PEMPHIGUS IN NORTHERN INDIA-CLINICAL STUDIES IN 34 PATIENTS

By

K. C. KANDHARI, F. R. C. P., (Edin), F. A. M. S.,
Prof. of Dermatology and Venereology, All India Institute of Medical Sciences,
New Delhi, India

and

J. S. PASRICHA, M. D.,
Registrar in Dermatology and Venereology, All India Institute of Medical Sciences,
New Delhi-16, India

Since the studies of Civatte (1943) and Tzanck (1948) who outlined the histopathological criteria for the differentiation of this fatal disease of unknown aetiology from other vesiculo bullous eruptions, the disease has been investigated from several aspects, including clinical studies on large series of patients reported by Gellis and Glass (1941), Combes and Canizares (1950), Sanders et. al. (1960) and Lever and White (1963).

The disease is not uncommonly met with by workers in the field all over the world, yet, reports from certain areas are very few. From Western part of India a series of 21 cases were reported by Desai and Rao in 1960.

MATERIAL AND METHODS

The present report is a compilation of clinical studies on 34 cases reporting to All India Institute of Medical Sciences in Northern parts of this country as observed over a period of four years. All the cases have shown characteristic clinical features and the diagnosis has invariably been confirmed by histopathological studies and demonstration of Tzanck cells in smears from the base of the bullae.

OBSERVATIONS

Details of the distribution of age, sex and the type of disease is shown in Fig. 1. There were 26 cases of pemphigus vulgaris, 5 cases of pemphigus foliaceous and 3 cases of pemphigus erythematosus. No case of pemphigus vegetans as such has been seen so far, although one case of the vulgaris type developed vegetating lesions in her joint folds during one of her relapses. Almost every case of pemphigus foliaceous or the pemphigus erythematosus variety has shown bullous lesions characteristic of the vulgaris type. But we have not seen any case who first presented like pemphigus vulgaris and later changed over to the other type except the single instance of change over to pemphigus vegetans type, cited above.

Most of the cases come from lower socio-economic group. There are 20 males to 14 females in our group. The age incidence has varied between 9 years, and 70 years, the age indicated for every patient being the age at which the

Received for publication on 13-2-65.

disease started in the individual. Maximum number of cases lie in the 4th and 5th decades but more interesting is the fact that 5 cases of this group are under 20 years of age, the youngest being 9 years when the disease started.

