Steroid-induced Psychiatric Syndromes
A Report of 14 Cases and a Review of the Literature

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(Received 8 February, 1983)
(Accepted 10 March, 1983)

Summary

Although it is well-established that psychiatric symptoms can develop in association with the administration of corticosteroids, the nature of this relationship is poorly understood. We reviewed 14 previously unreported cases of steroid-induced psychiatric syndromes, 79 cases from the literature and 29 studies of the clinical efficacy of steroids in various medical illnesses. Our findings indicate that severe psychiatric reactions occur in approximately 5% of steroid-treated patients, and that a large proportion of these patients have affective and/or psychotic symptoms. Psychiatric disturbances usually occur early in the course of steroid therapy. Female sex, systemic lupus erythematosus and high doses of prednisone may be risk factors for the development of a steroid-induced psychiatric syndrome. Treatment with steroid-taper, neuroleptics or electroconvulsive therapy is generally effective, although tricyclic antidepressants do not appear to be useful therapeutic agents. Most patients recover within several weeks of the onset of symptoms.

Introduction

The occurrence of psychiatric symptoms in association with the clinical use of corticosteroids and adrenocorticotropic hormone (ACTH) has been documented since the introduction of steroids as therapeutic agents over 30 years ago. However, the nature of this relationship has been difficult to evaluate. There are some studies in the literature which address limited aspects of this problem, but there are no adequately controlled comprehensive studies of the psychiatric effects of steroid therapy. Consequently, we reviewed case records at the University of Iowa Hospitals, previous case reports and other sources of information in the literature in order to improve our understanding of these disorders.
Methods

Review of the University of Iowa Hospital records from July 1976 through June 1981 revealed 14 cases of significant psychiatric syndromes occurring in association with the administration of steroid therapy. From a review of the case notes and the consulting psychiatrist's evaluation we were able to obtain the following information about each patient: age; sex; history of previous psychiatric illness; premorbid adjustment and personality characteristics; medical indication for steroid treatment; type, dose and duration of steroid treatment; history of other courses of steroid therapy; type and duration of psychiatric symptoms; response to treatment; outcome.

Review of the literature (Borman and Schmallenberg 1951; Galdston et al. 1951; Brody 1952; Clark et al. 1952; 1953; Cleghorn 1952; Lidz et al. 1952; Ritchie 1952; Rome and Braceland 1952; Glaser 1953; Toone and Irby 1955; Stern and Robbins, 1960; Train and Winkler 1962; Garner and Falk 1967; Baloch 1974; Villareal et al. 1974; Gilles and Shellshear 1975; Sergent et al. 1975; Blazer et al. 1976; Hall et al. 1979; Pies 1981; Kaufmann et al. 1982), revealed a total of 102 case reports of psychiatric symptoms occurring in association with the use of steroids. Twenty-three cases were excluded from further analysis. In two cases the development of psychiatric symptoms was more clearly associated with the withdrawal, than with the administration, of steroids (Clark et al. 1952; Ritchie 1952). One case was excluded because steroids were administered in an attempt to treat a psychotic disturbance (Rome and Braceland 1952). Sixteen cases were excluded because the case records revealed only mild isolated psychiatric symptoms without evidence of a recognizable psychiatric syndrome, or because the amount of data recorded was inadequate to make further analysis possible (Clark et al. 1952; Stern and Robbins 1960; Blazer et al. 1976). The remaining 79 case reports were reviewed for the same information noted above. A complete set of such data was not available in every case.

In an attempt to find additional information about the incidence and other aspects of steroid-induced psychiatric syndromes, we also reviewed 29 studies of the clinical efficacy of corticosteroids and ACTH in various medical illnesses. In these studies, the authors commented, in varying amounts of detail, on the occurrence of psychiatric side effects.

Parametric data were analyzed with the Student t-test, using Cochran's method for unequal variances when necessary. Categorical data were analyzed with the chi-square test, Fisher's exact test or McNemar's exact test, as indicated (Rosner 1982).

