TREATMENT OF CHRONIC ASTHMA WITH PREDNISOLONE AND THE NEWER STEROIDS

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This paper records the treatment of out-patients with chronic asthma by prednisolone administered in short courses and for continuous periods up to four years. A comparison of the effects of prednisolone with some of the newer steroid derivatives is also made.

Short-term Treatment: Controlled Trial

In order to determine whether prednisolone in relatively low dosage was effective when given in courses of one week's duration, 26 patients with asthma, who usually required the use of an atomizer or bronchodilator tablets several times daily, were selected. Each patient was given three sets of tablets—5-mg. tablets of prednisolone, a bronchodilator (phenoxymethazone 100 mg. or aminophylline 200 mg.), and dummy tablets—in sealed boxes. The contents were known only to the pharmacist, and the tablets were given in varying order. Instructions on the method of taking the tablets were:

1st and 2nd days, 4 tablets in divided doses
3rd and 4th days, 3 tablets in divided doses
5th and 6th days, 1 tablet night and morning
7th day, 1 tablet at night

Each patient was given a diary and was asked to keep a daily record of attacks of asthma and the number of bronchodilator tablets taken or aerosol administrations during each day of treatment.

Assessment was made by comparing (1) the number of attacks of asthma, (2) the quantity of symptomatic drugs employed as spray or tablet, (3) the number of asthma-free days, and (4) the patient's own preference. When prednisolone was compared with bronchodilators (aminophylline or methoxyphenamine) it was found that 19 of the 26 patients had fewer attacks during the week on prednisolone,* four had more attacks, and three had the same number. Fourteen used a smaller amount of other symptomatic remedies while taking prednisolone, eight used more, and four used the same. Comparison of prednisolone with the dummy tablets showed that 17 had fewer attacks on prednisolone,* three more, and six the same; while 19 used smaller quantities of symptomatic remedies while on prednisolone, four used more, and three the same. For the total number of patients (26) 58 asthma-free days were recorded on prednisolone, 29 on bronchodilator tablets, and 26 on dummy tablets. Of 20 patients who expressed a preference, 16 favoured prednisolone.

There appears to be little doubt that prednisolone given in this way can be effective in controlling asthma of moderate severity in a high proportion of patients. It was noticeable that while patients were on prednisolone, asthma-free days were usually recorded in the second half of the week.

Selection of Patients.—Further experience has now been obtained in 102 patients and has shown that two groups are particularly suitable for this form of short-term treatment: (1) those with mild or moderately severe chronic asthma which can usually be controlled by a bronchodilator in aerosol or tablet form, but who from time to time have more severe attacks which fail to respond to the usual remedies; and (2) those who develop a persistent disabling wheeze resistant to bronchodilators, often after respiratory infection. In both groups failure to treat the attack effectively may lead to hospital admission.

Results

Results were assessed initially on the basis of respiratory function tests (vital capacity, peak flow estimations), as well as the patient's report at attendance a week later. When repeated courses have been prescribed, the patient has been instructed to start treatment if the usual symptomatic remedies have failed to control attacks. In such cases subjective evidence has had to be accepted unsupported. The results are shown in Table I.

TABLE I.—*Results of Short-term Treatment*

	No. of Cases	No. of Courses	Good Response	Fair Response	Poor Response
Male	39	71	60	5	6
Female ..	63	285	237	21	27
Total ..	102	356	297	26	33

Fifty-one patients received two or more courses, including four who have had between 10 and 20, and four between 20 and 30, courses over a period of two to four years. Patients receiving multiple courses usually responded well, but variable responses were sometimes recorded.

Failure to respond was attributed to the employment of too small an initial dose or to infection in the majority; no reason for failure was determined in others. Side-effects prevented completion of the course in two. Infection appeared in most cases to be the reason for poor results in those who had previously responded well.

