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PART 1.—ORIGINAL ARTICLES.

*On Psychoses after Influenza.** By JULIUS ALTHAUS, M.D., M.R.C.P.Lond., Senior Physician to the Hospital for Epilepsy and Paralysis, Regent's Park.

The discussion which I have been invited to open is on a subject which is new to all of us, and which may, therefore, simply on this account, claim a share of our attention. Indeed, on searching the works of Clouston, Blandford, Savage, and others, as well as the extensive periodical literature which is at our disposal in the "Journal of Mental Science," the "West Riding Asylum Reports," and similar publications in France and Germany, the subject of mental affections occurring subsequently to influenza has hardly been mentioned with a single word previous to the epidemics of that distemper which we have recently passed through. Nor is there anything to be found on this subject in the numerous books and papers descriptive of influenza which have appeared before 1890. All that has been written on mental disorders in connection with influenza previous to that date refers to the *febrile* or *initial delirium* which may occur at any time during the progress of the feverish attack, and may, indeed, precede all other symptoms, setting in sometimes before there is any rise of temperature. This initial delirium has been described as long ago as 1510 by Sauvages, and later on by Huxham, Ash, Haygarth, Gray, Smyth, Rush; more recently by Lombard, Bonnet, and Pétrequin, and during the last epidemics

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by Ewald,[1] Joffroy,[2] Gwynne,[3] Creagh,[4] Nicholson,[5] Van Deventer,[6] Mairet,[7] and others. In the German Collective Investigation Report, edited by Leyden and Guttmann,[8] no less than 276 such cases have been collated. It is, however, not this initial delirium which we have met here to consider to-day, but those better defined psychoses which are prone to occur after the feverish attack is over, during, or some time subsequently to *convalescence*.

The only remark relating to our subject which I have been able to discover previous to 1890 is one made by Sir James Crichton-Browne,[9] who states in a valuable paper on so-called "acute dementia," published in 1874, that he has seen a chlorotic girl who had retained unimpaired intelligence until she was attacked by influenza, when she rapidly lost the use of her faculties, and became unable to think, speak, or move spontaneously. These four lines, therefore, constitute all the definite information which is extant on post-grippal psychoses previous to 1890. Sir J. Crichton-Browne has kindly informed me that the case just mentioned occurred after an attack of genuine influenza, and not a mere feverish catarrh; and that it was a case of certifiable insanity, and not mere initial delirium. The case is, therefore, of historical interest, as being the first undoubted instance of a real post-influenzal psychosis recorded in medical literature.

It is, however, not simply because the subject is new that it should claim our earnest consideration. To my thinking it should do so even more on account of its own intrinsic interest and importance, which become at once apparent, whether we look at it from a purely scientific or a more practical point of view. I believe it will be generally acknowledged that these post-grippal psychoses possess considerable scientific interest, inasmuch as they have been found to differ in many respects from other post-febrile insanities, with the special features of which we have long been more or less familiar; while on the other hand the comparatively large number of cases which have been met with, in general as well as in consulting and asylum practice, greatly exceeding that of psychoses occurring after other fevers, imparts to the subject naturally a higher degree of practical importance than that of some analogous conditions which are so rare that they may be considered as curiosities of medical practice and literature. Such is, for instance, the case with psychoses after measles, of which, as far as I am aware, altogether only four cases have been reported.

The literature of psychoses following influenza has since the recent epidemics become very large. Amongst the authors who have written on this subject I would particularly mention Savage,[10] Clouston,[11] Hack Tuke,[12] Flint,[13] Harrington,[14] Paine,[15] Richardson,[16] Kraepelin,[17] Jutrosinski,[18] Pick,[19] Ahrens,[20] Bartels,[21] Becker,[22] Mucha,[23] Solbrig,[24] Fehr,[25] Schmitz,[26] Weynerowski,[27] Mispelbaum,[28] v. Holst,[29] Krypiakiewicz,[30] Müller,[31] Munter,[32] Ladame,[33] Bidon,[34] Leledy,[35] Voisin,[36] Mairet,[7] Morselli,[37] Frigerio,[38] Christiani,[39] Lojacono,[40] Cantarano,[41] Hoge,[42] Ayer,[43] and myself.[44]

