is seen predominantly in young and middle-aged adults, is uncommon in children and rare in the elderly. In a recent series of 47 patients, 30, or nearly two-thirds, belonged to the 20 to 40 age group (Burke, 1961). The sexes are about equally affected. The disease is common in Negroes.

ETIOLOGY

Certain predisposing factors have been considered to play a part in the development of tinea versicolor. Poor hygiene, a marked tendency to sweating,

malnutrition, the wearing of woolen undergarments and tuberculosis have been implicated by most of the early clinicians. Burke (1961), in a careful investigation of the susceptibility factors in this disease, found no evidence that tinea versicolor patients as a group showed abnormally high sweating tendencies, but did find that about one-third of patients in her series had either more serious diseases or altered physiology due to pregnancy at the time tinea versicolor made its appearance. She also found that genetic factors seemed to play a definite role in a significant proportion of the patients. Not a single proved instance of paternal transference of susceptibility was noted, although 17 per cent of the patients showed genetic predisposition to tinea versicolor on the maternal side.

High endogenous or administered plasma cortisol levels were also found to act as a predisposing factor in the development of tinea versicolor. This was confirmed by Boardman and Malkinson (1961), who investigated a group of individuals suffering from chronic ulcerative colitis treated with ACTH and corticosteroids in doses so large that Cushingoid changes developed. Tinea versicolor appeared in many patients so treated. In experimental infection studies (Burke, 1961), clinical tinea versicolor was produced in one, possibly two, cases of Cushing's syndrome, in one patient on steroid therapy and in one individual with nutritional deficiency. Subclinical tinea versicolor was produced in two chronically ill patients on steroid therapy. With cessation of steroid therapy, and after bilateral adrenalectomy in one patient with Cushing's syndrome, *M. furfur* disappeared without therapy.

PATHOLOGY

The disease is presumed to be due to the presence of a fungus, *M. furfur*, which is seen microscopically in the horny layer of the skin. The fungus does not penetrate into the deeper layers, and the diseased scales can be easily scraped off the surface of the

