PSYCHOSES ASSOCIATED WITH
INFLUENZA

I. GENERAL DATA: STATISTICAL ANALYSIS *

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Sir William Osler\(^1\) succinctly remarks that apparently "almost every form of disease of the nervous system may follow influenza." This postulate is seemingly quite justified by the accretion of neuropsychiatric data from cases in the recent pandemic. The frequency of mental disturbances accompanying the acute illness in the epidemic has been the subject of frequent comment, and the wave of psychiatric material that followed in its wake was unexpectedly large and correspondingly interesting.

The literature on the mental diseases associated with influenza is remarkable for its paucity and the inadequacy of the communications, and this well applies to toxic psychoses in general. Bonhoeffer\(^2\) considered authoritative on the subject, ascribed this in a measure to the fact that "for most part communications concerning the psychoses accompanying or following infectious disease proceed from the pens of others than psychiatrists. . . . A practical knowledge of the frequency and nature of the (mental) diseases encountered can only be learned from material that includes both internal and mental diseases."

Precisely because of the latter point, the Psychopathic Hospital affords unusual and highly desirable opportunities for the study and evaluation of data concerning the influenzal psychoses. Not only are many cases sent to the Psychopathic Hospital seen early in the course of the mental disease, but in all instances careful collateral study is made from the physical, serologic and social standpoints. The average influenza patient cared for at home is not seen by a psychiatrist; the average institutional patient is usually seen late in the course of the mental disease, long after aid from the physical side is practicable.

For these reasons the series of cases observed at the Boston Psychopathic Hospital during the recent epidemic are of particular importance. This institution serves a varied function in the community, but primarily it is a clearing house for cases of mental disease, and above all for the study of incipient (or borderline) mental cases. All of the cases here presented were regularly admitted patients, affording a certain definite uniformity of methods of study of the clinical material.

DIAGNOSTIC METHODS

A word is in place as to the methods used in the diagnosis of the "influenza" and of the "psychosis." As to the former, the statement of the attending physician, substantiated by the descriptions offered by the family or friends, was in most cases the chief evidence. In a considerable number we were able to make or confirm the diagnosis intramurally. In a few instances we have only the patient's word. For the accuracy of these we have no criterion or proof. On the other hand, the ubiquity of the disease, the singularity of its symptoms and course, and the absence of intercurrent epidemics in Boston at that time make the diagnosis of an acute febrile illness of short duration with respiratory tract symptoms and disproportionate prostration comparatively simple. Finally, it is certain that the percentage of error in the diagnosis is under the circumstances probably less than the average error in diagnosis of acute illness of all kinds, at all times, by all physicians.\(^3\)

The psychiatric diagnoses in the Psychopathic Hospital are arrived at after this fashion. On the fifth day of the patient's stay, the case is presented to the entire staff by one of its members with the complete data of outside history, mental, physical and serologic examinations, and the special examinations, such as spinal fluid, roentgenographic, clinical chemistry, ophthalmoscopic and psychometric. At this time a preliminary diagnosis is made by vote. In a few cases this diagnosis is changed by or after the tenth day when the reconsideration of doubtful cases is made, usually at staff conference.

I hold no brief for the diagnostic ability of the staff of this hospital. I am glad to be able to refer to the statistical investigations of Lowrey,\(^4\) the well substantiated conclusion of which is that the diagnoses made here are in some 85 per cent. correct (as measured by longer observation in other institutions).

STATISTICAL DATA

The epidemic appeared in Boston about September 15. From that time until December 15, a period of three months, 100 cases of mental disturbance associated with influenza were admitted here. Of these 100, data are complete on only eighty, and except for some general statistics it is the latter number which is considered.

\(^*\) From the Psychopathic Hospital, series of 1918.
\(^1\) Osler, William: Principles and Practice of Medicine, New York, 1915.
\(^2\) Bonhoeffer, K., in Aschaffenburgs Handbuch, Leipzig and Vienna, 1912.
\(^3\) Lowrey, L. G.: An Analysis of the Accuracy of Psychopathic Hospital Diagnoses, Am. J. Insanity, to be published.