In approaching the study of psychoses after influenza it occurred to me that it might be useful to consider these affections in connection with other better-known post-febrile insanities. Mental diseases coming on after rheumatic fever, pneumonia, intermittens, the acute exanthemata, erysipelas, cholera, and whooping cough have, indeed, attracted the attention of numerous observers, more especially during the last forty years, in this country, as well as in Germany and France, and I need only remind you of the writings of Russell, Greenfield, Handfield Jones, Wilson Fox, Murchison, Clouston, Blandford, Savage, Tuke, Hermann Weber, Scholz, Jolly, Kraepelin, Boileau, Berthier, Christian, and others who have done so much for the elucidation of this subject. Indeed, the psychoses following rheumatic and intermittent fever were already known to Sydenham, Boerhave, Van Swieten, Musgrave, Hofmann, the elder Monro, and other physicians of the last century. In order to illustrate certain points in the natural history of all post-febrile psychoses, I have constructed a table based chiefly on Kraepelin's[45] collection of cases, on which are shown :—

1st. The number of well-observed cases which have been utilized ;
2nd. The influence of sex, age, and general and special predisposition ;
3rd. The duration of these affections ; and
4th. The eventual result, whether cured, uncured, or fatal.

I shall have frequent occasion to refer to this table in the course of my address, and now proceed to submit to you the more important points connected with our subject, which are still to some extent *sub judice*, and on which I would invite discussion by the eminent experts here present.

TABLE showing the number of Cases, Influence of Sex, Age, and Predisposition, Duration and Result in all Post-Febrile Psychoses.

Acute Infectious Diseases.	Number of cases utilized.	Influence of Sex.		Of Age.		Of Predisposition.		Duration.				Result.		
		Male.	Female.	Up to 30.	Above 30.	General.	Alcohol.	One week.	One month.	Twelve months.	Years.	Cured.	Uncured.	Died.
Rheumatic Fever ...	96	60·3	39·7	77	23	30	?	16	33	46	5	93·6	0	6·4
Pneumonia	43	82	18	40	60	41·4	16	70·7	19·5	9·8	0	89·5	0	10·5
Intermittent Fever ...	39	76	24	48	52	31	?	24	48	28	0	100	0	0
Variola	41	60·7	39·3	57.1	42·9	10·7	?	71·4	14·3	14·3	0	80	0	20
Scarlatina	16	60	40	58	42	19	?	87	0	0	0	87	0	13
Erysipelas	11	73	27	50	50	54	?	63	37			80	0	20
Typhoid Fever... ...	87	56·5	43 5	70·5	29·5	34·5	?	17	24	21	38	71·8	20·5	7·7
Cholera	19	68·4	31·6	37·5	62·5	21	?	18·8	56·2	25	0	100	0	0
Influenza	113	56 4	43·6	39	61	72·7	10 8	12·5	32·5	55	0	56·6	5·8	7·6

1. *Are psychoses after influenza more frequent than those which occur after other fevers?*

In one sense this question has already been answered in the affirmative. There is no doubt that the cases which have been recorded by various authors are absolutely much more numerous than those which have been described as following any other acute diseases. On my table the number given is 113, the next highest numbers being 96 for rheumatic fever, and 87 for typhoid fever. That number (113), however, does not approximately represent the whole of the cases which have been mentioned or cursorily described by authors, for I have only selected those which have been related with full detail. Thus the table does not include one of the 170 cases of post-grippal psychoses which have been at the disposal of the compilers of the German Collective Investigation Report,[8] and which, I regret to say, do not appear to me to have been as much utilized as they might have been.