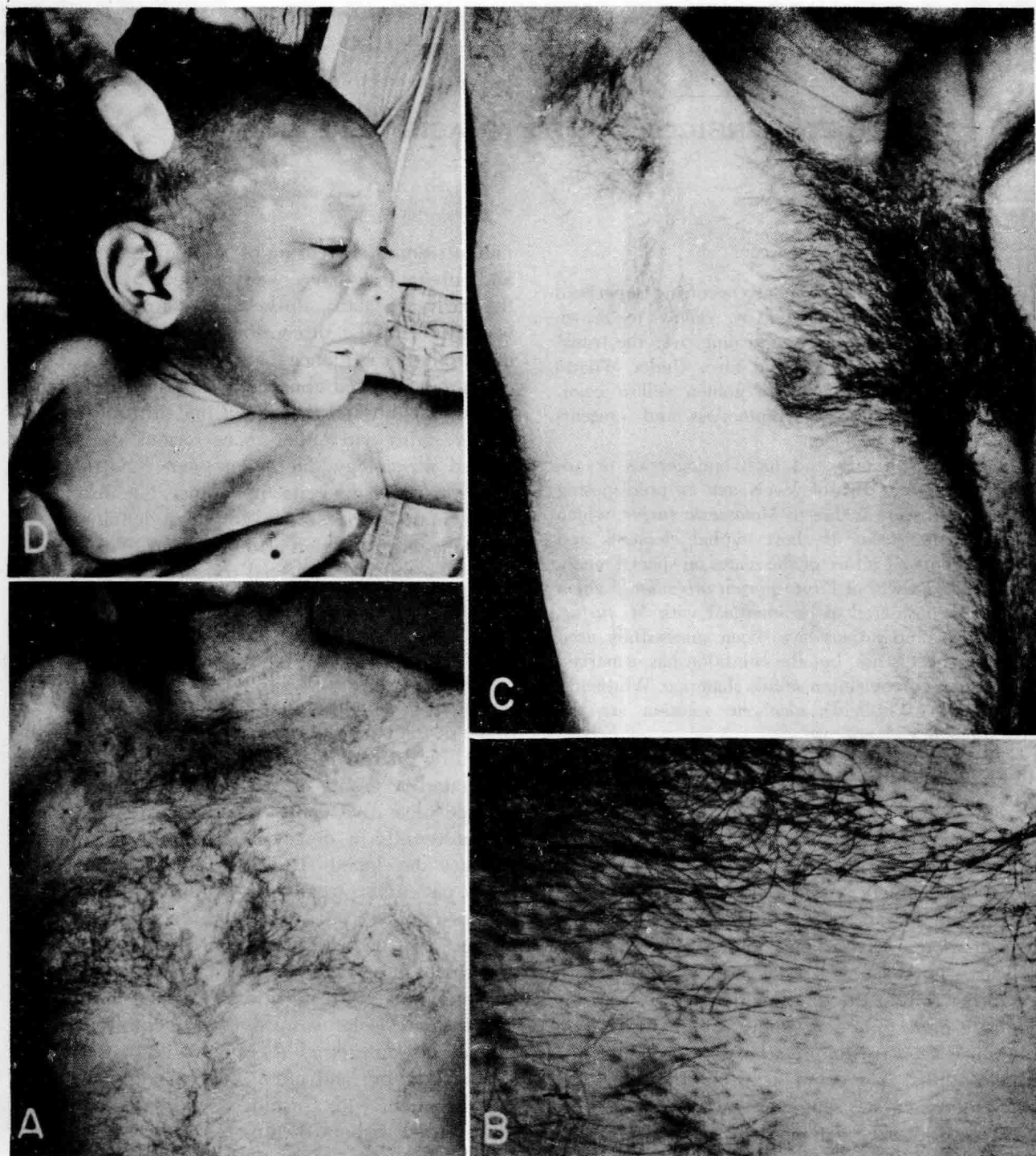


FIGURE 1.1

Tinea versicolor. A, B: A white patient with yellowish perifollicular and confluent lesions. C: White patient with lesions solidly confluent and hyperpigmented on the upper trunk. D: Negro infant with hypogammaglobulinemia with depigmented lesions of face and hyperpigmented lesions over right shoulder and upper trunk. The presence of depigmented and hyperpigmented lesions in the same patient is often helpful in diagnosis.

skin with the fingernail, a scalpel or any sharp object. The underlying skin appears to be normal and does not show a tendency to bleeding; there is no histologic evidence of inflammatory changes in the dermis.

Examination of the scales in potassium hydroxide shows the typical organisms: short, rather thick hyphal elements of various shapes and sizes, sometimes straight, but more often showing a wavy contour and irregular thickness, some with shapes resembling an S or a V. Round spores are the second constant element found in the scales. These are usually arranged in grapelike clusters. The spores vary in diameter and some have protruding budlike structures. Keddie *et al.* (1961) describe direct staining of vinyl plastic tape strippings of epidermal scales, using Gram, periodic acid-Schiff, Giemsa and acridine orange staining technics. A simpler technic has been described by Goldschmidt and Kligman (1961) employing adhesive-coated glass slides.

While the typical structures appear in scales from the lesions with great regularity and the microscopic examination of scales is diagnostically reliable, cultural attempts, though numerous, have been less successful. Panja (1946) discovered that by adding various oils to his culture medium, a great increase in the growth of fungi could be achieved, and he was able to isolate oval, yeastlike and mycelium-producing elements. Gordon (1951), using agar medium overlaid with oils, succeeded in culturing a series of lipophilic yeastlike organisms from lesions of tinea versicolor. In a high percentage of cases he also recovered a spherical organism, exacting in its nutritive requirements, which