Case 1.—A woman aged 57 had asthma which had begun eight months previously with an acute chest infection. Wheezing and dyspnoea on effort had persisted after the acute attack ceased. Vital-capacity readings over several weeks were repeatedly between 1,400 and 1,600 ml., with peak flow readings of 185 and 230 l./min. before a course of prednisolone was given. At the end of the course the vital capacity had risen to 2,800 ml. and the peak flow to 350 l./min. The improvement was maintained for some weeks.

Case 2.—An asthmatic woman aged 50 with advanced rheumatoid arthritis had previously been admitted in status asthmaticus on a number of occasions. She has had 30 short courses over a period of four years and has responded well to all except one. On this occasion she had a severe accompanying bronchitis. A recent fall led to a Colles fracture, but this appears to have been related to her rheumatoid arthritis rather than to any generalized osteoporosis of endocrine origin.

Case 3.—A man aged 53 suffered from persistent wheezing with superimposed acute attacks. After respiratory infection the vital capacity fell to 1,200 ml., with a peak flow of 185 l./min. The usual symptomatic remedies were ineffective. After a course of prednisolone the vital capacity rose to 3,500 ml. and the peak flow to 230 l./min.

*The preference for prednisolone, using these criteria, is significant at 1% level.

Case 4.—A woman aged 35 had recurrent severe attacks of asthma often associated with heavily infected sputum—23 courses were given over three years, with good results in 16, fair in four, and poor in three.

Side-effects

Two patients were unable to complete the course because of a " bursting " sensation in the chest. Three patients who had repeated courses increased in weight to a considerable extent (22 lb. (10 kg.) after 24 courses, 10 lb. (4.5 kg.) after 30 courses, and 8½ lb. (3.9 kg.) after 24 courses). One had recurrence of pain from a pre-existing duodenal ulcer. Apart from these six patients no side-effects were observed except in the doubtful case already referred to with a fractured arm. One patient died from acute asthma seven months after the third course of prednisolone; it was thought that this death was unrelated to the treatment.

Long-term Steroids

Long-term treatment was reserved for patients with repeated attacks of status asthmaticus, which were regarded as a hazard to life, or for those with severe disabling asthma which seriously interfered with, or prevented them from leading, a normal working life. No cases with primary bronchitis or with obvious evidence of organic emphysema were included. A favourable response to steroids was initially observed during in-patient treatment in most cases. Five subjects treated as out-patients were included in this series after several short courses of prednisolone had proved temporarily effective. All patients were supplied with a card stating the type of dose of steroid used and the date when treatment began.

In this series of 36 treated with prednisolone, 20 had had repeated attacks of status asthmaticus before starting treatment; the remaining 16 had intractable asthma which had failed to respond to other measures, and six of these had had isolated attacks of status asthmaticus. The average period of treatment with prednisolone was 20.7 months, and no patient is included who had less than six months' treatment. Eighteen of these cases also received treatment with the newer steroid derivatives (triamcinolone, methylprednisolone, and dexamethasone) for periods of up to 18 months, and six had been treated with corticotrophin (three) or cortisone (three) prior to treatment with prednisolone. The average total period of treatment with all steroids was 30.9 months.

All patients except five who lived too far from hospital were seen monthly for the first year, and at least every two months thereafter. An initial dose of 20 mg. of prednisolone was given and subsequently reduced to the lowest effective level: 12 cases were stabilized at 15 mg., 21 between 7.5 and 12.5 mg., and three at 5 mg. or less. The effect of treatment was assessed in three ways: (*a*) by measurement of respiratory function, together with recordings of the daily requirements of bronchodilator drugs; (*b*) by comparison of functional activity as judged by capacity for work and loss of time from work, including hospital admissions; and (*c*) subjectively by the patient's personal opinion of the effect of treatment. The final assessment was made mainly on objective evidence provided under the first two headings. The results of treatment are given in Table II.