Results

Incidence

In 11 uncontrolled studies (Margolis and Caplan 1951; Ward et al. 1951; Goolker and Schein 1953; Taran et al. 1953; Engleman et al. 1954; De la Riva 1958; Kirsner
et al. 1959; Nielsen et al. 1963; Treadwell et al. 1964; Cass et al. 1966; Rosenberg et al. 1976) involving 935 patients, the incidence of psychiatric symptoms was found to vary from 13% to 62% with a weighted average of 27.6%. Although the types of psychiatric symptoms were not specified in some studies, most of these symptoms appear to have been mild to moderate changes in mood without the development of a full affective syndrome. Other uncontrolled studies (Margolis and Caplan 1951; Bunim et al. 1955; Toone and Irby 1955; Kirsner et al. 1959; Cass et al. 1966; Hall et al. 1967; Marx and Barker 1967; Michael et al. 1967; Smyllie and Connolly 1968; Hayreh and Watson 1970; Cade et al. 1973; Sergent et al. 1975; Rosenberg et al. 1976) involving 2,555 patients, report the frequency of occurrence of severe psychiatric syndromes, or constellations of significant psychiatric symptoms. In these studies the incidence of psychiatric syndromes ranged from 1.6% to 50% with a weighted average of 5.7%. There was no difference ($\chi^2 = 0.167, df = 1, P > 0.50$) in average incidence when the studies reported before 1960 (5.4%) were compared with later studies (5.8%).

Further information regarding the incidence of psychiatric syndromes, as well as the causal nature of steroids in producing these reactions, can be found in 4 controlled studies in the literature. Kirsner et al. (1959) reported on 240 patients with ulcerative colitis who were treated with several different steroid preparations. Using the patients as their own controls, these investigators found that whereas 4.2% of the patients had experienced a psychotic disturbance at some time in their life prior to the initiation of steroid therapy, 6.3% suffered a psychotic disturbance while receiving steroids. Marks and Barker (1967) also studied patients with ulcerative colitis. Of 50 such patients who were treated with steroids, 12% experienced a psychotic disturbance, whereas only 2.6% of 80 control patients had similar reactions.

Smyllie and Connolly (1968) reviewed the case records of 550 patients who had been treated with steroids for various respiratory diseases. They compared these patients with 499 patients who had not received steroids over the preceding year. The 2 groups were approximately matched for age, sex, type of illness, and year of entry to hospital. Mental disturbance, defined as “serious enough to require psychiatric advice and treatment”, was found in 1.8% of the steroid-treated group and in 3.2% of the control group. This difference was not statistically significant ($\chi^2 = 2.09, df = 1, P > 0.10$).

The clearest evidence that steroids produce psychiatric disturbances was reported in a study of patients with lupus nephritis who were randomly assigned to 4 treatment groups, 2 of which involved the use of prednisone (Cade et al. 1973). “Overt psychoses” developed in 32% of the prednisone treated patients and in only 3.8% of the patients who did not receive prednisone. This finding was highly statistically significant (Fisher’s exact test, $P = 0.012$).

**Types of psychiatric syndromes**

As previously mentioned, changes in mood or affect, such as mild euphoria or depression, are the psychiatric symptoms most frequently seen in association with steroid use. There are no clearly satisfactory methods of categorizing the psychiatric
syndromes seen in association with steroids, in large part because the presence and severity of individual symptoms can fluctuate dramatically during the course of the illness (Hall et al. 1979). One approach to classifying these disorders is to define them on the basis of the predominant psychiatric syndrome seen during the course of the illness. Table 1 lists the frequency of different types of predominant psychiatric syndromes seen in the 79 case reports in the literature. Depression is the most common psychiatric disturbance, accounting for over 40% of the cases, and over 75% of the patients suffered from an affective syndrome. Ten percent of the patients had a delirium characterized by a clouding of consciousness, disorientation, changes in psychomotor activity, and rapid fluctuations in symptoms. Fourteen percent of the cases suffered from a psychotic disorder without evidence of a significant mood change or features of a delirium. Disturbance in reality testing was present in 71% of the patients, whereas 29% had no evidence of psychotic features.