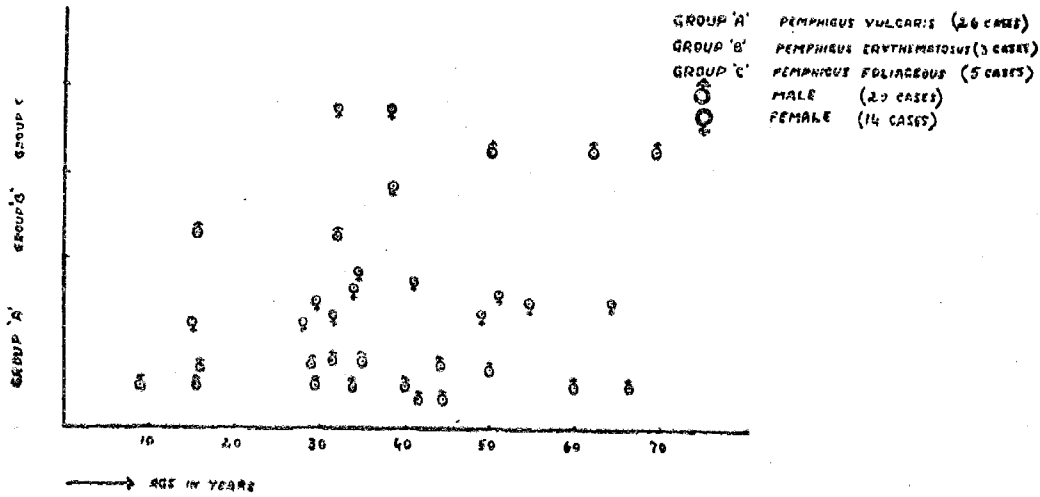

Fig. 1

The characteristic clinical lesion has been the classical flaccid bulla arising on normal skin. Almost every case at one stage or the other showed such lesions, though at the time the patient first presented himself for examination, the lesions were not always bullous. They were either raw areas, crusted lesions, pyodermic lesions or only pigmented macules and on a few occasions the correct diagnosis was delayed because of this varied presentation. In 2 patients the initial diagnosis was a pyoderma till the lack of response to proper antibiotic therapy lead us to further investigations and thus the correct diagnosis. In 2 other cases, the bullous lesions were tense and situated in groups on erythematous patches in a symmetrical fashion. The presentation simulated erythema multiforme bullosum, particularly because in one of these cases high constitutional toxicity and fever were also present and the duration was very short. Further follow up however, and a histopathological study of the blister decided the diagnosis.

Involvement of buccal mucous membrane was present in 27 cases and often it had preceded the skin lesions by several months. In addition to buccal lesions, 4 cases had ulcerations in the nose with episodes of epistaxis and 1 case developed ulcerations on the vocal cords with hoarseness. In two cases, a conjunctivitis of one or both eyes had been associated, but without any ulcerations, while unlike this, mucous membranes, mostly showed irregular ulcerations of a variable size. No proved case of pemphigus with mucous membrane lesions alone has been seen by us, in the present series. 7 cases (3 of the foliaceous variety, 2 of pemphigus erythematosus and 2 of the vulgaris type) never showed any mucous membrane lesions. It seems that cases of pemphigus foliaceous and pemphigus erythematosus show a much less tendency to mucus membrane lesions.

Most of the cases were asymptomatic but paraesthesias on raw areas were quite troublesome. Apart from this, some cases, more so of the foliaceous type complained of severe pruritus and burning.

All cases were treated with cortico-steroids and they showed a good response. Among the steroids, we have been using, as a routine, prednisone or dexamethasone, with the addition of A. C. T. H. on occasions. Some patients did not show a good response to prednisone; then a change over to dexamethasone and/or the addition of A. C. T. H. was useful. In two patients, it was only the injectable dexamethasone that brought about a remission. The initial daily dosage had been 6-8 tab, (30-40 mg.) of prednisone. But in cases who did not show a response within a few days, the daily dosage was increased to 12 or 16 tab. (60 or 80 mg.) of prednisone. Most of our patients could be controlled with a daily dosage of 12 tab. Two cases needed equavalents of 22 tab and 20 tab. (11 mg. and 10 mg.) of dexamethasone for their remissions respectively.

The controlling dose of steroid used to be maintained till the lesions healed completely. The daily dosage was then reduced slowly by 1 tablet after every 3 days if the total daily dosage was more than 6 tablets, otherwise reduction was made by $\frac{1}{2}$ tab after every 3 days. Most of the patients were discharged from the hospital on a maintenance dose of 3 or 4 tab. a day.

On a few occasions (7 times in 6 patients) we ventured to go against the rule and reduced the dosage more drastically from 12 tab. to 4 tab. a day with the simultaneous addition of A. C. T. H. (to stimulate the endogenous production of steroids). So far we have not observed any untoward effects and certainly recommend this schedule for further trials.

In subsequent attacks, the controlling dose had been quite often higher than that in the previous attacks (Fig. 2 and 4) and thus it became more and more difficult to manage such cases.