It can be seen that males responded rather better than females, and that in this series there was no appreciable difference between those cases with a history of status asthmaticus and those with only chronic asthma. Twenty-nine cases are continuing with steroid treatment.

TABLE II.—*Results of Long-term Treatment*

	No.	Excellent	Good	Slight	No Improvement
Cases with previous history of status	M 9	3	5	0	1
	F 14	1	7	3	3
Cases of chronic asthma	M 8	2	5	1	0
	F 5	2	1	2	0

Excellent = Bronchodilator drugs required only occasionally. Maximum vital capacity maintained throughout treatment.
Good = Considerable reduction in amount of bronchodilator drugs required. Vital capacity improved but not normal.
Slight = Improvement claimed by patient but not demonstrable by objective methods.

There were 10 failures, which include those assessed as receiving only slight benefit. Severe emotional factors were present in two of these patients (in one there was considerable doubt whether the tablets were taken regularly); associated bronchiectasis was present in two; repeated attacks of bronchitis occurred in one; in one patient depression developed as a side-effect and necessitated reduction of dosage to an ineffective level; in one, respiratory function tests showed a diffusion defect in addition to spasm. One patient whose asthma deteriorated during the summer months as a result of grass-pollen sensitivity died at home in status asthmaticus in June, while still taking prednisolone in doses which had previously controlled her symptoms. Two patients claimed to be greatly improved, but objective confirmatory evidence of this was not obtained. In several cases successful treatment seemed to depend upon the use of initiative in adjusting the dose of steroid according to the severity of respiratory symptoms—increasing the dose during exacerbations and reducing it during periods of improvement. It was noted that, even in those assessed as having an excellent result, the forced expiratory one-second volume and the peak flow usually persisted at a level well below normal.

Side-effects

Side-effects occurred in nine cases—there was facial mooning with gross increase of weight in three, and hirsuties in one of these. In four cases there was a moderate increase in blood-pressure; all were women of middle age, and three of them had received regular treatment for more than three years. Purpura was recorded in two, dyspepsia in two, and depression in one. More than one side-effect was recorded in two patients. One other developed ulcerative colitis while being successfully treated for asthma. In only one case (the patient with depression) was treatment terminated on these grounds.

Deaths

Three deaths were recorded—one, already referred to, during an attack of severe asthma while receiving treatment. Two others died in status asthmaticus within two months of terminating treatment, which had been given for 6 and 14 months respectively. In both the dosage was gradually reduced before treatment ceased.

Case Histories

The following case histories were typical. The results in Cases 5 and 6 were regarded as " excellent," and in Cases 7 and 8 as " good."

Case 5.—A boy aged 16, with a history of lifelong severe asthma and flexural eczema, was sent to Switzerland, where he remained well for over a year but relapsed at once on returning home, and was admitted to hospital in status

asthmaticus on three occasions within two months. He remained almost completely free from symptoms during 16 months on prednisolone 15 to 12.5 mg. daily and then on triamcinolone 8 mg. for six months, and methylprednisolone 10 mg. for 10 months. Occasional attacks of asthma developed, particularly when visiting friends who kept cats and dogs. On one occasion after skin-testing with extracts of animal hairs he developed acute anaphylactic symptoms with urticaria, wheezing, and collapse which nearly resulted in his death. He had had methylprednisolone 4 mg. three hours before the tests were carried out. During the two years and eight months of treatment no other symptomatic remedy was used, and his vital capacity remained within the normal range and the peak flow was usually normal. Any attempt to reduce the dose below the figures stated led to increased wheezing. Growth appears to have been retarded, but he was small for his age before treatment was started.