he named *P. orbiculare*. This organism was also cultured from 2 of 8 apparently normal skins. Gordon's attempts at experimental inoculation of human beings and animals with cultures of *P. orbiculare* failed to produce tinea versicolor. More recently, Burke (1961) has presented evidence pointing to a possible relationship between *M. furfur* and *P. orbiculare*. Sternberg and Keddie (1961) have demonstrated by immunofluorescence studies a common antigen between *P. orbiculare* and *M. furfur*. More work, however, will have to be done before the identity of the two organisms can be definitely established.

CLINICAL FEATURES

The disease is characterized by yellowish to dark brown patches or continuous sheets of scaling over

the chest and abdomen. The sternal and interscapular regions are most commonly affected; the shoulders, neck and face are less often involved. The scalp may occasionally be affected, and the lesions may simulate those of seborrheic dermatitis. Scaling may be obvious or it may become apparent only after scratching the surface with a fingernail or some other sharp object. Rubbing the suspected area with a wisp of cotton wool soaked in ether helps to make minimal degrees of scaling become more obvious.

As the name "versicolor" implies, the color of the patches is not always uniform but may vary. The patches are usually café au lait brown, but may be yellow to brown, dark, very pale, or of a reddish hue. Pityriasis versicolor alba (achromia parasitica) is a variant of the disease in which the affected patches appear white against the surrounding skin. It has been suggested that this appearance is due to the fungus-affected areas of skin filtering out ultraviolet rays and thus preventing normal pigmentation. As, however, this form of tinea versicolor may occur without any history of exposure to the sun, it is more likely that the fungus may have a direct effect on the mechanism of pigmentation of the skin. Jelliffe and Jacobson (1954) describe blotchy depigmentation of the groin, perineum, buttocks and face associated with tinea versicolor in Negro infants in Nigeria and Jamaica.