Diagnostic Groups.—For the sake of statistical convenience and clarity it is desirable to introduce here a diagnostic grouping which will be elaborated on later in the paper. The psychiatric diagnoses in this series of cases vary, of course, within wide limits, including nine of Southard’s eleven major groups of mental disease. On the basis of numerical preponderance, however, they are readily classifiable into four groups:

Group I comprises those cases generally agreed to be states of delirium, dependent on the acute infection. “Infection-toxin delirium” seems to me better than the recognized reversal of the phrase, namely, “toxic-infectious,” since from the name the latter may legitimately be interpreted to include incidents of delirium tremens superimposed on pneumonia.

Group II comprises the cases of frank dementia praecox.

Group III comprises the other forms of psychoses encountered which were thought to fit more or less precisely the generally recognized entities.

Group IV comprises the cases in which there was enough doubt or difference in opinion on the part of the staff to justify leaving the case unclassified. That is to say, this is a group in which we did not feel certain of any one diagnosis.

On the basis of this grouping, the numerical incidence of the cases was as shown in Table 1 and Chart 1.

The large size of Group IV will be remarked. It is here appropriate to point out that in many of these cases time will be the great diagnostician. Already one of the patients included in that group has returned to the hospital with this time a clear picture of dementia praecox. A forecast of probabilities, to be accepted only at its face value, is chiefly interesting in its confirmation of the results in the established groups. In other words, the indications from the unclassified group would seem only to augment in numbers the tendencies pointed to by the data of Groups I, II and III. Thus of that group, at the present time, three cases seem most likely to have been forms of delirium and three of dementia praecox; six cases are between those two diagnoses, and the remaining four cases are of other types. On a basis of probabilities, the totals of the eighty cases, plus the probabilities in the remaining twenty cases of the hundred, are presented in Table 2 and in Chart 1.

From Tables 1 and 2 there appears at once the most conspicuous and remarkable fact of the present data. This is the unexpected frequency of dementia praecox as a postinfluenzal psychosis. It occurred more frequently in this hospital than all other psychotic forms combined, delirium excluded, and even more frequently than the delirium which should be the most common. In the latter cases, however, the fallacy is quite obvious, since the great majority of deliria are never sent to a hospital for mental diseases. In fact, it may be parenthetically remarked that some authors do not recognize delirious states as psychoses, the chief reason being, however, that there is no established definition of psychosis, rather than that the nature of delirium is not appreciated. However, the strength of the first comparison is undiminished, and becomes more remarkable on further consideration. This is, of course, necessary, since not all of the cases of dementia praecox were storms from a clear sky. The matter will be considered in detail below.

Sex.—The 100 cases comprise forty-three males and fifty-seven females. The eighty cases more extensively studied comprise thirty-four males and forty-six females. In both groups the proportions are the same, the females preponderating by 57 per cent. to 43 per cent.

On the basis of the tentative groupings detailed above, the sexual distribution appears as in Table 3. The chief deduction from this table is the predominance of the female sex in the patients presenting the picture of dementia praecox. Relative equality obtains
elsewhere despite the influence of alcohol in augmenting the proportion of males in Group III (e.g., acute alcoholic psychoses).

Age.—The age range was from 16 to 69, the youngest patient being a male, the oldest a female. The youngest woman was 18, the oldest man 61. The average of all was 31.7 years, without marked differences in the sexes (e.g., for Group I, males, thirty-three; females, thirty-one).

The average ages of patients in the diagnostic groups appear in Table 4. There is a statistical suggestion from this table of the bizarre hypothesis that the age is a factor in the determination of the form of resultant psychosis. Thus below, say 18, no serious mental complication is common. In the succeeding decade the tendency is toward the development of dementia praecox; in the next decade, toward some other psychotic entity. It is not pretended that this theory is to be taken entirely, but neither is it wholly to be ignored. Nothing that contributes to the further elucidation of the question, "Why does a specific individual develop dementia praecox?" should fail to receive consideration.