Case 6.—A man aged 47. Asthma had begun in a severe form two years previously after an operation for nephrectomy. He had spent 17 weeks in hospital on four occasions during this time and was virtually unable to work. He started treatment with prednisolone 15 mg. for nine months, his weight rising from 123 to 157 lb. (71.2 kg.) in this time: the dose was then reduced to 10 mg. for 10 months, during which he remained well and his weight remained constant. For the next year the dose was reduced to 7.5 mg. without ill effect; the weight fell during this time from 157½ to 147 lb. (71.4 to 66.7 kg.). In the subsequent 10 months he remained well on methylprednisolone 6.4 mg. with a further loss of 6 lb. (2.7 kg.) in weight. During the three and a half years of treatment, apart from occasional wheezing, he has had two attacks of bronchitis, on one occasion remaining in bed for one week, during which he received chlortetracycline. This was the only period of time lost from work. Whereas he had previously taken regular bronchodilator tablets and used an atomizer, he now had no symptomatic treatment other than steroids. The vital capacity was within the normal range except on those occasions when he had bronchitis.

Case 7.—A man aged 61 had had asthma for four years. During this time he was off work for three years and had 12 hospital admissions in status asthmaticus. From April to July, 1956, he was maintained on 15 mg. of prednisolone daily: this was then reduced to 10 mg. with some deteroriation, and 20 mg. daily was taken till February, 1959. His weight, which was 172 lb. (78 kg.) prior to his illness, rose from 156 to 185 lb. (70.8 to 83.9 kg.). Triamcinolone was substituted; he remained well on 8 to 12 mg., and his weight fell to 179 lb. (81.2 kg.). He then resumed prednisolone (10 to 15 mg.) and his weight rose by 3 lb. (1.4 kg.). An atomizer was used from time to time, especially in the second year of treatment; his vital capacity remained between 3,300 and 4,400 ml. except on a few occasions when it fell below 3,000 ml. No time was lost from work over the whole period of 48 months' treatment. During a holiday in Switzerland each year his asthma cleared completely and he was able to climb mountains: he could then omit steroid therapy until his return to England.

Case 8.—A woman aged 57 had had asthma for 21 years. She complained of constant wheezing, was unable to do her housework, and used a spray for up to 50 times daily. Prednisolone 15 mg. daily was given for nine months, 10 mg. for five months, and 7.5 mg. for two months. She was subsequently treated with triamcinolone 4–8 mg. for six months, and dexamethasone 0.75–1 mg. for 10 months. During the first six months of treatment she was admitted to hospital for a period of two weeks with bronchitis, which followed influenza, and for 10 days with asthma and bronchitis; subsequently she remained well and was able to perform her housework without added symptomatic remedies. Her vital capacity, which averaged 1,330 ml. during a period of control observation, rose to an average of 1,720 ml. on 15 mg. and fell to 1,440 ml. during the period on 10 and 7.5 mg. It subsequently rose to 1,600 ml. on dexamethasone 0.75–1 mg. Expiration remained prolonged, and an expiratory wheeze was constantly present on auscultation. Respiratory function thus remained considerably below the normal range in spite of clinical improvement. Her weight increased from 144 to 164 lb. (65.3 to 74.4 kg.) while receiving 15 mg. of prednisolone, remained constant on 10 and 7.5 mg., but fell to 150 lb. (68 kg.) on triamcinolone 6 mg. daily, rising again to 174 lb. (78.9 kg.) during the 10 months on dexamethasone 0.75–1 mg. daily.

Comparison of Prednisolone with Newer Steroids

Eighteen patients whose symptoms were regarded as satisfactorily controlled with prednisolone were switched to a comparable dose of triamcinolone, methylprednisolone, or dexamethasone. They were maintained for periods of at least six months on each preparation, unless there was evidence of deterioration or unpleasant side-effects. Most patients received two of these preparations and some all three. They were encouraged to adjust the dosage of the new preparation to achieve the same result as they had been getting from prednisolone.