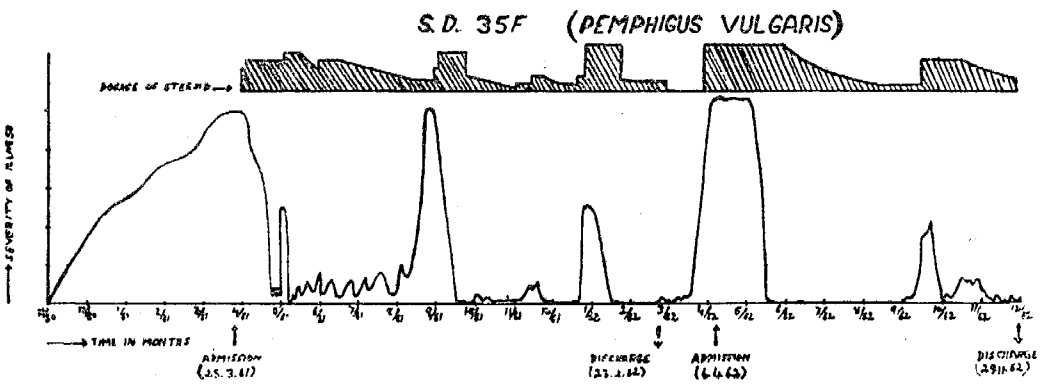

Fig. 2

Adjuvant treatment included antacids, anabolic hormones and a high protein diet. Salt was restricted when the dosage was high and diuretics (usually Esidrex) given whenever oedema on feet made its appearance.

Side effects from steroid therapy were quite frequent. Increase in weight and Cushing's type of obesity were commonly seen. Other side effects included occasional epigastric pain, oedema on feet, osteoporosis with pain in the back and steroid acne Hypertension was seen in a few cases. One patient developed large linear atrophic striae and another case died of uncontrolled tuberculosis. With a schedule of 15 gr. (1.0 gm.) potassium chloride for every 2 tab. of prednisone and restriction of sodium chloride in diet, no case of electrolyte imbalance was observed.

The course of the disease had been invariably attended with remissions and relapses, but the pattern varied for each patient, hence any prognostic forethought was not possible. A few graphs showing the extent of clinical involvement of skin (based roughly on the ' Formula of 9 ') along with the level of steroid dosage are shown in Fig. 2, 3 and 4. As a general rule, cases of pemphigus foliaceous showed longer remissions and also a longer life span as compared to those of the vulgaris type.

Duration of the disease in individual patients till the end of June 1964, is shown in table I. There were 8 cases in whom the diseas e was known to be of more than 3 years duration and they are alive. Three of these cases are pemphigus vulgaris type, 3 of pemphigus erythematosus variety and 2 of pemphigus foliaceous. This observation also supports the general view that cases of pemphigus foliaceous and pemphigus erythematosus have a longer life span.

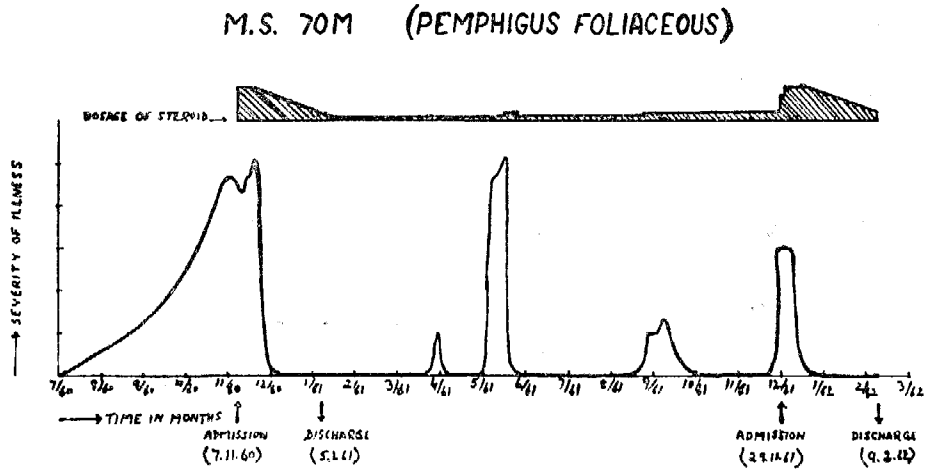

Fig. 3

TABLE I—Duration of disease in months.