Time Factors.—The two principal considerations concerning temporal factors are the duration of the influenza, particularly in relation to the psychoses engendered, and the chronology of the influenza and respective psychoses.

Taking up first the matter of the duration of the influenza, we at once encounter a large factor of unreliability. In the first place, there might be some theoretical objections to the designation of any particular moment as the terminal moment of a specific attack of influenza.

This can be pragmatically circumvented by assuming that the influenza terminates when the fever abates, that is, when the temperature returns to normal and there remains. Not only, however, are many of the patients not informed by their physicians of the precise date of this termination, but in not a few cases the physicians themselves evidently did or do not know. However, the difficulty was actually more apparent than real, because in most cases in which it was not known it could be estimated from the relative time spent in bed, the subjective symptoms, etc.

TABLE 5.—DURATION OF ATTACKS OF INFLUENZA, FROM HISTORIES

<table>
<thead>
<tr>
<th>Uncomplicated Influenza:</th>
<th>Range of duration</th>
<th>From 2 to 17 days</th>
<th>Average duration (59 cases averaged)</th>
<th>6 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza with Known Pneumonia:</td>
<td>Range of duration</td>
<td>From 3 to 25 days</td>
<td>Average duration (19 cases averaged)</td>
<td>13 days</td>
</tr>
</tbody>
</table>

On this working basis the facts presented in Table 5 were obtainable. The reputed duration of the acute illness was, as may be observed, quite variable; but the listed cases fall into four rather clearly defined groups: those of a duration of less than five days, those of from five days to a week in duration, those lasting from eight days to two weeks, and those exceeding that length of time. Thirty-six per cent. of all the cases fall into the second group. On this basis, Table 6 is presented to show the relative frequency of each, and of the development of dementia praecox as the specific psychosis. The same is represented graphically in Chart 2, in five day periods.

The conclusions justifiable from these statistics are, first, that the duration of the influenza or influenza and pneumonia precipitating mental diseases is probably not appreciably greater than that of the average attacks of influenza or influenza and pneumonia in the present epidemic. The frequency of pneumonia (about 25 per cent.) is certainly larger than that obtaining generally, but this may in part be due to the fact that at least two thirds of our "pneumonia" patients were brought here, more or less moribund, because of the deliria of profound toxemia.

The second conclusion concerns the tendency of dementia praecox to show no constant relation to the duration of the influenza attack precipitating it. As

TABLE 6.—INCIDENCE OF PSYCHOSES AND PARTICULARLY OF DEMENTIA PRAECOX ACCORDING TO DURATION OF INFLUENZA

<table>
<thead>
<tr>
<th>Duration of Influenza</th>
<th>Number of Cases, Cases of Dementia Praecox</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Forms No. Per Cent.</td>
<td></td>
</tr>
<tr>
<td>From 1 to 4 days</td>
<td>18 6 33</td>
</tr>
<tr>
<td>From 5 to 7 days</td>
<td>29 10 32</td>
</tr>
<tr>
<td>From 8 to 14 days</td>
<td>18 5 28</td>
</tr>
<tr>
<td>From 15 to 22 days</td>
<td>12 4 33</td>
</tr>
</tbody>
</table>

large a percentage of cases of dementia praecox followed the briefer attacks as followed the most prolonged and presumably more severe.
In the matter of the chronological relationships between the influenza and the psychoses, graphic presentation is most helpful.

Chart 3 presents the average interval between the somatic and psychotic episodes. To be more precise, it represents the relative chronology of the fever accompanying influenza and the manifestation of psychotic symptoms following it. As will be noted in all instances save the deliria, the psychosis began on the average after the fever had abated. This interval varies from less than two days in the alcoholic psychoses to 8.5 days in the cyclothymic psychoses.