This high incidence of affective syndromes and of psychotic features is confirmed by our findings that among 14 cases, 8 suffered from an affective syndrome and 9 had psychotic features (Table 2). However, our series differs from the previous case reports in that a manic syndrome (50%) was much more commonly seen in our patients than was a depressive syndrome (7%). This difference was statistically significant (Fisher's exact test, \( P = 0.021 \)).

**Duration of steroid treatment**

In our series, the duration of treatment with steroids before the onset of psychiatric symptoms ranged from 1 day to 54 days (Table 2). The median duration of treatment was 11 days. Forty-three percent of the cases developed symptoms during the first week of treatment, 57% within the first 2 weeks, and 93% within 6 weeks of the initiation of steroid therapy. These figures are very comparable to those obtained from the 70 case reports in the literature which documented the necessary

<table>
<thead>
<tr>
<th>Psychiatric syndrome</th>
<th>Psychotic features</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Depression</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Mania</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Depression/mania</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Psychosis</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Delirium</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>56</td>
<td>23</td>
</tr>
</tbody>
</table>
information. Although the range of duration of treatment before the onset of symptoms was greater in the cases in the literature (1 day–210 days), the median was very similar (11.5 days). In addition, symptoms developed in 39% of the cases within the first week of treatment, in 62% of the cases within the first 2 weeks of treatment, and in 89% of the cases within the first 6 weeks of steroid treatment.

**Steroid dose**

Evidence regarding the relationship of the dose of a specific steroid, prednisone, to the development of a psychiatric syndrome is summarized in Table 3. The dose-response effect of prednisone on the induction of psychiatric symptoms was most clearly demonstrated in the Boston Collaborative Drug Surveillance Project (1972) in which 676 patients who received prednisone therapy were evaluated for the development of acute psychiatric syndromes. These investigators found a statistically significant increased incidence of psychiatric disturbances with increasing average daily doses of prednisone (Table 3). Subsequent studies by Sergent et al. (1975) and Rosenberg et al. (1976), as well as a collection of 22 case reports in the literature (Train and Winkler 1962; Gilles and Shellshear 1975; Sergent et al. 1975; Blazer et al. 1976; Garner and Falk 1967; Hall et al. 1979; Pies 1981; Kaufmann et al. 1982) appear to substantiate these findings (Table 3). The evidence from our series also supports this dose-response effect; only 23% of the patients had been receiving less than 40 mg/day of prednisone before the onset of symptoms, whereas 77% had been receiving greater than 40 mg/day. Combining our case reports with those in the literature, we were unable to find any significant correlation between the average daily dose of prednisone and the duration of treatment before the onset of symptoms, the duration of symptoms or the type of psychiatric syndrome.

**Other courses of steroid therapy**

Although our sample size was too small to investigate this issue, the combination of our case reports with those previously reported in the literature (Clark et al. 1952; Clark et al. 1953; Glaser 1953; Train and Winkler 1962; Baloch 1974; Sergent et al. 1975) produced a total of 17 patients with a steroid-induced psychiatric syndrome who had received other courses of steroid therapy. Six of these patients had experienced severe psychiatric symptoms during other courses of steroid therapy, whereas 11 patients had not. Statistical analysis, comparing the response to the first course of steroid treatment with the response to the second course, provided no evidence that the presence or absence of a psychiatric disturbance during the initial course of steroid treatment predicted the response to a subsequent course of treatment (McNemar's exact test, \( P = 0.79 \)).