TABLE III.—*Comparison Between Newer Corticosteroid Preparations and Prednisolone on a Tablet-for-Tablet Basis*

	No. of Patients Treated	Effects Compared with Prednisolone on a Tablet-for-Tablet Basis		
		Better	Same	Worse
Triamcinolone (4-mg. tablets)	11	4	5	2
Methylprednisolone (4-mg. tablets)	8	0	6	2
Dexamethasone (0·5-mg. tablets)	12	4	0	8

There appeared to be minor individual differences only between these preparations and prednisolone in controlling symptoms of asthma. The numbers involved are small, but it was noticeable that several patients appeared to do less well on dexamethasone and spontaneously replaced this preparation with another steroid: this was partly due to unpleasant side-effects. In two a second course of dexamethasone was also terminated by the patient after a short period.

Side-effects and Effect on Weight

Triamcinolone.—Eleven patients were treated, 10 of them for six months or more. Seven showed a fall of 5 to 10 lb. (2.3 to 4.5 kg.) during the six months on triamcinolone. Most of these were already overweight as the result of treatment with prednisolone. One girl of 18, however, put on 5 lb. (2.3 kg.) in a month with acute mooning of the face and deterioration of flexural eczema while receiving 8 mg. daily; treatment was stopped. On returning to prednisolone 15 mg. daily, her weight fell by 15 lb. (6.8 kg.). Dexamethasone (1 mg. daily) subsequently caused an increase in weight of nearly 20 lb. (9 kg.) in three months. Other side-effects included purpura and haematuria (1), dyspepsia (3), vertigo (1), and transient proteinuria* (1), but were mild. Altogether side-effects were observed in seven cases.

Methylprednisolone.—Eight cases were treated, seven for six months or more. Three showed loss of weight of 3–5 lb. (1.4 to 2.3 kg.). Three who had already lost weight while receiving triamcinolone remained constant at the lower level on methylprednisolone. Transient proteinuria and purpura were observed in the same patients who showed this during triamcinolone therapy.

*This patient also showed proteinuria on prednisolone.

One patient complained of swelling of the face and some deterioration of asthma: she reverted to prednisolone after two months.

Dexamethasone.—Twelve patients were treated. Eight reverted to prednisolone within two months. There was an increase in weight in six patients, in contrast to the tendency to lose weight on triamcinolone and methylprednisolone. Two patients gained 28 and 20 lb. (12.7 and 9 kg.) in three months on 1 and 1.5 mg. daily. Two patients complained of sleeplessness, associated with heartburn in one. Another had palpitations and retention of urine which he likened to the effects of ephedrine. Some side-effects were present in six cases.

Discussion

In spite of general agreement that corticosteroids have a temporarily beneficial effect in asthma, there are few references to their short-term use in the treatment of exacerbations in out-patient clinics. Short courses of prednisolone given over a period of seven or eight days have been found to be beneficial in a high proportion of cases: they may abort severe attacks in some patients subject to intermittent asthma, or terminate periods of persistent wheezing occurring after infective episodes. Even repeated courses at intervals of a few weeks over several years have not been associated with harmful side-effects, though some patients have increased in weight. The majority began to improve within 24 hours of taking steroids: many stated that their condition during the last three or four days of treatment had been dramatically improved. Recurrences were not uncommon within a few days of the end of treatment, but these were usually less severe and could be controlled by other means.

The main reasons for failure in individual cases were that the initial dose might be inadequate or that the period of one week was too short for complete control to be achieved. The dosage has to be adjusted to suit the needs of individual patients. Infection of the bronchial tract, with production of purulent sputum, may antagonize the effect of steroids, and in such cases larger doses of these should be given along with antibiotics. It is important to recognize that there may be a delay of 24 to 48 hours before a response is obtained, during which time symptomatic treatment with bronchodilator drugs should be continued. Close medical supervision is obviously necessary, even though in certain instances it may be left to the patient to decide when to initiate treatment.