Occasionally, papular lesions may be present. These are usually around a follicular opening (Burke, 1961). The perifollicular location of the lesions of tinea versicolor suggests a relationship between the fungus and the sebaceous discharge from the follicles.

Wood's light may be of help in the diagnosis of tinea versicolor. The affected areas may show a yellowish or whitish fluorescence or appear a yellowish brown or bronzy color under this light. Lesions in areas exposed to the sun may not exhibit fluorescence.

The occurrence of tinea versicolor and erythrasma in the same patient has been recorded (Nikolowski and Stähle, 1949) and is said to be a relatively common combination. In the recorded case, the two conditions existed in adjacent patches and both erythrasma and tinea versicolor lesions were found in the same axilla. The patient was subject to marked sweating. Pityriasis versicolor and erythrasma were also seen in 3 patients by Sarkany (1961).

Tinea versicolor is usually symptomless, although mild itching may be a complaint. Advice is usually sought because of the embarrassment caused to the

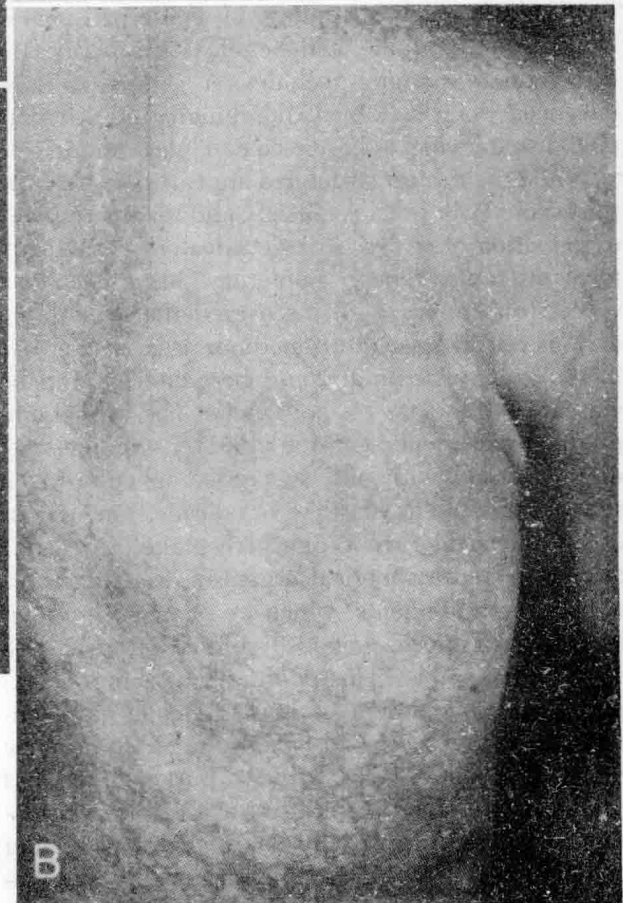
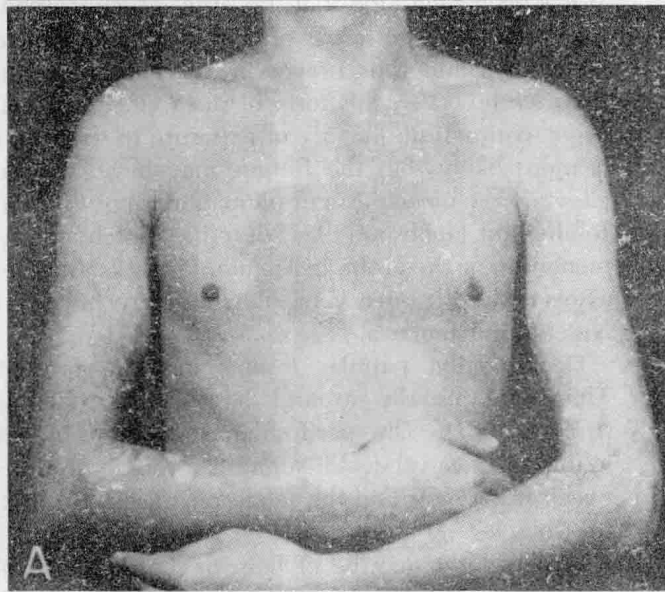
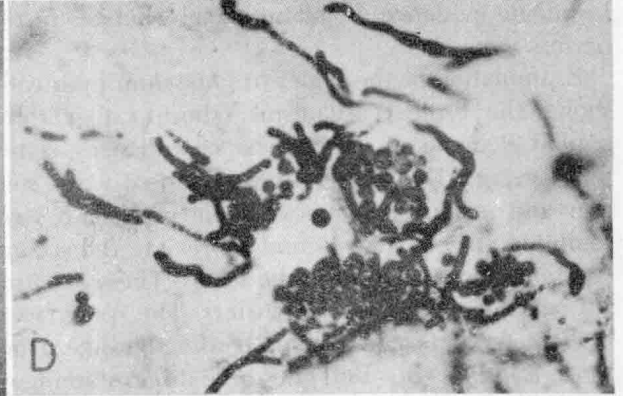
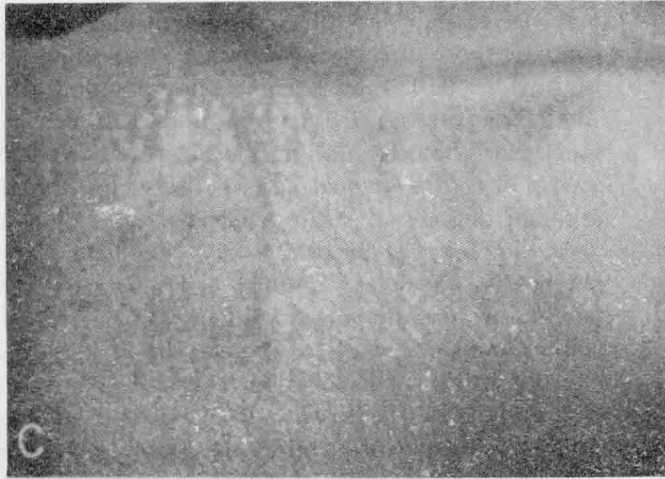