**Age**

The patients in our series tended to be slightly older (mean age 50 years) than those patients which had previously been reported in the literature (mean age 38 years). When all cases were considered together the age ranged from 8 years to 71 years with a mean of 39.6 years. This age distribution is very similar to the range (4–84 years) and mean (42.7 years) age found in over 1400 patients treated with
<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Past psychiatric history</th>
<th>Premorbid personality</th>
<th>Medical illness</th>
<th>Steroid treatment</th>
<th>Other treatment</th>
<th>Psychiatric syndromes</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62</td>
<td>M</td>
<td>N</td>
<td>NL</td>
<td>Kidney transplant</td>
<td>Prednisone 29</td>
<td>N</td>
<td>Mania Y</td>
<td>Haloperidol</td>
<td>Recovery</td>
</tr>
<tr>
<td>2</td>
<td>61</td>
<td>F</td>
<td>N</td>
<td>ABNL</td>
<td>Idiopathic</td>
<td>Prednisone 40</td>
<td>N</td>
<td>Depression Y 60</td>
<td>Steroid taper</td>
<td>No effect</td>
</tr>
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<td>3</td>
<td>48</td>
<td>F</td>
<td>N</td>
<td>NL</td>
<td>Asthma</td>
<td>Prednisone 60</td>
<td>N</td>
<td>Mania N 14</td>
<td>Recovery</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>62</td>
<td>M</td>
<td>N</td>
<td>ABNL</td>
<td>Crohn's disease</td>
<td>Prednisone 60</td>
<td>N</td>
<td>Mania Y 23</td>
<td>Recovery</td>
<td></td>
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<td>5</td>
<td>58</td>
<td>F</td>
<td>N</td>
<td>NL</td>
<td>COPD</td>
<td>Prednisone 60</td>
<td>N</td>
<td>Delirium N 7</td>
<td>Recovery</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>F</td>
<td>N</td>
<td>ABNL</td>
<td>Asthma</td>
<td>Prednisone 60</td>
<td>N</td>
<td>Mania Y 27</td>
<td>Recovery</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>48</td>
<td>M</td>
<td>Y</td>
<td>NL</td>
<td>Lung cancer</td>
<td>Dexamethasone</td>
<td>Y</td>
<td>Mania Y 21</td>
<td>Recovery</td>
<td></td>
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<tr>
<td>8</td>
<td>53</td>
<td>F</td>
<td>N</td>
<td>ABNL</td>
<td>Asthma</td>
<td>Prednisone 100</td>
<td>Y</td>
<td>Mania N 30</td>
<td>Recovery</td>
<td></td>
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<tr>
<td>Case</td>
<td>Age</td>
<td>Sex</td>
<td>Race</td>
<td>Diagnosis</td>
<td>Duration of Treatment</td>
<td>Psychiatric Symptoms</td>
<td>Treatment</td>
<td>Recovery</td>
<td></td>
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<tr>
<td>9</td>
<td>22</td>
<td>F</td>
<td>N</td>
<td>NL</td>
<td>Prednisone 70</td>
<td>Psychosis Y</td>
<td>Steroid taper</td>
<td>Recovery</td>
<td></td>
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<td>10</td>
<td>18</td>
<td>F</td>
<td>N</td>
<td>ABNL</td>
<td>Prednisone 60</td>
<td>Psychosis Y</td>
<td>None</td>
<td>Recovery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>53</td>
<td>M</td>
<td>N</td>
<td>NL</td>
<td>Prednisone 97</td>
<td>Mania Y</td>
<td>Steroid taper</td>
<td>Recovery</td>
<td></td>
<td></td>
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<tr>
<td>12</td>
<td>62</td>
<td>M</td>
<td>Y</td>
<td>ABNL</td>
<td>Prednisone 20</td>
<td>Delirium Y</td>
<td>Lithium carbonate</td>
<td>Recovery</td>
<td></td>
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<tr>
<td>13</td>
<td>71</td>
<td>M</td>
<td>N</td>
<td>NL</td>
<td>Prednisone 60</td>
<td>Delirium N</td>
<td>Steroid taper</td>
<td>Persistent memory impairment</td>
<td></td>
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<tr>
<td>14</td>
<td>36</td>
<td>M</td>
<td>N</td>
<td>NL</td>
<td>Prednisone 48</td>
<td>Delirium N</td>
<td>Steroid taper</td>
<td>Recovery</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ABNL = abnormal; COPD = chronic obstructive pulmonary disease; NL = normal.

a Duration of treatment before the onset of psychiatric symptoms.

b Cases 7 and 12 developed a psychiatric syndrome during other courses of steroid therapy; cases 8, 9, and 14 did not.
TABLE 3
DOSE-RESPONSE EFFECT OF PREDNISONE ON THE INDUCTION OF PSYCHIATRIC SYNDRomes