This chart is a partial verification of Bonhoeffer's principle, that "in general one may say that the later in the convalescence the psychosis begins, the more doubtful is its symptomatic character and the more frequently does it bear the stamp of endogenous psychic disturbances." It is also a valuable witness to Bonhoeffer's theory of the elaboration of the endotoxins as a result of stimulation by acute infection toxins, the former bringing about the psychoses.

An analysis of this interval by five day periods is presented in Chart 4. This chart has reference to the day of onset of the psychosis, as compared to the days of the influenza; that is, those cases of psychosis manifested during the first five days of the illness make up the first pillar, those during the second five days the second pillar, etc.

The conspicuous evidence offered by this chart is the tendency of simple delirium to occur early in the course of the disease, the postinfectious or "collapse" delirium being quite exceptional; and, on the other hand, the uniform rate of incidence of dementia praecox throughout the postinfluenzal period. Thus no cases of delirium occurred after the fifteenth day, whereas there were as many cases of dementia praecox between the twentieth and twenty-fifth days as between the first and fifth, or any other period. Further time studies have been made of the dementia praecox cases, but these must be omitted here for want of space.

SYMPTOMATOLOGY

A representative but synthesized case history reads as follows:

During the convalescence from influenza, Miss X suddenly became excited and rushed from her bed into the street, screaming. She was recaptured and confined in bed, but seemed to be bewildered, deluded and hallucinated. The motor excitement faded: the perverted ideation became augmented, and the family physician advised the Psychopathic Hospital. At about this stage the diagnosis is always in more or less doubt between various obvious possibilities. Subsequently the symptoms follow in most cases a more or less stereotyped course and the diagnosis becomes clear; that is, one case will progressively clear up and the patient be sent home recovered, with a diagnosis of postinfluenzal delirium; another will manifest more and more evidences of schizophrenia and be committed with a diagnosis of dementia praecox, etc.

Depression is traditionally the postinfluenzal symptom par excellence. Osler comments on it; most writers in psychiatry as well as general medicine follow suit. But depression as an emotional state of the psychoses following influenza is not strictly comparable with the depression which presumably is common after the disease in nonpsychotic subjects. (I am aware of one instance in which a mild tendency toward hypomania rather than the reverse was observed in a normal young man, and so recognized by himself.) Aside from a few cases of postinfluenzal depression in which the diagnosis was in doubt between the normal and the psychotic, depression was in this series distinctly uncommon. Only three cases of the depressed phase of manic-depressive psychosis were encountered. Only about a fourth of all the cases showed any depression at any time, and it was rarely constant when present.

The heterogeneity of symptoms is manifest from the divers forms of psychoses presented. Certainly the most common two are delusions and hallucinations. The delusions are of all sorts: somatic, referred, paranoid, transformation, grandeur, etc. One sort or another were present in seventy of eighty cases. Hallucinations in one or more fields occurred in all of the cases diagnosed dementia praecox, and in all of the cases of delirium, and in two thirds of the remaining cases. The constancy of hallucinations in delirium as here seen might arouse curiosity as to why Regis and others have specified a particular "hallucinatory" type of delirium (confusion mentale aigue), as if hallucinations were not generally present.

No cases were monosymptomatic. In the first two groups, however, there were characteristic symptoms. In the deliria, it is amnesia. This was present in all cases, either as an amnesia during the acute psychotic period for past events (including the paramnesia of the Korsakow syndrome) or an amnesia after the acute psychosis for events transpiring during it, or, as not infrequently occurred, both. The second form is an integral symptom of delirium, but it is not an absolute differential point, as it occasionally occurs in dementia praecox and some other forms.

In the dementia praecox cases the characteristic and omnipresent symptom was schizophrenia, used in the symptomatic sense. As this is, in fact, the criterion of the diagnosis of dementia praecox, the foregoing statement is axiomatic. A more remarkable fact is the occurrence of distinctly schizophrenic symptoms in cases in which the patients quickly recover and which are necessarily diagnosed delirium. Six cases were left in doubt because of this fact, and one third
of the cases diagnosed delirium showed at one time or another frankly schizophrenic symptoms.