FIGURE 1.2

Tinea versicolor. A, B: White patients who demonstrate the typical small depigmented macules which often become confluent in areas over the upper trunk and arms. C: Slightly scaling and perifollicular lesions over the clavicle in a Negro. D: Photomicrograph of the organisms in scales; both round, yeastlike and hyphal forms are present. Gram's stain $\times 1000$, before 30% reduction. (A and B, courtesy London Institute of Dermatology.)

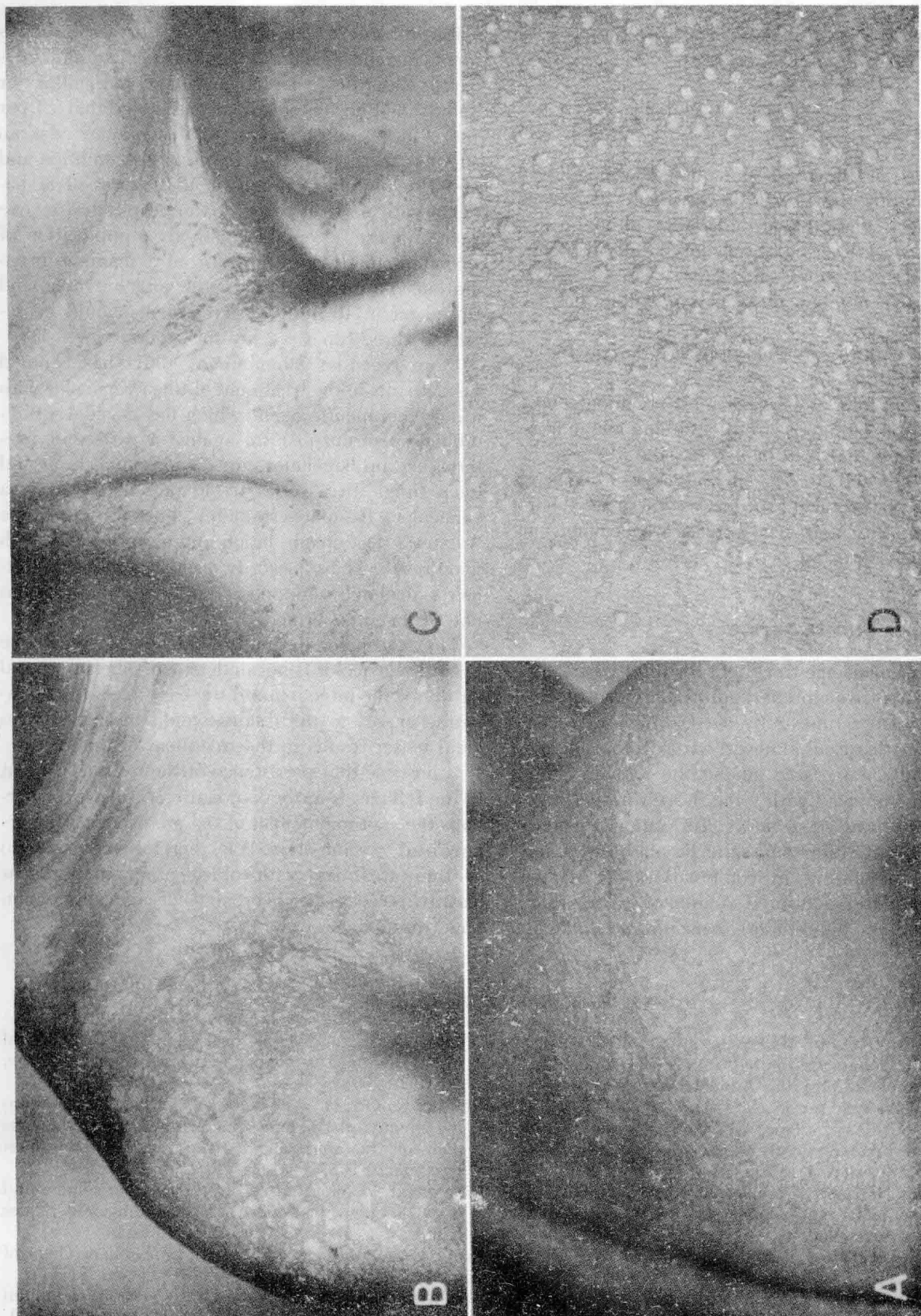


FIGURE 1.3

Tinea versicolor in Negro skin. A, B: Small, barely scaling depigmented macules. **C:** The less common, elevated hyperpigmented form. **D:** Close-up to demonstrate the perifollicular localization of the process in early lesions.

patient by the lesions, which may give the appearance of dirt to the lay observer.

DIAGNOSIS

Diagnosis is based on the clinical appearances and the finding of *M. furfur* in the scales. Potassium hydroxide preparations are adequate, although imprint slides, as described by Goldschmidt and Kligman (1961), are more satisfactory. These can be stained in a number of ways, including Gram's method.

Routine culture confirmation is not practicable at the present time.

Tinea versicolor is perhaps most commonly misdiagnosed as vitiligo. Careful examination, microscopic examination of the scales, and the use of Wood's light should help in diagnosis. Chloasma and other pigmentary disorders, erythrasma, seborrheic dermatitis, and even pityriasis rosea may at times cause confusion.

TREATMENT AND PROGNOSIS

There is no specific treatment for tinea versicolor. Although numerous preparations have been recommended, none is uniformly successful, and recurrence of the disease is almost the rule. Robinson and Yaffe (1956) enumerated among the remedies that have been employed with some success in the treatment of pityriasis versicolor, sulfur, salicylic acid, a combination of sulfur and salicylic acid, resorcinol (resorcin) alone and in combination with other drugs, β -naphthol, saturated solution of sodium thiosulfate (sodium hyposulfite), benzoic and salicylic

acid ointment, tincture of iodine, chrysarobin ointment, mercury bichloride, sulfuric acid, mild mercurous chloride (calomel) ointment, pyrogallol, tar and turpentine. These authors suggested that a 1 per cent solution of selenium sulfide ointment was an effective method of treatment for this condition and noted involution of lesions in their series of 28 patients with no recurrence of the eruption after one year. A more acceptable method of application of selenium sulfide is in the form of a shampoo preparation. This is applied to the affected area and rinsed off in 10 minutes. Treatment should be repeated three times weekly for several weeks.

More recently, Zimmerman (1961) has claimed good results in the treatment of tinea versicolor with a new therapeutic agent which has a wide antimicrobial spectrum *in vitro* against a variety of bacteria, certain flagellates, and various superficial and deep fungi. In a series of 40 patients with tinea versicolor, 9-aminoacridinium 4-hexylresorcinolate was used as a cream, lotion and aerosol spray with good result. The superiority of this agent over Whitfield's alcoholic solution or Whitfield's ointment has not yet been confirmed.

The reason for the high incidence of recurrence in tinea versicolor is not understood. The superficial nature of the infection and the easy access of therapeutic agents to the lesions would be expected to yield better results in the treatment of this disease. It is possible that persistence of the causative agent in the follicles is a frequent cause of relapse, or perhaps the continued effect of the predisposing factors may lead to reinfection. It is, therefore, advisable to continue treatment with topical preparations for at least two weeks after overt signs of clinical infection have disappeared.

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