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Mean dose (mg/day)</th>
<th>(%) with psychiatric syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt; 40</td>
<td>41-80</td>
</tr>
<tr>
<td>The Boston Collaborative Drug</td>
<td></td>
<td>(1.3)</td>
<td>(4.6)</td>
</tr>
<tr>
<td>Surveillance Program 1972</td>
<td>676</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sergent et al. 1975</td>
<td>28</td>
<td>&lt; 40</td>
<td>41-80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(33)</td>
<td>(50)</td>
</tr>
<tr>
<td>Rosenberg et al. 1976</td>
<td>107</td>
<td>&lt; 100</td>
<td>101-180</td>
</tr>
<tr>
<td>Case reports</td>
<td>22</td>
<td>&lt; 20</td>
<td>21-40</td>
</tr>
<tr>
<td>Ul cases</td>
<td>13</td>
<td>&lt; 20</td>
<td>21-40</td>
</tr>
</tbody>
</table>

*In the Rosenberg et al. (1976) study the dose of prednisone represents the maximum daily dose of prednisone; the mean daily dose was not reported.

b In the case reports sections, the figures in parentheses represent the percent of cases receiving that average daily dose of prednisone.

steroids in various clinical trials (Margolis and Caplan 1951; Goolker and Schein 1953; Levin et al. 1953; Bunim et al. 1955; Kirschner et al. 1959; Treadwell et al. 1964; Michael et al. 1967; Hayreh and Watson 1970; The Boston Collaborative Drug Surveillance Program 1972; Cade et al. 1973; Chan et al. 1981). The striking similarity in age distribution between these two groups suggests that age is not a risk factor for the development of a steroid-induced psychiatric syndrome.

Sex

There were an equal number of males and females among our 14 cases. However, of the 79 cases reported in the literature, 68% were females and only 32% were males. When cases with systemic lupus erythematosus (SLE) or rheumatoid arthritis (which have 9:1 and 3:1 female-to-male ratios, respectively) were excluded, there was still a female predominance (58% vs. 42%), although it was less marked.

More convincing evidence that the incidence of steroid-induced psychiatric syndromes is higher in females can be found in a review of clinical trials in which the incidence of psychiatric syndromes was reported by sex (Boland 1951; Taran et al. 1953; Bunim et al. 1955; Toone and Irby 1955; Nielsen et al. 1963; Cade et al. 1973). In these studies, 19.7% of steroid-treated females developed a psychiatric disturbance, whereas only 3.3% of the males did. This difference was highly statistically significant ($\chi^2 = 16.9, df = 1, P < 0.001$). This finding remained highly significant, (17.3% versus 2.6%) even when patients with SLE were excluded.

Coexistent medical illness

The incidence of psychiatric syndromes in patients who receive steroid therapy
for SLE (Drinkard et al. 1970; Cade et al. 1973; Sergent et al. 1975) or pemphigus (Rosenberg et al. 1976) is 32.9% and 20.6%, respectively. Both these incidence rates are significantly higher \((P < 0.001)\) than the 5.7% incidence seen when all diseases are considered together. The incidence of steroid-induced psychiatric syndromes in patients with lymphoma (Hall et al. 1967), multiple sclerosis (Cass et al. 1966), ulcerative colitis (Kirsner et al. 1959; Marx and Barker 1967), or rheumatoid arthritis (Boland et al. 1951; Margolis and Caplan 1951; Levin et al. 1953; Bunim et al. 1955; Toone and Irby 1955) does not significantly differ from the expected incidence.

**Past psychiatric history and premorbid personality**

None of our 14 cases had a past history of psychiatric illness unrelated to steroid therapy. Six (43%) were thought to have evidence of a premorbid personality disorder. Among 41 cases in the literature, 17% had a prior history of psychiatric illness unrelated to steroids. Fifty-two percent of 29 cases were reported to have had an abnormal premorbid personality. No comparable control data were available which could be used to determine whether past psychiatric illness or premorbid personality disturbances were risk factors for the development of a steroid-induced psychiatric syndrome.

