The Wild Fire (Pemphigus Foliaceus) of Brazil

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THE WILD FIRE (PEMPHIGUS FOLIAEUS) OF BRAZIL

One of the reports attracting most attention at the X Pan American Sanitary Conference was that on virus diseases, prepared by Dr. G. Travassos and presented by the Brazilian delegation. Of special interest was the paragraph dealing with the form of pemphigus known in Brazil by the name of fogo selvagem, or wild fire, in which it was stated that the etiology has been linked with a filterable virus found in the blood of patients (Lindenberg). While it has not yet been possible to verify this thesis, much interesting information has been collected by Brazilian observers in the last two decades. The problem is sufficiently important for the State of São Paulo to have established a special Service and hospital ("Adhemar de Barros" Institute) for study of the disease, and the epidemiological picture of its course in Brazil appears to afford a basis for revision of the accepted concepts in regard to it.

Early writers stated that pemphigus foliaceus was "neither epidemic nor contagious." Others have ignored its existence insofar as any manifestations peculiar to the tropics are concerned. The cause has been attributed to toxins (said by Ormsby to be the most popular theory), to neuropathic influences, and to the Bacillus pyocyaneus (Hazen). Dermatologists apparently agree that, whatever its origin, the condition is rare.

The Brazilian experience contradicts a number of these views. First, all Brazilian authors agree on the contagiousness of fogo selvagem. Second, the disease is far from rare, as is shown by the fact that the São Paulo Service of Pénfigo Foliáceo (created in September, 1938) had, by June 6, 1941, 500 cases registered, of which from 15 to 20% had proven fatal. The "Adhemar de Barros" Institute, inaugurated September, 1940, had by June of the following year hospitalized 117 cases. Orsini de Castro reported in 1927 that in 15 years, 70 cases of pemphigus foliaceus had been registered in Belo Horizonte (200,000 inhabitants); another figure is 108 in 15 years. In 1937, Vieira reported that in São

1 "Actas X Conferencia Sanitaria Panamericana," 1938, p. 103.
5 Manson describes a tropical "pemphigus contagious" which does not seem to resemble the pemphigus foliaceus of Brazil, and does not mention the latter (Manson-Bahr, P.: "Manson's Tropical Diseases," 10th ed., 1936, p. 532); Still refers only to Manson's "pemphigus contagious," classing it as Impetigo (Strong, R. P.: "Still's Diagnosis, Prevention and Treatment of Tropical Diseases," Blakiston, 1942, p. 1602.)
7 Vieira, Note 3.
8 Lindenberg, Note 2.
"Adhemar de Barros" Institute (Hospital for Pemphigus Foliaceus Cases—first of its kind), São Paulo, Brazil. (Photograph courtesy of Dr. João Paulo Vieira, São Paulo.)
WILD FIRE

Pemphigus Foliaceus. (a), (b), (c), Initial outbreak; (d) Invasion period of the disease. (Photographs courtesy of J. P. Vieira, São Paulo.)
Carlos, São Paulo, (population 30,000) there had been 40 cases in 10 years; in a Jau fazenda or plantation (population 200) there were eight cases in 10 years; in one ward of a hospital 10 or 15 beds were always occupied by pemphigus cases.

INCIDENCE OF PEMPHIGUS FOLIACEUS (175 CASES)

Incidence of Pemphigus Foliaceus in São Paulo State, Brazil (175 cases).
(From the graph by J. P. Vieira, São Paulo, 1942)

Although the clinical symptoms of pemphigus foliaceus in Brazil are the same as those found elsewhere, the subjective phenomena (itching, burning, acute pain) are much more severe, and have given rise to the popular name for the condition. The disease occurs in the interior of São Paulo, Minas Gerais, Goiás, Matto Grosso, and Baía; and has apparently not been reported in the coastal area from Santos to Rio. It has a tendency to form endemic foci which are in turn the sources for the formation of new foci.

The first recorded observations of the disease were apparently those of A. Cerqueira, who saw cases in Baía in 1900 and earlier, according to hospital records. The first studies in São Paulo State were those made by Caramurú Paes Leme, who in 1902 published a thesis in which he confused the disease with Tokelau, an error later corrected by L. Gualberto, Lindenberg, O. da Fonseca Filho, J. P. Vieira, and others. At the seventh Brazilian Congress of Medicine and Surgery in 1917,

INCIDENCE OF PEMPHIGUS FOLIACEUS WITH RELATION TO COLOR, SEX, AND NATIONALITY (IN 460 CASES)