The assessment of long-term steroid therapy presents considerable difficulty, but, provided regular information is available, it is possible for a reasonable estimate to be made. Such information includes measurement of respiratory function, records of attacks of asthma and of symptomatic remedies other than steroids, together with capacity for work and time lost on account of asthma. Vital-capacity readings have been used as the main measure of respiratory function: in the course of treating patients with cortisone it had been found that the vital-capacity recordings in the main ran parallel to F.E.V.1. Timed vital-capacity readings were, however, made on occasion and latterly measurements of peak flow rate were also recorded. Evidence acquired in this way confirms the findings of others (Phear *et al.*, 1960; Somner *et al.*, 1960) that many patients who have been leading the lives of chronic invalids may be restored to normal activity, and that this improvement may be maintained for a number of years. In the present series seven cases have remained continuously improved for over four years and nine for over three years. No tendency to acquire tolerance to any individual steroid has been observed, and in some cases the maintenance dose has been gradually reduced. Temporary increase in dosage is often necessary. As Lowell *et al.* (1953), Davies and Williams (1955), and Somner *et al.* (1960) have pointed out, infections of the bronchial tract undoubtedly antagonize the effect of steroids and limit their usefulness in asthmatics.

Serious side-effects have not been recorded in this series. Increase in weight, sometimes considerable in extent, has been common, particularly during treatment with prednisolone and dexamethasone; dyspepsia has been controlled by antacids, and in one case by substituting keratin-coated tablets of prednisolone for the usual preparation; there has been no evidence of the development of peptic ulceration. It has been found exceedingly difficult to terminate treatment in those patients who have responded well. All successfully treated cases showed a level of dosage which could be reduced only at the expense of an increase in the number of asthmatic attacks, and consequently in the quantity of other symptomatic remedies employed: a quantitative relationship could in most cases be established between the degree of improvement as measured by vital capacity or reduction in the use of bronchodilator drugs and the daily dose of corticosteroid administered. There was often a similar relationship between the dose of steroid and the gain in weight. Of the seven patients in this series in whom treatment has been gradually terminated, two have died in status asthmaticus within three months of cessation of treatment. Two other patients, not included in this series, who had received treatment with cortisone for six months, also went into severe status asthmaticus shortly after treatment ceased, and one of these died. Asthmatics treated with steroids for six months or more appear to be subject to a special risk of death from the effects of their disease for some time afterwards, and steroids in large doses should be prescribed at once if status asthmaticus develops in such patients; those suffering from other chronic diseases, such as rheumatoid arthritis treatable by steroids, are not exposed to a comparable potentially fatal hazard.

Bearing these facts in mind, this form of treatment appears to be justified in middle-aged or elderly patients with recurrent attacks of status asthmaticus or disability so severe as to prevent working. This group is known to have a poor prognosis with a high mortality (Rackemann, 1940; Leigh and Rawnsley, 1956; Pearson, 1958). It is particularly inadvisable to begin treatment in young people till all other means of controlling their attacks have failed. Nevertheless, the present series includes 11 patients between 10 and 30 years of age; eight of these had had repeated attacks of status asthmaticus, two were chronically disabled, and one was treated primarily for severe flexural eczema associated with relatively mild asthma.

Comparison of the effects of the newer steroids with prednisolone indicated that, although the former were more potent on a weight-for-weight basis, they offered little advantage in the treatment of asthma. Triamcinolone and methylprednisolone sometimes led to beneficial loss of weight in those who had shown a marked increase on prednisolone. Neustadt (1959) has also drawn attention to weight loss, accompanied by weakness, in some cases of rheumatoid arthritis treated with triamcinolone; none of our patients complained

of weakness. Dexamethasone, on the other hand, appeared to favour weight gain and in some cases development of acute Cushingoid changes. Similar observations have been made by others (Falliers and Bukantz, 1959; Friedlaender and Friedlaender, 1959; Neustadt, 1959; Stresemann, 1959). Occasionally patients appeared to respond more favourably to one particular steroid than to others.