**Duration of psychiatric syndromes**

Among our cases the duration of symptoms ranged from 2 days to 60 days, with a mean of 21.0 days, irrespective of treatment. In 56 cases from the literature, the duration of symptoms ranged from 1 day to 150 days, with a mean of 22.0 days. Among these 56 cases, 38% had symptoms lasting less than one week, 55% less than 2 weeks, and 93% less than 6 weeks.

When all 68 cases were considered together, patients who developed a delirium had a significantly shorter duration of symptoms (mean ± SD 5.4 ± 3.7 days) than did patients with either a depressive (26.7 ± 36 days) or manic (23.8 ± 18 days) reaction \((P < 0.05)\). There were no statistically significant differences in the duration of symptoms among the depressive, manic or psychotic (19.3 ± 18.8 days) groups.

**Outcome**

Ninety-three percent of our cases had a complete recovery from their steroid-induced psychiatric syndrome; 1 patient (case 13) continued to have some mild impairment in cognitive function during the time of follow-up. Among the cases in the literature for which outcome was specified, 93% had a complete recovery, 4% had continued or recurrent psychiatric symptoms, and 3% committed suicide.

**Treatment response**

Table 2 lists the response to various forms of treatment among our cases. When our cases were combined with those in the literature, we found that clinical recovery occurred in 92% of 36 patients treated with steroid taper only, 84% of 25 patients who received neuroleptics only, 100% of 8 patients treated with neuroleptics and steroid taper or lithium, and 100% of 11 patients who received electroconvulsive
therapy. However, none of the 6 patients who received tricyclic antidepressants improved with that therapy.

Discussion

Our review of 29 studies of the clinical efficacy of corticosteroids in medical illness revealed the average incidence of steroid-induced psychiatric syndromes to be 5.7%, with a maximum incidence of 50%. These findings are quite similar to those reported in a review of the literature over 20 years ago (5% and 58%, respectively) (Smyth et al. 1960). These similarities suggest that the overall incidence of these disorders has not changed despite differences in the types of steroids used, or other changes in prescribing practices. The variation in incidence among the studies is probably due to a number of factors including steroid dose, sex distribution of patients, underlying medical illness and definition of severe psychiatric disturbance.

The causal nature of corticosteroids in producing psychiatric syndromes is apparent from the controlled studies in the literature, 3 of which demonstrated a higher incidence of psychiatric syndromes in steroid-treated patients than in controls (Kirsner et al. 1959; Marx and Barker 1967; Cade et al. 1973). Smyllie and Connolly (1968) did not find a higher incidence of mental disturbance in their steroid-treated patients; however, over 94% of their patients were receiving less than 20 mg/day of prednisone. Because there is a dose–response effect of prednisone on the induction of psychiatric symptoms, this finding suggests that their steroid-treated patients would not be expected to have a significantly higher risk of developing a psychiatric disturbance than their controls.

The distribution of types of psychiatric syndromes found in our review of 79 cases in the literature is very similar to that reported by Ling et al. (1981). These authors found that among 55 anecdotal cases (of which 46 were included in our 79 cases), 40% had a depressive syndrome, 31% had a manic syndrome, 11% had both manic and depressive symptoms and 16% experienced acute psychotic reactions. Our findings also confirm the high incidence of psychotic features (58%) found by these authors.

In our 14 cases, a manic syndrome was more commonly seen than was a depressive syndrome. This difference might possibly be related to the higher frequency of prednisone use in these 14 cases (93%) than in the cases from the literature (24%). However, among the 22 cases in the literature in which prednisone was used, the incidence of a depressive syndrome was 45.5% and the incidence of a manic syndrome was 36.4%. This finding demonstrates that prednisone administration is not associated with a greater frequency of manic reactions than is the administration of other types of steroids. Since most of our cases were identified because they had been referred for psychiatric consultation, a more plausible explanation of our findings may be that nonpsychiatric physicians feel more comfortable managing a depressive syndrome than a manic one.