TOTAL NUMBER OF BRAZILIANS

TOTAL NUMBER OF FOREIGNERS

Incidence of Pemphigus Foliaceus in São Paulo State, Brazil, with Relation to Color, Sex, and Nationality (460 cases). (From the graphs by J. P. Vieira, Diretor do Serviço de Pênfigo Foliáceo, São Paulo, 1942.)
Pemphigus Foliaceus. (a) Invasive phase of the disease; (b) Generalized form; (c) and (d) dystrophic form. (Photographs courtesy of J. P. Vieira, São Paulo.)
Pemphigus Foliaceus. (a) Severely foliaceus form; (b) Hyperpigmented type (in a Japanese); (c) Herpetiform type; (d) Dystrophic form, with alopecia. (Photographs courtesy of J. P. Vicira, São Paulo.)
The characteristic, elementary lesion in _fogo selvagem_ is a serous purulent bulla, often located on the face, thorax, or the legs, and the eruption tends to become generalized. There is a period of evening fever, which may become very high and even fatal, though the fatal cases are in the minority. At various periods the disease must be distinguished from Duhring's dermatitis (in which the general health continues to be good and the localizations differ from those of pemphigus foliaceus), sub-acute pemphigus with extensive bullae (Brocq's type); true acute infectious pemphigus, and bullous impetigo. Nikolsky's sign is an important aid in diagnosis; it is always present in pemphigus foliaceus.

The _fogo selvagem_, once initiated, may develop into one of four types: acute, sub-acute (most common), super-acute (ending fatally after a short period of illness) or chronic (frustrate; extensively bullous; intensely foliaceous; pustulous and bullous; dystrophic; hyperpigmented; papillomatous or verrucose; erythrodermic; or herpetiform). In the chronic form there is ankylosis of the large joints, due to mineral loss and disturbances of the calcium metabolism with symptoms of osteoporosis. The nails are involved, with change of color (sometimes yellowish, as if dipped in iodine—J. P. Vieira's sign) and sometimes bleached and lifeless; they may drop off and are rapidly replaced. Great epidermic exfoliation accompanies this process. The nail color change usually appears about six months after the onset of the disease. In some cases itching is a predominant symptom, but not generally; the sensation is usually one of warmth or burning. In some cases the generalization of the bullae persists for a long period. As the general health improves, the bullae become sparser, larger, and painful. In addition to notable hyperpigmentation, there is papillomatosis, or a thickening of the epidermis, lesions persisting without complete restoration of the skin. On passing the fingers over the cutis of these chronic patients, one finds a roughened condition in the persisting lesions. These, under the microscope, reveal histologic bullae, para-keratose, keratoses, and granulose. Other phenomena observed in cases of pemphigus foliaceus in Brazil have been palmar and plantar keratoses, alopecia, papillomatosis of the scalp, pediculate lesions, elephantiasis of the ears due to lymphangitis (first reported by Vieira), and muscular atrophy. The hypertrophy of the ears is probably due to an associated infection. There are also endocrine disturbances, with dystrophy of the organism and physical transformation almost amounting to a change in sex, the disease running a graver course in women than in men. Of 35 male patients in the Alemar de Barros Hospital, 24 showed symptoms of testicular insufficiency. 12 of these had testicular retention and 27 out of 36 cases were impotent, five azoospermic, and four oligospermic. These changes are not observed in frustrate or initial forms of the disease. Of 44 women, 41 suffered from amenorrhea. Folliculin treatment brought about restoration of menstruation, and some improvement.
Pemphigus Foliaceus, São Paulo State, Brazil. Principal Localizations at Beginning of Disease; Age at which Disease Became Manifest (460 cases). (From the graphs by J. P. Vieira, São Paulo, 1942.)
Pemphigus Foliaceus. (a) and (b) Facies; (c) Severely foliaceous form; (d) Invasion period. (Photographs courtesy of J. P. Vieira, São Paulo.)
Pemphigus Foliaceus. (a) Familial pemphigus foliaceus. Left, frustrate form, right, invasion period; (b) Regression of the disease; (c) Hands of a patient; (d) Regression (back of patient "b"); (e) Hands of a chronic case (case "f"); (f) Chronic pemphigus foliaceus of 30 years duration. (Photographs courtesy of J. P. Vicira, São Paulo.)
in health, in nearly all these cases. Death may ensue from syncope, cardiac insufficiency, nephritis, an intercurrent disease, and, often, after extensive pleural effusions. Vieira recently reported that according to his study of 460 cases of pemphigus foliaceus, the maximum incidence of the disease was between the ages of 14 and 18. The lowest age of incidence was from 4 to 4.5 years.

The disease is more common in women; 60% of 460 S. Paulo cases. (Of 88 cases in the "Adhemar de Barros Hospital" 54% were women; 26 cases were children, 11 boys and 15 girls; the youngest was six years old.) Some require hospitalization in the second month of illness; others have had the disease for as much as 10 years before internment; the oldest case in the "Adhemar de Barros" had had it for 27 years.