Though most of the patients in this series were thought to have responded satisfactorily to steroids while under observation as in-patients or to repeated short courses in out-patients, the failure rate of long-term treatment is high (28%). This may in part be due to the cautious selection of patients who, with one exception, were severely incapacitated and who were regarded as having a poor expectation of life. Arnoldsson (1958) reported the persistence of moderate-to-severe asthma in 20.1% of 144 cases treated with steroids, and Phear *et al.* (1960) reported poor results in 12% and moderate improvement in 10% of 50 cases.

Though reasons for failure, including infection of the respiratory tract, organic disease of the lungs, severe emotional stress, or psychopathic personality, may often be detected, in some cases no satisfactory explanation can be found. Investigation of respiratory function showed that even those who had done best were seldom restored completely to normal. Lowell *et al.* (1953) have made similar observations. In assessing the effect of treatment it is important to remember that relief of symptoms does not necessarily imply restoration of normal respiratory activity.

Although serious side-effects are few it is still too early to assess the final effects of steroid therapy when continued for many years.

Summary

Short courses of steroids given in tapered doses over eight days are often effective in controlling exacerbations of asthma, though relapses are common.

Long-term steroid therapy may in some cases be maintained with continued benefit for a number of years.

If such treatment is terminated after six months or more the patient shows a tendency to relapse severely and sometimes fatally. Particularly careful supervision is therefore required during the ensuing months.

The newer range of modified steroids, though more potent on a weight-for-weight basis, have little advantage over prednisolone.

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JEJUNAL BIOPSY IN MALABSORPTIVE DISORDERS OF THE ADULT

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The terminology of the malabsorptive disorders remains unsatisfactory, and our knowledge of the relationship between coeliac disease in the infant and "idiopathic steatorrhoea" in the adult is by no means complete. Most investigators now consider that tropical sprue is basically a different condition from "idiopathic steatorrhoea," and the latter term is not regarded as a satisfactory designation for the non-tropical disorder. The term "sprue syndrome" has been used in relation to all these conditions, and the more embracing phrase, "malabsorption syndrome," is often employed to include not only these disorders but numerous others which may result in clinical features commonly found in patients with intestinal malabsorption of the "sprue" type. However, the term "malabsorption syndrome" is clearly unsatisfactory, since the clinical features vary so greatly that the word "syndrome" is inappropriate.

The introduction of a peroral method of jejunal biopsy by a modification of Wood's gastric biopsy tube (Shiner, 1956) or by a biopsy capsule (Crosby and Kugler, 1957) is a great advance which is likely to increase our knowledge considerably, particularly if a satisfactory peroral method of ileal biopsy can also be developed.

The Literature

Paulley (1954) reported mucosal atrophy in the small intestine of four patients with idiopathic steatorrhoea. The specimens were obtained at laparotomy. Shiner (1959), analysing her material obtained over a period of three years, reported that two types of mucosal abnormality might be found in the steatorrhoea group of disorders. Subtotal villous atrophy, with short and flat or non-existent villi, occurred in 21 patients with idiopathic steatorrhoea, in one with tropical sprue, and in one with post-gastrectomy steatorrhoea. Partial villous atrophy, with short clubbed villi, was found in two patients with idiopathic steatorrhoea, in one with post-gastrectomy steatorrhoea, in two with tropical sprue, in one with tuberculous enteritis, in one with the "loop syndrome," and in one with malnutrition and steatorrhoea.

Fone *et al.* (1960) gave the results of jejunal biopsy in 58 patients with "idiopathic steatorrhoea." Of these, 27 were considered to have a "flat" mucosal appearance with absent villi. In another 27 cases there were "abnormal villi" that were short, broad, and squat. In patients with the flat appearances the main presenting feature was diarrhoea, while severe anaemia was not a feature and malabsorption of cyanocobalamin was rare. In the patients with "abnormal villi" the main features were malaise and mild diarrhoea or severe anaemia of relatively short duration. Colicky abdominal pains were a feature in some patients. Malabsorption of cyanocobalamin was not infrequent.