AFFECTIVE DISORDERS ARISING IN THE SENIUM

I. THEIR ASSOCIATION WITH ORGANIC CEREBRAL DEGENERATION

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INTRODUCTION

THE importance of the psychoses of later life has been demonstrated by Cook, Dax and Maclay (1952), who found that 15 per cent. of patients admitted to mental hospitals in this country were aged 65 or over. Our own corresponding figure (derived from a Mental Hospital serving a county with a mixed rural and residential area) is 20 per cent. for the year 1953. Furthermore, it has been shown by Roth (1955) that about one-half of all admissions aged 60 and over are suffering from affective disturbances, and that of these over one-half have had no psychiatric illness before that age. Robertson and Brown (1953) report a similar proportion with late onset in their material.

There are a number of problems related to this large subgroup of affective disorders of late onset. Our previous investigations had shown that affective psychosis in old age differed from those with organic psychosis in the following respects: (1) Pattern of outcome with relatively high discharge and low mortality rates (Roth and Morrissey, 1952; Roth, 1955); (2) Psychological test performance (Roth and Hopkins, 1953; Hopkins and Roth, 1953); (3) The rarity of symptoms such as dementia, the amnestic syndrome, or prolonged clouding of consciousness in the clinical picture, even on follow-up study several years after admission. The results supported our hypothesis that affective disorder in old age is a separate nosological entity with evidence that is objective and independent. But although the findings suggested affinities between old age affective disorder as a whole on the one hand, and the manic-depressive and other functional affective illnesses of earlier life on the other, it remained to be ascertained whether the features described were equally characteristic of those cases suffering their first attack after the age of 60, and of those falling ill for the first time in early and middle life. The possibility remained, for example, that an organic factor in the aetiology of the group of late onset was concealed by dilution with cases in which this was unlikely to enter. A comparison of the two groups could therefore be expected to reveal whether cerebral degeneration was likely to be important as a cause of those affective illnesses that first appear in old age. Moreover, if the results suggested that the organic factor was unimportant and that the two groups were uniform in this respect, further comparisons might yet

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bring to light factors associated to a significant degree with breakdown early or late in life.

It is with an examination of the possible part played by organic cerebral degeneration in the group of late onset that this paper is concerned; in the remaining papers of this series, the evidence obtained as to the importance of other factors, hereditary and environmental, will be described.

METHOD

Patients suffering from affective disorder were divided into two groups as follows:

1. *An early onset group* in which the first attack of psychiatric illness occurred before the age of 60.

2. *A late onset group* in which there was no record of psychiatric disorder before 60.

The former group was considered for practical purposes to represent the manic-depressive and other functional affective psychoses; the latter, depressive illness occurring in the senium in which cerebral degeneration might be an aetiological factor. This involved an assumption that the group of early onset was likely to be largely free from organic taint. That this is probably true, is shown by a number of lines of evidence. No genetic relationship between manic-depressive and organic psychoses has yet been demonstrated (Sjögren, 1948; Stenstedt, 1952) and the incidence of dementia among groups of manic-depressive patients has seldom been placed higher than 1 per cent., a figure which can be accounted for in terms of fortuitous coincidence (Lundquist, 1945; Sjögren, 1948). In relation to our own material it is in the decade 50–59 years that cases of doubtful aetiology would have arisen. Of the 29 per cent. of the early onset group that had their first illness in this period, only 9 cases relapsed within two years, while in the remaining 17 the mean interval until the next attack was $12\frac{1}{2}$ years. Such long remissions largely exclude the possibility of organic cerebral causation for psychiatric symptoms, whereas frequent relapse is not necessarily incompatible with functional aetiology. Any organic taint in the early group is likely therefore to have been confined to rather less than 10 per cent. of the cases. However the possibility of bias due to organic causation of affective psychosis starting in middle age was examined (and eliminated) by an analysis of the results obtained.

Accordingly, we can examine our groups for clinical and psychometric evidence of degenerative change, and if the assumption that they contribute to affective disorder in later life is correct we ought to find them relatively more often in the late onset group. Also relevant to this problem in view of the different pattern of outcome between the functional and organic psychoses of old age (Roth, 1955) is a comparison of the follow-up results. The procedure here followed is, therefore, to compare the subgroups in detail in respect of:

(1) Clinical signs of organic nervous system disease and cerebral involvement; (2) Psychometric test results; (3) Outcome. In each case comparable data are available for the organic psychoses.

SELECTION OF MATERIAL

Selection of cases for study was made for 367 consecutive admissions aged 60 and over during the 18 month period August, 1951, to January, 1953, and was based on the presence of a *manic or depressive symptom-complex* of at least a few weeks' duration. One hundred and eighty-nine cases were found to fulfil

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these criteria, of whom 175 were considered to belong to the group of affective disorder proper, and 14 to the organic groups. The latter cases showed a mixed symptomatology consisting of a variable depressive mood change and sometimes typical depressive ideation in a clear organic setting (i.e. with dementia, a chronic amnestic syndrome, or with prolonged or fluctuating confusion); they are referred to as "mixed cases". There were 120 cases of senile, arteriosclerotic and acute confusional psychoses, and 58 cases with other diagnoses, admitted during the same period (Table I).

One-third of all cases were studied individually, and the remainder from their hospital records. Social histories were available in the majority.