Less than 6 months	...	...	...	4 cases
7 months to 12 months	...	...	...	7 cases
13 months to 24 months	...	...	...	12 cases
25 months to 36 months	..	...	...	3 cases
37 months to 48 months	...	...	...	6 cases
More than 48 months	...	...	...	2 cases
		Total	..	34 coses

Out of 34 cases, 18 patients are known to be living. Further follow up of 11 cases has been difficult as they would not communicate and it is not known as to how many are surviving. 5 cases are known to have died since. All these five cases had been of pemphigus vulgaris variety and co-incidently all of them were males. 4 cases died in the hospital while the 5th case was at home at the time of his death. One patient possibly died of pulmonary tuberculosis as he showed an active focus concomitently while the remaining three developed hypotension almost suddenly at a time when paradoxically their clinical condition seemed to have somewhat improved. On two of these cases we were able to perform autopsy, and the only significant findings were revealed an extreme degree of adrenal cortical atrophy in both cases and myocytolysis of cardiac muscle in one.

DISCUSSION

Pemphigus, as it is known today, presents itself in four closely related variants, namely pemphigus vulgaris, pemphigus foliaceous, pemphigus erythematosus and pemphigus vegetans; pemphigus vulgaris being the variety most commonly met with. Factors which determine the type of disease manifested in a particular individual are unknown, but racial predisposition may be one of them, since pemphigus foliaceous (Fogo Selvagem) is the most prevalent type in South

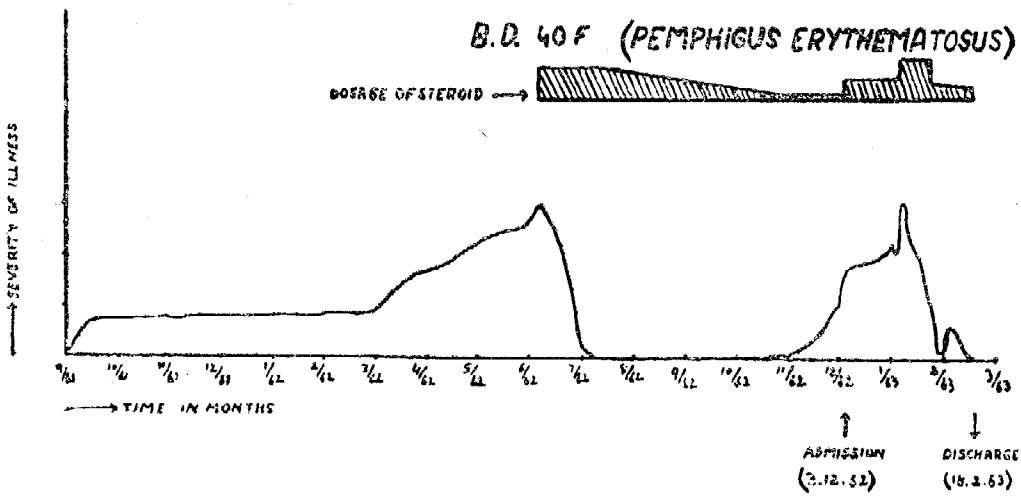

Fig. 4

America and Desai and Rao (1960) have reported a similar preponderance in South India attributing it to racial differences in the North and South Indians. Influence of the climatic and geographical conditions on the manifestations of the disease need further study.

Pemphigus can occur at any age, although the maximum number of cases occur in the 4th and 5th decades. Lever (1950) reported a case aged 11 years. The youngest patient in our series is 9 years. He presented with recurrent pyogenic lesions all over the body (Fig. 5 and 6) along with mucous membrane ulcerations.