Individual observers have seen many more cases of post-grippal psychoses during the last year or two than of other post-febrile insanities during a lifetime. Thus Savage[10] has reported upwards of fifty cases, Leledy,[35] twenty-two, Jutrosinski,[18] twenty, Hack Tuke,[12] eighteen, van Deventer,[6] eleven (in addition to twenty cases of initial delirium), Mairet,[7] eleven (in addition to six cases of initial delirium), myself,[44] nine, six of which I have reported, and many others a somewhat smaller number—all within a comparatively short period. Clouston,[11] indeed, states broadly that the poison of influenza destroyed the cortical energy to a much larger extent than any of the continued fevers or zymotics—nay, that its effects on the mental condition of Europe during the years of its prevalence far exceeded in destructive powers all those diseases put together. It left the mental tone of Europe lower by some degrees than it found it, and no epidemic of any disease on record has had such mental after-pains. There is thus good evidence to show that the absolute number of cases of these psychoses greatly exceeds that of other post-febrile insanities. But is this frequency also relatively greater—that is, when we compare it with the extremely large number of cases of the parent affection which have occurred? It is this latter question which I would submit more particularly to your consideration. Influenza has recently assumed the character of a pandemic rather than that of an epidemic, and an element of doubt is thus introduced which it would be desirable to clear up. Jastrowitz, who has drawn up the report on 170 cases in

the German Collective Investigation Report,[8] is of opinion that psychoses are not only absolutely but also relatively more frequent after influenza than after other fevers, and from the data which are at my disposal I have arrived at the conclusion that the only other acute disease which can at all compare with influenza in this respect is typhoid fever.

2. *What is the influence of sex and age in the causation of these affections?*

Kirn[46] states that females are more liable to them than males, and Jutrosinski[18] thinks that both sexes are about equally prone to them. A glance at my table, however, shows the male sex to be throughout more liable to post-febrile psychoses than the female. This difference is most marked for pneumonia, viz., 82 against 18; and least so for typhoid fever, viz., 56 against 44. For influenza the numbers are 56·4 and 43·6.

The influence of *age* on the production of post-febrile psychoses does not seem to be so uniform as that of sex, for although persons below thirty years of age appear to be on the whole more liable to them than those upwards of thirty, there are exceptions to this rule. For influenza the numbers are 39 for the younger and 61 for the older set of persons. I have compared the prevalence of post-grippal psychoses in the several decades of life, and find the three decades between 21 and 50 years af age to be more prone to them than the five decades at the two extremities of life (63 to 37). We find here a close analogy to what happens in cerebral syphilis leading to mental affections, which are also much more frequent between 20 and 50 years of age than at any other time of life; while, on the other hand, after rheumatic fever, small-pox, scarlatina, and typhoid fever patients are more liable to suffer before than after thirty years of age.

3. *What is the influence of predisposition?*

Hereditary or acquired predisposition is, from the table, seen to play a considerable part in the production of all post-febrile psychoses, and in none more so than in the post-influenzal (72·7). Predisposition includes heredity, a history of previous psychoses or neuroses in the patient himself, previous brain-injury, alcoholism, anæmia, the presence of some degeneration such as syphilis, or senile decay, the menopause in women, and grief or shock after the feverish attack. The influence of a neurotic tendency, however, has often been exaggerated, from sheer force of habit rather than from accurate observation. Thus Mairet[7] mentions the case of a woman who had no hereditary or personal antecedents whatever, yet includes it in a series of

others as strongly predisposed to brain disease. In nine cases of post-influenzal psychoses which I have seen (six of which I have reported),[44] predisposition existed only in two; of eighteen cases reported by Hack Tuke,[13] ten were predisposed and eight not so; of three cases described by Mucha[23] only one was predisposed; and Kraepelin,[17] Ladame,[33] and Jutrosinski[18] evidently go too far in looking upon predisposition as the exclusive ætiological factor in these conditions. On the other hand, the gravity and duration of these insanities are unquestionably increased by predisposition. The influence of alcoholism is seen to have been active in 10·8 per cent.