The ages from 15 to 19 and from 25 to 29 seem to be the most susceptible. *Fogo selvagem* attacks both natives and foreigners, though most frequently Brazilians; it attacks both whites and blacks, most commonly the former. In S. Paulo, no cases have been reported in the coastal zone where nutrition is admittedly poor; this would seem to eliminate avitaminosis as a cause. The disease is found in the purple- or red-earth, sandy-soiled area. In Minas Gerais, the chief foci are the Charity Hospital area of the Capital and the Minas Triangle, on the Goiaz border; and in S. Paulo, the north-eastern, north-western and western parts of the State. Further north, pemphigus foliaceus has appeared on the borders of the Araguaia, and it is frequently found in Mato Grosso. In S. Paulo, the infected zones are generally in the vicinity of streams, where large numbers of *simulidae* are found. *Triatoma* are also prevalent in some foci, as are bats, bugs, rats, and fleas. Sanitary conditions are always poor. The disease is most common in rural areas, although autochthonous cases have been reported from interior towns and cities. Altitudes vary from 530 to 935 meters; two of the towns affected (Franca and Ribeirão Preto) have temperatures of from 17.3 to 23.5°C.

**Experimental work.**—Lindenberg, after failing to find a visible microscopic cause of pemphigus foliaceus, decided that, in view of the obviously infective nature of the condition, a virus must be responsible, and in 1937, he announced this conviction and the successful experimental transmission of the disease in rabbits by injection into the testicle of serum from the blood of pemphigus cases. He was able to carry

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11 Vieira, Notes 9 and 2; *Bol. Acad. Nac. Med.*, June, 1941, p. 33. José Ricardo Cuinares (An. Paul Med. & Cir., 245, mzo. 1942), in a preliminary report on 18 cases, observed that all had contracted the disease before puberty, that 17 showed disturbances in growth (stature), only one being apparently normal, that 4 had been backward in stature growth before the disease, 5 had been at a stationary stage at its onset; and 7 showed a stationary condition in regard to height after the onset of the disease. The dwarfism appears to be pituitary. Improvement was shown after endocrine treatment. Commenting on this paper, Vieira observed that the maximum incidence of pemphigus foliaceus was between the ages of 14 and 18; and Artom considered its appearance in infancy as one of the characteristics differentiating it from European pemphigus. José Aranha Campos in the same journal (p. 249) remarked that since 1938 he had been observing that certain *fogo selvagem* cases revealed a marked tendency to endocrinological disturbances. Family studies showed in some cases an apparently hereditary disposition to such disorders, including hyperpituitarism, and thyroid-pituitary deficiency. When the disease began before puberty, the usual changes of that stage did not occur; the victims remaining children, without development of the gonads, but without cretinism. Studies in women revealed cases in those who had borne children and in those who had not. Endocrinological anomalies of the dental arch were also seen. Vieira added that it was probable that mal-nutrition was a factor, inasmuch as pemphigus attacked the rural zones, where nutrition was poorer.


13 However, José Aranha Campos (An. Paul. Med. Cir., 250, mzo. 1942) reported cases with nutritional disturbances such as hypopituitarism, hypothyroid, and hypogonad obesity, often of family type and occurring before onset of the disease.
the virus through several passages in animals and to transmit the disease to guinea pigs. Vieira and collaborators have not been able to confirm these results, but are still experimenting along this line.

Vieira and his coworkers have also made extensive studies of the chemical composition of the blood in pemphigus foliaceus. Among 48 or 50 cases, acidosis was found in certain patients; an increase in plasma was always seen; the protein index was always inverted, etc. The low alkaline reserve suggests the desirability of a special diet. Of 86 hemocultures, 70 were negative; 13.9% were positive for streptococcus; 4.6% positive for staphylococcus; streptococci isolated included two of the inert group; one, non-virulent, of the viridans; nine of the hemolytic (five virulent, two non-virulent, two undetermined); staphylococci: four strains, all albus.

Treatment.—To date cures (10%) have been obtained only when energetic treatment has been carried on from the very early stages of fogo selvagem. Vieira declares that the essentials are hygiene, antiseptic baths, quinine by mouth (one gram daily), and protection of the skin with boricated vaseline. Experiments with arsenicals and sulfanilamides have not been satisfactory and are not recommended. About 15% of cases may become well spontaneously, but the benefits of hospitalization are nevertheless very great.

Control.—Control measures recommended are: widespread knowledge of the symptoms so that early treatment is assured; confinement of the sick in special hospitals; home isolation of frustrate forms; intensive educational work; prevention of the entrance of carriers into healthy zones. By decree of September 17, 1938, the State of Sâo Paulo created the Pemphigus Foliaceus Service (Serviço de Pénfigo Folidáceo), and a hospital (the “Adhemar de Barros” Institute) was opened in September, 1940 for pemphigus cases. The Ministry of Education of Brazil was authorized in 1939 to spend 128,400,000 for the completion of a Hospital in Ponta Porã, Mato Grosso, for cases of this disease (60 beds, to be increased gradually to 100 beds).
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