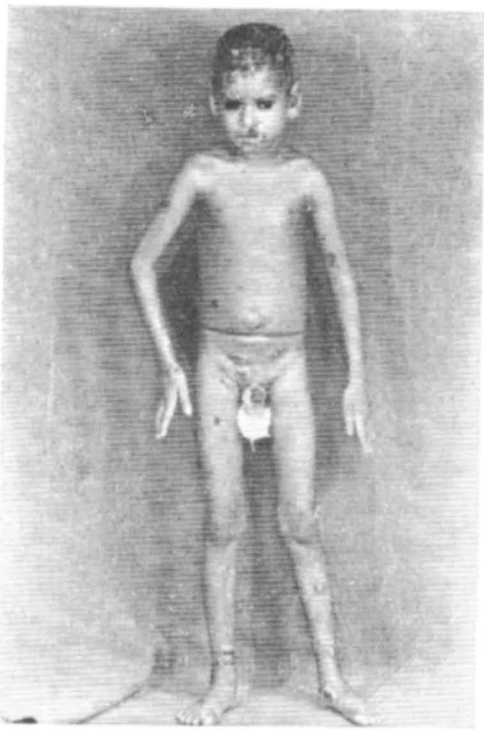

Fig. 5

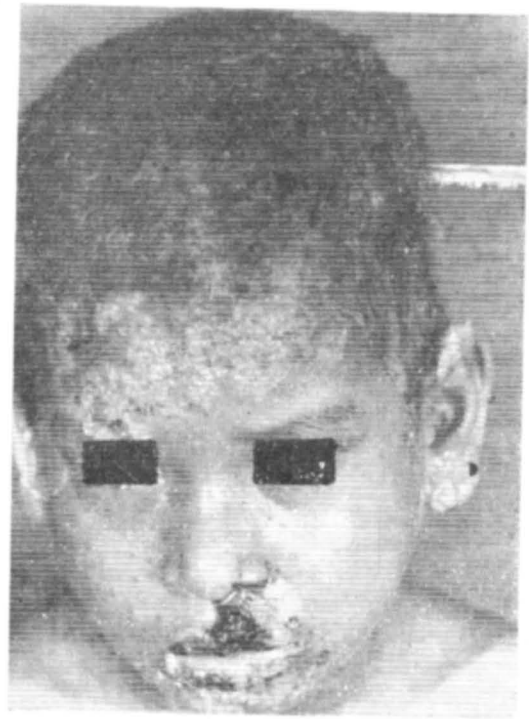

Fig. 6

The first diagnosis was a pyoderma for which he was treated but without any response. During this period he developed a bulla which was studied histopathologically. It showed intra-epidermal split and acantholysis (Fig. 7 and 8). Administeration of prednisone brought about a dramatic improvement. All the lesions healed leaving behind hyperpigmented and hyperkeratotic areas (Fig. 9) a characteristic, which we have constantly observed in pemphigus lesions only. Alternative possibilities of Juvenile dermatitis herpetiformis, Benign pemphigus of Hailey and Hailey and bullous impetigo were considered, but a combination of diffusely scattered isolated lesions, involvement of buccal mucosa, lack of family history, lack of response to proper antibiotic, a rapid healing on steroids and the residual hyperpigmented hyperkeratotic lesions made us suspect this case to be that of pemphigus. Histopathology settled the issue in favour of this suspicion

rather than of any other possibility. We hope to observe this case further for the course it takes. Young age usually goes against the diagnosis, but we have 4 other cases aged 15 years, 15½ years (2 cases) and 16 years too and in another hospital we have recently seen a case of Pemphigus aged 11 years. Thus it seems that age is no bar to suspect the diagnosis when the clinical signs are suggestive and later histopathology is unequivocal in favour of the diagnosis, though younger the patient less likely the disease.

The disease usually manifests with bullous eruptions diffusely scattered on skin. Almost any skin area can be involved. The bullae are usually flaccid, but