4. *What is the relative influence of the fever and the grippo-toxine in the production of these psychoses?*

Fever and a special virus may be looked upon as the chief causative agents of all post-febrile insanities, but their influence differs remarkably in the different forms of these diseases. The fever (that is, increased temperature and cardiac action) is of the first importance in the delirium of inanition or collapse, which follows upon the crisis in pneumonia and the acute exanthemeta, when in consequence of a sudden fall of temperature and simultaneous slowing of the heart's action, too little nutritive material is carried to the cortex, causing sudden exhaustion of the highest controlling centres, and setting free the uncontrolled energy of the lower centres, which is manifested by maniacal excitement. In the production of post-typhoid psychoses, on the other hand, the toxine of the malady seems to be more important than the fever, and the same I believe to be the case in influenza. In the latter complaint the fever is habitually too short and too slight to have much influence upon the nutrition of the cineritious matter; and the prostration of mental and physical strength is habitually so profound as to be utterly inexplicable except by assuming poisoning of the nerve-cells by the grippo-toxine. Indeed we shall see presently that in the majority of cases of post-influenzal psychoses the feverish attack has been peculiarly mild. This holds good chiefly for the melancholia and the general paralysis which occur after influenza; while for the delirium of inanition, which also occurs, the fever must chiefly be held responsible.

Seeing how greatly cases differ in their clinical features, I am inclined to think that there must be great differences in the composition of the virus in different cases. Pfeiffer[47] has, in his latest description of the influenza bacillus, laid stress upon the circumstance that its size is found to vary considerably, some rodlets being very much larger than others; and it

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is conceivable that in cases where the larger-sized bacillus predominates, or shows particular vitality, the toxine secreted by it may have a more deleterious influence on the nerve-cells of the cortex than the smaller kind of bacteria. In the same way Koch was enabled, in the beginning of the recent epidemic of cholera at Hamburg, to predict, from the size and vitality of the comma bacillus, or "vibrio," as some people now call it, that the outbreak would be a particularly severe one. Another important point is that psychoses are chiefly apt to occur after slight cases of grip which have been neglected, showing an analogy with some forms of syphilis, in which grave tertiary lesions tend to appear where the primary and secondary symptoms have been so slight as to attract little attention, and have therefore been insufficiently treated.

5. *What is the duration of post-influenzal psychoses?*

While insanities after the acute exanthemata, erysipelas, and pneumonia tend to get well in a week, those occurring subsequently to rheumatic, typhoid, and intermittent fever, and influenza, have generally a longer duration. Only 12·5 per cent. of post-grippal psychoses got well in a week, against 87 per cent. for scarlatina; 32·5 more had recovered within a month, and 55 lasted beyond a month. The latter were chiefly cases of the severer forms of melancholia in aged persons, and of general paralysis, while those which lasted a comparatively short time, were either cases of the delirium of inanition or of the slighter forms of melancholia in young persons.

6. *What is the proportion of cured, uncured, and fatal cases?*

Insanities after intermittent fever and cholera show a hundred per cent. of recoveries, while after small-pox and erysipelas we have 20 per cent. of deaths, after scarlatina 13, after pneumonia 10·5, after typhoid 7·7, and after influenza 7·6. The percentage of uncured cases after the latter is 35·8, and cured 56·6, so that the prognosis of post-influenzal psychoses appears to be tolerably favourable.

7. *Is there any relationship between the severity of the feverish attack and the subsequent occurrence of psychoses?*

I have divided the available cases into three classes, viz., slight, medium, and severe, and have found that 55·2 of these psychoses have come on after comparatively mild attacks of grip, 27·6 after severe attacks, and 17·2 after such of medium intensity.