Group III is too heterogeneous to allow of any such representation. The specific psychoses were so far as diagnosticated more or less true in type, and this is not the place to review the symptoms of the recognized psychoses.

Motor excitement and emotional acceleration were not conspicuous except in Group III. Here both the alcoholic psychoses and the cyclothymoses (especially manias) showed the characteristic hyperkinesis and hyperthyemia.

**Diagnostic Groups**

The four groups used throughout this paper are, of course, by no means as homogeneous as their captions might suggest, and it is proposed to analyze, in a degree, their componenty. The lack of space prohibits illustration by means of case histories or even abstracts, but as these are to appear later, it is perhaps desirable to present here only the structural framework of the series.

**Group I.**—The cases diagnosed "toxic-infectious delirium" or "delirium with infectious disease" (American Medico-Psychological Association nomenclature) embrace three forms of delirium.

These forms are not based, as by Kraepelin, on ambiguities, such as "confusion" and "exhaustion," or as by Bonhoeffer, on the predominant symptom. They are based on the most simple and the only uniform factor, namely, time. It is in our experience here quite impossible to follow either Kraepelin or Bonhoeffer in distinguishing types of delirium. On the other hand, the deliria are in all cases of one of three types: prefebrile delirium; (cum-) febrile delirium, or postfebrile delirium. Either of the first two may be prolonged over into the subsequent period. This classification is so preeminently valuable from a pragmatic standpoint, and the subdivisions of the German writers so bewildering and so conducive to ambiguous descriptions, that for the present I feel that no further justification is required.

Statistically, there were in the present series one, possibly two, cases of prodomal delirium type.

Of the typical delirium concomitant with fever, the present series includes twelve. Of these patients, seven died. In one instance the fever abated two weeks before death.

Of the postfebrile deliria there were three, one of which was fatal. In one of the other two the delirium lasted two weeks.

Any general hospital could probably furnish more examples of all of these types than a psychopathic hospital. These cases are in a sense representative of the more severe forms of delirium.

Neurologic signs were not infrequently present. I am elsewhere reporting with Myerson an instance of severe bilateral optic neuritis which occurred in but one case, although all eye grounds were examined as a routine. One woman, aged 40, with typical delirium, presented absent pupillary and patellar reflexes, with muscular fibrillation. Several cases were noted with transient Argyll Robertson pupils. Convulsions were rare, occurring in only one case, and incidently in one fatal case in one of our nurses, not included in this series.

The spinal fluids were examined in most cases, and in only one instance was there any inexplicable change. This was a case of postfebrile delirium, with slight increase of albumin and globulin, and a mild midzone gold reading; Wassermann tests were negative. These negative findings do not coincide with the postmortem findings on spinal and cerebral fluids of patients dying of influenza, in which Southard and Canavan have found marked changes. (See note on Meningeal Reactions in Influenza, in preparation.)

**Group II.**—The patients who developed dementia praecox during or soon after an attack of influenza may be differentiated into three important groups. These are: (1) those with preexistent indications; (2) those with morbid family history, without previous tendency, and (3) those with neither. Of the first class there were, of course, two varieties: those with previous attacks of acute psychosis, dementia praecox episodes, and those who, without previous episodes, manifested a tendency to the exclusive, egocentricity, etc. In both of these types the acute psychotic episode seems to have been precipitated by the influenza, a process frequently mentioned in the literature, but by no means understood.

The patients in whose family history there appear pathologic elements—a psychot with a father, a feebleminded brother, etc.—are separately grouped because of the possible contribution of these elements.