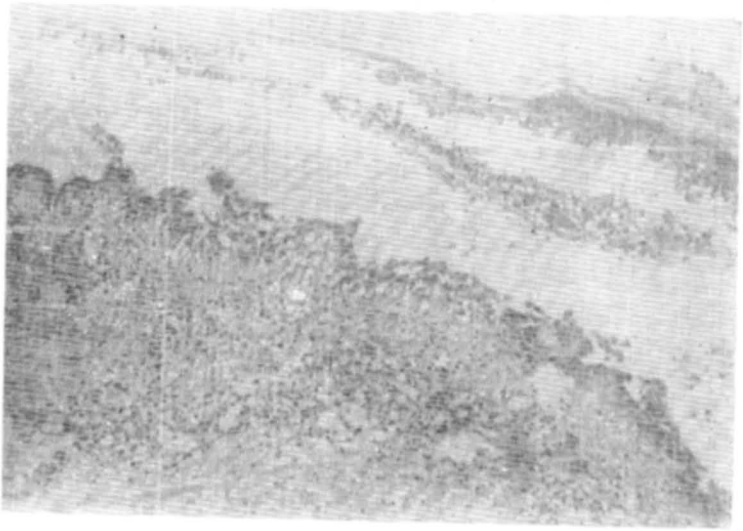

Fig. 7

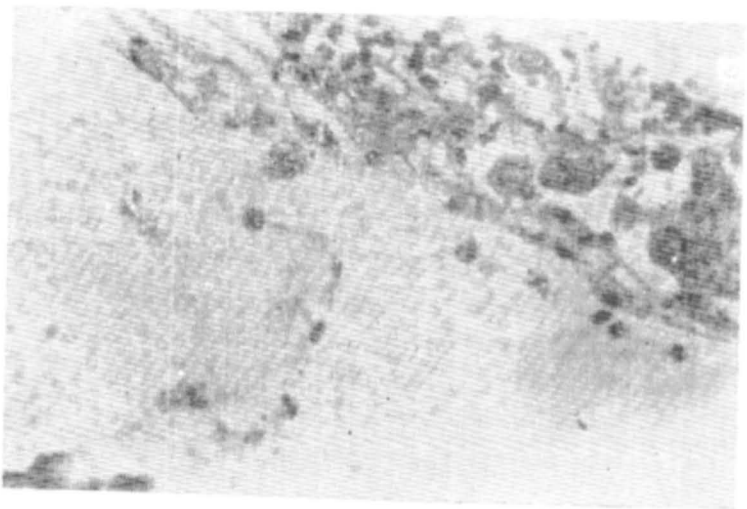

Fig. 8

occasionally they may be tense or they may be surrounded by erythema. Secondary changes of crust formation or purulent discharge may dominate the clinical picture. Sometimes the only type of lesion seen is a dry crust and when the process is activated, there is peripheral extension of bullae which also form underneath the crusts. With serous discharge under and around the crusts which now become separated from the base, a characteristic appearance is given to the lesions which deserves the name of " FLOATING CRUSTS "—Crusts floating on a pool of serous discharge. We have observed such lesions in at least two cases and regard this as a highly diagnostic clinical sign. When the clinical diagnosis is in doubt, a histopathological study and demonstration of Tzanck cells must always be undertaken. Some people (Graham et. al. 1963) have demonstrated acantholytic cells in other dermatoses as well, but the frequency with which these cells can be demonstrated in pemphigus far exceeds that in other dermatoses, and Tzanck test still remains a diagnostic procedure of great value.

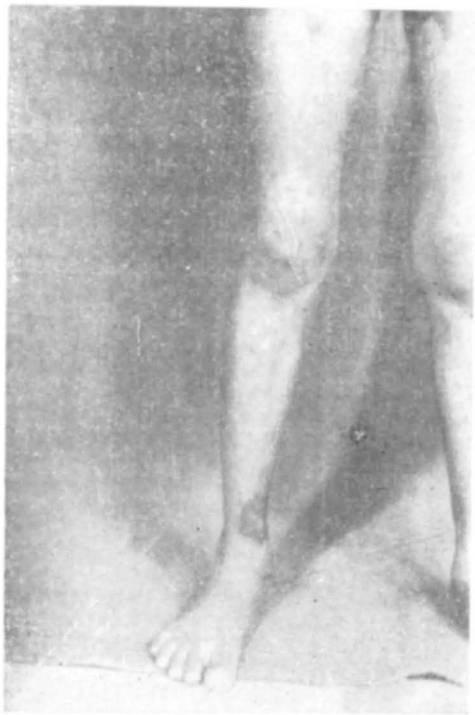

Fig. 9

Involvement of mucous membranes prior to skin lesions is another clinical sign of great importance. Although we have not seen any proved case with only buccal lesions, we admit that there must be several of them who have not yet shown skin lesions. Buccal mucosa is most commonly involved, but at times other mucous membranes may be the site of ulcerations. Some patients show a greater tendency to mucous membrane lesions.