8. *What length of time may elapse between the feverish attack and the outbreak of the insanity?*

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This is a very important point, involving the question of *post hoc ergo propter hoc*. Are we justified in attributing a psychosis to influenza when it occurs, say, three or four months after the feverish attack? In former years insanity has been referred to typhoid fever when there had been an interval of five or even ten years between the two events. The effects of injury to certain parts of the body, more especially as promoting the subsequent growth of tumours in the injured parts, seem to corroborate this view. I think, however, that we shall be more safe in looking upon a psychosis as really consequent upon some preceding infectious disease when it occurs:—

(1st) During convalescence from the latter; and

(2nd) Within six months after the attack, provided that no other causes have been at work during the interval; and also provided that the patient has, since convalescence, shown some symptoms of disturbed balance of brain-power, even where this did not amount to an actual psychosis.

A study of those cases in which the interval between the feverish attack and the outbreak of the psychosis has been accurately stated, has led me to the conclusion:—

(1st) That those psychoses which are characterized by delirious exaltation and mania are prone to follow very close upon the feverish attack, and begin, indeed, sometimes immediately after the crisis;

(2nd) That insanities distinguished by depression and melancholia are apt to appear somewhat later, viz., between a few days and a few weeks after the attack; and

(3rd) That general paralysis of the insane may be the latest of all, the interval between the attack and the first unmistakable appearances of the psychosis having amounted to as much as six months in a case recorded by Krypiakiewicz.[30]

9. *Is there any special form of insanity induced by influenza which does not occur after other fevers?*

Kirn[46] speaks of a typical grippal psychosis characterized by acute mania and confusion, while Mairet[7] considers true "folie grippale" to consist of melancholic delirium. Most observers, however, have come to the conclusion that there is no special form of insanity which could be considered as connected with influenza *per se*.

In the paper read before the Section I have fully described the clinical features of the various forms of psychoses which are apt to follow the feverish attack; but want of space prevents me from reproducing that description here. I will, therefore, only state that there are three principal forms of post-in-

fluenzal insanities, viz.: 1st. Acute hypochondriacal melancholia, with lethargy and loss of volitional power (41·2 per cent.); 2nd. Weber's[48] delirium of collapse, or inanition, and confusion, with hallucinations, followed by stupor (27·2 per cent.); and, 3rd. General paralysis of the insane of an extremely rapid (galloping) course (6·2). To these forms may be added—4th. The *pseudo-influenzal* psychoses, that is, various forms of mental disturbance, such as intermittent or circular insanity, delirium tremens, mania, etc., in persons with a long history of hereditary or acquired tendencies, in whom the feverish attack is only the accidental exciting cause of a disturbance which would also have occurred from any other cause, or perhaps no cause at all (25·4 per cent.). While, therefore, no actual specificity is shown to exist in post-grippal psychoses, they differ from other post-febrile insanities by presenting a greater variety in their clinical features; inasmuch as the first group mentioned is similar to the mental affections occurring after typhoid and rheumatic fever and whooping cough, while the second group resembles the psychoses chiefly seen after the acute exanthemata, pneumonia, and the puerperal state. After influenza, however, we see cases belonging to both groups indiscriminately, and, in addition to them, cases of general paralysis, which is hardly ever seen after other fevers. Indeed, Mickle[49] states that only in 12 out of 3,374 male general paralytics, and in one female out of 910, fevers were assigned as the cause, and that even these might perhaps be all explained away.

10. *How does influenza affect those previously insane?*

In some asylums the patients appear to have been much less affected by influenza than the attendants and other sane persons living in the institution, while in others no such difference has been observed. Leledy[35] states that in the asylum of Beauregard, near Bruges, which contains 400 inmates, only 15 patients had influenza, while the attendants and other employés suffered almost to a man. Of these 15 persons, only three were men, and twelve women. On the other hand, Mucha[50] found that in the asylum of Göttingen 15·3 per cent. of the male and 33·3 of the female patients had influenza. The attendants there suffered in much the same ratio, viz., 13·3 per cent. of males and 32 per cent. of females. Some light may perhaps be thrown on this singular circumstance by what happened in the hospital for the insane at Gladesville, New South Wales, where Sinclair, quoted by Ashburton Thompson,[51] found that the attendants suffered more in three different buildings than the