Our 14 cases and those in the literature suggest that adverse psychiatric reactions to steroid therapy usually occur early in the course of treatment. This pattern is also
confirmed by the report of Smyllie and Connolly (1968) who observed that during a 3-year follow-up of patients receiving steroids, most of the psychiatric reactions occurred within the first month of treatment. This time clustering of psychiatric symptoms may be due to the dose–response effect of steroids and consequently it may reflect the prescribing pattern for steroids; that is, steroids are frequently administered with an initial large dose and subsequent tapering of the daily dose.

Although early investigators were unable to find any consistent relationship between the dose of steroids and the onset of psychiatric disorders (Goolker and Schein 1953), it is clear from the evidence summarized in Table 3 that increasing doses of at least one steroid, prednisone, are associated with an increased risk of a psychiatric reaction. Our failure to find any significant correlation between the average daily dose of prednisone and the duration of treatment before the onset of symptoms, the duration of symptoms or the type of psychiatric syndrome is consistent with the findings of other investigators (Clark et al. 1953; Glaser 1953).

The lack of association between the psychiatric responses to the first and second courses of steroid treatment demonstrated in this study confirms the opinions of other investigators (Clark et al. 1953; Guze 1967; Hall et al. 1979). This finding implies that the presence or absence of a psychiatric reaction to a previous course of steroids is not helpful diagnostically in assessing patients who develop psychiatric symptoms while receiving steroids. In addition, this evidence suggests that it is not reasonable to withhold further steroid therapy solely on the basis of a history of a steroid-induced psychiatric disturbance.

Age does not appear to be a risk factor for the development of steroid-induced psychiatric syndromes. However, females do appear to be at higher risk than males. This difference cannot be explained by the higher incidence of a predisposing medical illness (SLE) in females. It was not possible though to control for a possible influence of steroid dose on the higher incidence of steroid-induced psychiatric syndromes seen in females.

Patients with SLE clearly have a higher incidence of psychiatric disturbances in association with steroid administration than do patients with other medical illnesses. Although psychiatric symptoms can be a manifestation of SLE alone, Cade et al. (1973) clearly demonstrated a significantly higher incidence of psychiatric reactions in patients with SLE who received steroid therapy than in controls. Thus, although steroid treatment is not a necessary nor a sufficient cause for the development of psychiatric symptoms in patients with SLE, these two factors are additive in producing a higher incidence of psychiatric symptoms than would be seen in the presence of either factor alone. It should be noted though, that the possible influence of sex or steroid dose could not be controlled for in this analysis.

It is not possible to determine from our data whether past psychiatric illness or premorbid personality disturbances are risk factors for the development of a steroid-induced psychiatric syndrome. Although some early investigators felt that a history of psychosis was a contraindication to steroid therapy (Copeman et al. 1954), other investigators found no evidence that prior psychiatric illness predisposed patients to the development of a mental disturbance during steroid therapy (Clark et al. 1952, 1953; Lewis and Fleminger 1954; Hall et al. 1979). The only controlled
data on this topic were reported by Goolker et al. (1953) who found no differences among 3 categories of premorbid personality adjustment in the incidence of mental disturbances during steroid therapy.

Although some patients have a protracted course, over 50% of cases recover within 2 weeks and over 90% are well within 6 weeks of the onset of symptoms. Patients with a delirium have a significantly shorter duration of symptoms than do patients who develop an affective syndrome.

Our data, as well as that previously reported in the literature, indicate that most patients with a steroid induced psychiatric syndrome experience a complete recovery, although a small percentage of patients have persistent symptoms. The outcome data also indicate that suicide potential must be carefully assessed in these patients. Treatment with steroid-taper, neuroleptics or electroconvulsive therapy, depending on the clinical picture, is generally effective in these patients. However, tricyclic antidepressants do not appear to be useful therapeutic agents, and may actually exacerbate the symptoms induced by steroids (Hall et al. 1978). Prophylactic treatment with lithium carbonate has been reported in a single study to be useful in decreasing the incidence of steroid-induced psychiatric syndromes (Falk et al. 1979).

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