The group in which there was no previous indication, no evicened tendency and no morbid family history is certainly the momentous group of this series. It is subdivided into those complicated by parturition, and those due solely to the influenza. In this group the influenza (and parturition) seemed to act by directly inducing a process for which there were no previous indications. There are as yet insufficient data to conclude that the infectious process may be the direct etiologic factor (perhaps via some such mechanism as Bonhoeffer proposes) of dementia praecox. Nevertheless the evidence which these cases constitute for the organic view of dementia praecox, as held by Alzheimer, Dide, Deny, Southard, Regis, Rosanoff and others, is of considerable weight. What effect it

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Chart 4.—Influence of duration of influenza on time of onset of resultant psychoses. Abscissas represent time periods in five day groups; ordinates, number of cases.
will have on the view of “curable dementia praecox,” of which only rumors have thus far reached us ex bello, no one can say.

The numerical frequency of the foregoing subdivisions of Group II appears in Table 7.

**Group III.**—This heterogeneous group includes cases of the usual psychoses which were precipitated in acute form by the influenza. This does not relate to their permanence, since forms of manic-depressive psychosis will likely all prove transient; of neurosyphilis, presumably permanent. All began during the defervescence of, or convalescence from, the influenza. The cases of neurosyphilis are included, as the others, because although it is indisputable that the neurosyphilitic process precedes the influenza, the symptoms were so exaggerated or the process so accelerated that for the first time the conduct of these patients became such that institutional care was considered necessary.

**TABLE 7.—SUBDIVISIONS OF THE DEMENTIA PRAECOX GROUPS**

<table>
<thead>
<tr>
<th>With present indications</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite episodes</td>
<td>3</td>
</tr>
<tr>
<td>Disposition only (including I parturient)</td>
<td>6</td>
</tr>
<tr>
<td>With morbid family history (including I parturient)</td>
<td>4</td>
</tr>
<tr>
<td>With neither personal nor familial predilection</td>
<td>13</td>
</tr>
<tr>
<td>Influenza plus parturition</td>
<td>2</td>
</tr>
<tr>
<td>Influenza (or pneumonia) alone</td>
<td>11</td>
</tr>
</tbody>
</table>

An outline with the numerical frequency of each group appears in Table 8.

**Group IV.**—This group of cases of dubious diagnosis consists of sixteen cases. Of these, three were most likely postfebrile delirium; six were indistinguishable between postfebrile delirium and episodic dementia praecox; three, in my opinion, will likely prove to be dementia praecox, and five remain undiagnosed because of unusual combinations of symptoms, insufficient data, etc.

The striking point in this group is the frequency of difficulty in distinguishing between postfebrile delirium and dementia praecox. There is no time here to dilate on this theme, or to recall the references to this difficulty made by the French authors who regard dementia praecox as essentially a toxic psychosis. It is sufficient to indicate that this fact, and the presence of schizophrenic symptoms in one third of the cases diagnosed delirium, add considerable force to the

**TABLE 8.—STATISTICAL ANALYSIS OF GROUP III**

<table>
<thead>
<tr>
<th>So-called “functional psychoses”</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclothymia</td>
<td>9</td>
</tr>
<tr>
<td>Manic phase</td>
<td>3</td>
</tr>
<tr>
<td>Depressed phase</td>
<td>3</td>
</tr>
<tr>
<td>Mixed phase</td>
<td>1</td>
</tr>
<tr>
<td>Psychoneurosis</td>
<td>1</td>
</tr>
<tr>
<td>Paranoia (Kraepelinian)</td>
<td>1</td>
</tr>
<tr>
<td>Recognized organic psychoses</td>
<td>12</td>
</tr>
<tr>
<td>Alcoholic psychoses</td>
<td>5</td>
</tr>
<tr>
<td>Neurosyphilitic psychoses</td>
<td>2</td>
</tr>
<tr>
<td>General paresis</td>
<td>1</td>
</tr>
<tr>
<td>Diffuse form</td>
<td>1</td>
</tr>
<tr>
<td>Arteriosclerotic psychoses</td>
<td>2</td>
</tr>
</tbody>
</table>

suggestion made above from the statistics in Group II, concerning infectious processes as the possible etiology in some cases of dementia praecox.