patients, but that in the main building, where the percentage of male patients attacked was only 0·5, the female patients suffered to the extent of 41·5 per cent. This apparently unaccountable occurrence was eventually explained by the female patients having been employed in a laundry, to which infected clothing had been sent from another building. As soon as the female patients began to wash this clothing their side of the house began to suffer. The male side of the house being completely separated from the female side, and males not having been employed in laundry-work, they no doubt for this reason escaped infection. What happened in Charenton[35] is again different. There almost all attendants suffered, but not one of them seriously, while amongst the patients only the aged and those suffering from general paralysis, apoplectic and senile dementia, succumbed to the epidemic. Insanity, therefore, did not appear to be a protection against grip; but where the insane were spared, this seemed to be owing to their being isolated, and therefore less exposed to infection than others who moved freely about.

The effect of the feverish attack on the insane appears likewise to have varied very much in different asylums. The mental condition has either been left unchanged, or improved, or become aggravated. Mucha[50] tells us that in the asylum of Göttingen the influence of influenza on the mental affection was practically *nil*. On the other hand Leledy[35] states that the fifteen patients at Beauregard, who had influenza, appeared to be particularly lucid during the attack. Some who had been violently delirious became quiet; there was no difficulty in keeping them in bed, and they were altogether more manageable than previously.

In some recent cases decided benefit appears to have occurred. Metz[52] mentions the case of a man, aged 33, who had been eleven months in the asylum for maniacal excitement with delusions, when he was seized with grip. The feverish attack lasted two days, and almost immediately after the crisis the patient became rational, and could be discharged a few weeks subsequently. Journiac[35] speaks of a similar case which occurred in a sister of charity, aged 48; but nothing is said about the further progress of these cases. Leledy[35] reports the case of a lad, aged 15, who was much improved by an attack of influenza, but had to be readmitted three months after his discharge, when he was as bad as ever. Van Deventer[6] has described the case of a hysterical girl, aged 9, who had been subject to attacks of confusion with occasional lapses of

consciousness, and appeared to recover after an attack of influenza.

It seems possible that a condition of anæmia, with contraction of the arterioles of the brain, may be improved by the sudden congestion of the cerebral blood vessels which occurs during the feverish attack; on the other hand it is even more easy to conceive that a congestive or sub-inflammatory state of the brain and its membranes may be aggravated by such an incident. Cases of this latter kind appear, indeed, to have been much more numerous than those in which improvement was noticed. Instances in which the result was quickly fatal have been reported by Van Deventer,[6] Bartels,[21] and Leledy.[35]

11. *What treatment should be resorted to in the different forms of post-influenzal psychoses?*

Change of air and scene, and avoidance of excitement and worry, are useful in the whole class of these affections. Insomnia, which is generally present, should be combated by prolonged warm baths, and such medicines as paraldehyde, sulphonal, trional, and amylen-hydrate. For the anorexia which is so common, bitter tonics and dainty dishes should be prescribed, while for general debility a combination of strychnine and arsenic is invaluable. In the depressive form of insanity, alcohol, in the form of champagne or whisky and Apollinaris water, is generally necessary; and the constant current of electricity, applied to the præfrontal lobes and the bulb, tends to clear up melancholia.

In the delirium of inanition and confusional and delusional insanity, hypodermic injections of morphine and atropine, followed by the free exhibition of alcoholic stimulants, are useful. When collapse threatens, hypodermic injections of ether and camphorated oil (1 grain in ten minims) should be employed. Bromide of ammonium combined with strychnine is indicated after the acute stage of this affection has passed off.

For general paralysis of the insane after influenza I can recommend mercury, together with large doses of iodide of potassium, while alcoholic stimulants must be strictly prohibited. Avoidance of excitement and of physical and mental efforts is in these conditions more especially important.

Where insanity after influenza appears to be grafted upon pre-existing neuroses or psychoses, each case has to be treated on its own merits. It is chiefly in this class of cases that determined attempts at suicide are made, and the patients should therefore be watched with special care.

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