The disease as a rule remains limited to the skin and mucous membranes. The internal organs are largely spared. Postmortem finding of adrenocortical atrophy could be attributed to the exogenous steroid therapy, but the role of disease itself in producing adreno-cortical stress and later exhaustion-atrophy cannot be ruled out and is rather more likely since the same was reported by Goldzieher in 1948 when steroid therapy was not even known. Significance of myocytolysis seen in one case is not known. The terminal hypotension may be having its origin in the damaged heart muscle.

Morbidity of the disease in our cases seems to be much less. Most of the cases could be brought under control with an equavalent of 60 mg. of prednisone compared to 120-240 mg. (24-48 tab. of Prednisone) reported by Lever (1963) and 300-400 mg. by Grace, The maximum daily dose that was ever given to a case was an equavalent of 110 mg. of Prednisone.

As there is no universally accepted schedule of steroid therapy, we have contrived our own regime and find that it works well. The subject of gradual reduction of steroid dose has perhaps been overemphasized. The adventure of dropping the dose under cover of added A. C. T. H. therapy has double advantage. Firstly it reduces the total quantity of steroid given to a patient and hence its side effects, and secondly it enables a case to be relieved from the hospital much earlier. Simultaneous addition of A. C. T. H. seems to afford some protection from a sudden relapse possibly by stimulating the adrenal cortex undergoing atrophy, to produce endogenous steroids and thus reduce the level of maintenance dose.

Mortality rate in our cases again is not high. In the series reported by Combes and Canizares (1950) the average survival period was 9.5 months. 44% of the cases had died during the first 9 months. Only 12% lived for more than 3 years. In another group reported by Sanders et. al. (1960) 25% cases died in the first year and almost 50% in the first 3 years. In comparison, out of 34 cases in our group, 23 cases have already had the disease for more than 12 months and only 5 are known to have died. The survival periods of these five cases have been 24 months (1 case), 12 months (3 cases) and 7 months (1 case). Out of 11 cases in whom the duration of the disease is less than 12 months, 4 have already died, another 4 cases are those in whom the disease has started only recently and remaining 3 have been lost to observation. Thus the exact duration of the disease in them is not available. In 8 cases, the disease has already been present for more than 3 years. All these observations are a sufficient proof of the fact that the disease in our part of the world has shown somewhat milder character and comparatively low mortality-a fact which is more spectacular in face of the comparatively lower dosage of steroids administered.

SUMMARY

A review of 34 cases of pemphigus seen over a period of 4 years at the A. I. I. M. S. Hospital, New Delhi is presented. Stress is laid on the variety of

clinical lesions that these cases present. Some features which help to make an early diagnosis are also outlined. A comparatively low morbidity and mortality of this disease in our part of the world is pointed out ~~that~~ and the mode of treatment of these cases at our hospital is discussed.

ACKNOWLEDGEMENTS

In the end, we gratefully acknowledge the help given to us by the Photographic Section, A. I. I. M. S. and Mr. R. C. Gupta, Stenographer, for typing the manuscript.

REFERENCES

1. Civatte, A. (1943): Annde Dermat. et. Syph. 3 : 1.
2. Combes, F. C. and Canizares, O. (1950): Arch. Derm. and Syph. 62 : 786.
3. Desai, S. C. and Rao, S. (1960): Hautarzt. 11/10 : 445.
4. Gellis , S. and Glass, F. (1941): Arch. Derm. and Syph. 44 : 321.
5. Goldzieher (1945): Arch. Derm. and Syph. 52 : 369.
6. Grace, A. W.: (Personal communication).
7. Graham, J. H., Bingul, O. and Burgoon, C. B. (1963): A. M. A. Arch. Derm. 87 : 118.
8. Lever, W. F. (1950): J. Invest. Derm. 14 : 205.
9. Lever, W. F. and White, H. (1963): A. M. A. Arch. Derm. 87 : 12.
10. Sanders, S. L., Brodey, M. and Nelson, C. T. (1960): A. M. A. Arch. Derm. 82/5 : 717.
11. Tzanck, A. (1948): Ann. de Dermat. et. Syph. 8 : 205.