Another classification of the diagnostic groups is suggested by the facts presented. The influenza acts in two ways: as an exciting factor for a process not previously manifest, and as an exciting factor for rendering visible a previously latent or semilatent process. Thus the cases of manic-depressive psychosis with first attack following influenza illustrate well the first tenet, and the augmentation of neurosyphilitic processes the second. Our knowledge concerning both methods is at present in a clouded state, and only much careful study of series of cases such as the present will elucidate the matter.

From such a point of view the cases of this series may be presented numerically as in Table 9.

**TABLE 9.—NUMERICAL SUMMARY ACCORDING TO WAY INFLUENZA ACTED**

<table>
<thead>
<tr>
<th>Latent Processes Acted</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia praecox</td>
<td>6</td>
</tr>
<tr>
<td>Manic-depressive psychosis</td>
<td>3</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>3</td>
</tr>
<tr>
<td>Alcoholic psychoses</td>
<td>4</td>
</tr>
<tr>
<td>Other psychoses</td>
<td>5</td>
</tr>
<tr>
<td>Unclassified</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>32</td>
</tr>
</tbody>
</table>

**Processes Instigated:**

<table>
<thead>
<tr>
<th>Delirium</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia praecox</td>
<td>17</td>
</tr>
<tr>
<td>Manic-depressive psychosis</td>
<td>3</td>
</tr>
<tr>
<td>Other psychoses</td>
<td>6</td>
</tr>
<tr>
<td>Unclassified</td>
<td>12</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>48</td>
</tr>
</tbody>
</table>

The course of the psychoses has in general been indicated in connection with the individual groups. The delirious patients either recover mentally and physically or die. Those diagnosed as having dementia praecox are all alive at the present time except two, who died within the month. There have been no deaths in Groups III and IV. Necropsy results will appear later.

Statistically the present status and probable prognosis is represented in Table 10.

**TABLE 10.—COURSE OF THE PSYCHOSES**

<table>
<thead>
<tr>
<th>Groups</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient</td>
<td>10</td>
<td>0</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Intermittent by death</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Permanent</td>
<td>23</td>
<td>7</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

**SUMMARY AND CONCLUSIONS**

1. One hundred cases of mental disease associated with influenza in the recent pandemic have been studied at the Boston Psychopathic Hospital. Eighty of these have been intensively analyzed.

2. The variety of mental disturbance manifested is wide, embracing in this series nine of Southard's eleven groups of mental disease. For convenience they are readily classifiable into four groups: delirium, dementia praecox, other psychoses and unclassified. Of these the second (dementia praecox) is the largest group numerically.

3. That age may be a factor in determining the form of psychosis evolved is suggested by an analysis of the average ages of the groups.

4. Analysis of the time relations proves that the duration of the influenza attacks in the patients developing psychoses is not appreciably greater than the average as reported in the present epidemic, nor does the duration modify the form of psychosis developed.

5. There is in most instances an interval between the termination of the influenza and the first manifestation of symptoms of psychosis, the averages varying from two to eight days in all save the febrile delirium. Herein, Bonhoeffer's principle of the relation of interval and complexity of the psychoses is supported.

6. The symptomatology is as complex as the nosology. Delusions and hallucinations are the most common symptoms, and depression is relatively infrequent contrary to the case in mentally normal subjects.

7. The states of delirium encountered are best classified as of three forms, on a temporal basis: pre-febrile delirium (prodromes), (cum-) febrile delirium, and post-febrile delirium (collapse delirium,
exhaustion, delirium, confusion, etc.). This accounts for all cases and avoids ambiguity.

8. Neurologic signs were few; ophthalmoscopic examination negative, save for one instance of bilateral neuritis, and spinal fluid examination negative save for one instance of modified colloidal gold reaction.

9. An organic basis for some instances of the picture denoted dementia praecox is supported by the preeminent frequency of its occurrence in this series (31 per cent), the age factor above mentioned, the frequency of schizophrenic symptoms in otherwise typical cases of delirium, and the occurrence of several (six or more) cases in which a diagnosis could not be made between delirium and dementia praecox, despite the presence of all diagnostic aids.

10. The psychiatric prognosis in influenza justifiable on the basis of the present series may be expressed in general as delirium (with recovery), death or dementia praecox. This excludes cases of previous psychotic basis, such as alcohol and neurosyphilis.

ATROPIN AND INDUCED ANTI-ANAPHYLAXIS
AS A PROTECTION AGAINST ACUTE ARSHPHENAMIN REACTIONS

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The acute nitroprusside or anaphylactic reaction to the intravenous injection of arsphenamin has become rather familiar to the profession through the peculiarities of certain brands of the drug that have of late years been placed on the market. In the management of a few cases, or in the treatment of young, robust persons, the average acute reaction may be an annoyance rather than a critical complication. None the less, it has resulted fatally, and in the enfeebled or in those with grave constitutional ailments it may give rise to alarming situations. There is also a type of patient who needs the drug, but who, instead of an occasional reaction, exhibits a persistent marked idiosyncrasy which subjects him to repeated anaphylactic storms with progressive injections that may force an abandonment of this form of medication.

Hence, for the means of the control of acute reactions due to the administration of arsphenamin have been confined to special care in the preparation of the patient (catharsis and empty stomach), caution in the alkalinization of arsphenamin solutions, and to the use of the epinephrin solution suggested by Milian1 in from 5 to 10 minin doses as a means of controlling the reaction after it develops. Epinephrin may also be used as a prophylactic, as noted, for instance, by Berman.2 This drug, however, administers a shock of no mean intensity by its powerful effect on the vascular system, so that I have seen occasions in which patients have for the moment seemed in as much risk of serious damage from the therapy as from the original arsphenamin reaction. The frequency of nitroprusside crises during the period in which German

made arsphenamin and neo-arsphenamin were being supplied to this country by submarine furnished an incentive to the development of a less vigorous propylaxis for the reaction, which could be relied on to make repeated injections possible even if the face of a marked idiosyncrasy on the part of the patient. It occurred to me that such a propylaxis might be based on the clinical resemblance of the nitroprusside crisis and the reaction produced by imperfectly alkalinized arsphenamin solution to anaphylactic shock. A physiologic means of combating anaphylactic shock, it seemed to me, might protect against acute nitroprusside crisis, and at the same time have theoretical interest as an indirect demonstration of the true anaphylactic nature of the phenomenon. This seemed the more worth while because of the theory, recently advanced by Schamburg, Kolmer and Raisz,3 that the reaction was due to the physiologic effect of an impurity (substance X) rather than to anaphylaxis per se.

Support for the belief that the nitroprusside crisis is a form of anaphylactic shock rests on more than mere clinical analogies. Swift4 early undertook to explain the reaction as a form of shock by showing that guinea-pigs could be passively sensitized to a mixture of guinea-pig serum and arsphenamin solution, subsequent injection develop a true anaphylactic response. Since, however, the older conception of anaphylaxis required that a previous sensitizing dose of the allergy-producing agent be administered, the explanation of Swift seemingly failed to cover those cases in which nitroprusside crisis developed on first injection.

The development of the newer physical conceptions of the mechanism of anaphylactic shock, made possible by the work of Bezredka and Strobel,5 Kopaczewski and Mutermilch,6 Jobling and Petersen,7 Novy and De Kruif8 and numerous other investigators, has done away with the objection to Swift's explanation. One of the essential facts in the production of anaphylactic shock may now be regarded as a change in the dispersion of the colloids of the blood serum. An investigation which has special application to the problem of arsphenamin reaction in its relation to anaphylaxis is that of Friedberger and Tsuneoka,9 who found that the injection of a powder, such as kaolin, into the blood stream, gives rise to anaphylactic shock. MacKee,10 among others, observed in 1912 that the intravenous injection of arsphenamin in acid solution produced a precipitate, and a reaction in the patient proportional to the concentration of the solution and the rate of injection, that is, the rate of formation of the precipitate in the blood stream.