TABLE I

All Admissions Aged 60 and Over During 18-month Period, August 1951–January 1953. The "Mixed Cases" are Referred to in the Text

Group of					Male	Female	Total
Affective Disorder	..	..	..	..	59	116	175
Senile, arteriosclerotic, and acute confusional psychoses	..	..	..	..	49	71	120
"Mixed Cases"	..	..	..	..	6	8	14
Other Admissions	..	..	..	..	13	45	58
Total	..	..	..	..	127	240	367

"Mixed" Cases. In the "mixed" group the affective symptoms were seen in nearly every case in the setting of arteriosclerotic psychosis. In a previous study (Roth, 1955) such cases were in fact classified with arteriosclerotic psychosis. They have, however, been included here, though under a separate heading, so as to ensure that no case that could conceivably have been diagnosed as affective psychosis was left out of consideration. It was felt also that the relative contribution of the early and late onset groups to these intermediate cases had some bearing on the problem under investigation, and might throw some light on the problem of overlap presented by these cases in which affective and organic features were combined. In 8 of these "mixed" cases organic features were present from the beginning of the illness; the remainder had exhibited a phase of affective disturbance lasting months or years before the appearance of organic symptoms, although features unrecorded in the notes might have betrayed an organic component in the illness at an earlier stage or at onset.

It may here be pointed out that we have not excluded *all* patients with organic signs from the affective groups proper. Allocation of cases to the organic groups were made only when the psychiatric picture itself had consistent organic colouring, with dementia, prolonged confusion, or the presence of an amnestic syndrome. Localized disease of the nervous system (such as unilateral tremor, an old hemiplegia, or paralysis agitans), or equivocal signs of cerebral disturbance such as mild degrees of memory defect, or transient confusion, did not contra-indicate a diagnosis of affective disorder. It remains pertinent therefore to examine the frequency of such conditions in our two groups; for although not warranting a diagnosis of organic psychosis proper, they could nevertheless point to organic cerebral degeneration as a factor underlying the affective disturbance, and one which might subsequently transform the clinical picture. A difference in the importance of organic factors in causation between the two groups ought moreover to be reflected in a difference in the frequency with

which features indicative of an organic psychosis proper as well as signs of cerebrovascular disease are observed at follow-up.

We have made no attempt to give separate consideration to cases of involutional depression. However, as already pointed out, any assumptions implicit in treating all cases of "early" onset as one group of affective disorders, for the purposes of our study, were tested in a number of ways.

Description of material—Numbers. Of the 175 patients with affective disorder proper, 86 belonged to the early and 89 to the late onset group. Of the 14 mixed cases, 5 belonged to the early and 9 to the late onset group.

Sex ratio. Males. The early onset group contains 64 males, of whom 21 belong to the early, and 43 to the late onset group. Of 124 *females* 70 belong to the early, and 54 to the late onset group. The difference in sex ratio between the groups is significant at the 1 per cent. level of chance.

Age. The mean ages of the two groups are significantly different at the 1 per cent. level (early onset group 65·7 years, late onset group 70·4 years). Table II shows the age and sex distributions in the two groups and in the mixed cases.

Previous psychiatric illness. Forty per cent. in the early onset group had had one, 30 per cent. two, and 30 per cent. three or more previous attacks before

TABLE II

Sex Distribution and Mean Ages in Two Groups with Affective Disturbance: in Each Group Cases Belonging to the Organic Psychoses are Shown Separately ("Mixed" Cases)

	Early Onset			Late Onset			
	Affective	"Mixed"	Total	Affective	"Mixed"	Total	Totals
Females ..	67	3	70	49	5	54	124
Males ..	19	2	21	40	4	44	65
Total	86	5	91	89	9	98	189
Mean Ages	65·6	67·2	65·7	70·2	72·3	70·4	68·1

the age of 60. Of the late onset group, about 38 per cent. had had attacks since the age of 60, but before the present admission. Forty per cent. of the early onset group had their first attack before 40 years of age, 24 per cent. in the period 40–49, and 29 per cent. between 49 and 60.

SYMPTOMATOLOGY AND MENTAL TEST PERFORMANCE

The findings described were present on admission or observed during the first few weeks in hospital.

1. *Symptomatology*

Clinical signs of intellectual impairment and cerebral disease. The frequency of signs and symptoms suggestive of organic disease in the two groups is shown in Table III. Memory defect and "Confusion" were recorded whenever even a question of their presence arose in the hospital records or interviews. By "confusion" is meant a state of diminished awareness causing impaired contact with, and incorrect interpretation of the immediate environment (e.g. disorientation); both these symptoms are, of course, often associated in severe and sustained form with organic cerebral disease. This incidence is relevant to the present problem, for although there is much evidence to suggest that transient confusion in the acute stage may occur in affective disorders of functional aetiology, its presence in old age, even in this form, is prone to be attributed to some organic contribution to the aetiology. Likewise, mild degrees of memory

impairment in old people are often attributed to early dementia. Thirty-three individuals (17 per cent.) showed one or both of these signs (memory defect, which was nearly always for recent events such as admission to hospital, was associated with confusion in all but three cases). It can be seen in Table III that despite the preponderance of organic cases (mixed cases) in the late onset group, the incidence in the two groups is almost identical. Among the affective

TABLE III

Symptomatology in Two Groups Aged 60 and Over with Affective Disorder. "Mixed Cases" Showing both Organic and Affective Features are Shown Separately

	Group of: Early Onset			Group of: Late Onset			Total
	Affective	"Mixed"	Total	Affective	"Mixed"	Total	
Memory defect	6	5	11	6	8	14	25
Confusion ..	10	5	15	8	7	15	30
Focal neuro-logical signs	4	1	5	5	1	6	11
Dementia ..	0	2	2	0	2	2	4
Number of individuals affected	12	5	17	13	9	22	39
Total in Group	86	5	91	89	9	98	189

groups proper, confusion and memory defects were probably associated with the affective disturbance *per se* in 10 per cent. of cases, a figure which agrees closely with Lundquist's (1945) finding among 135 manic-depressive patients. Seven of our patients were suffering from manic or excited states.

Focal signs indicating recent central nervous system disease were found among 5 patients in the early, and 6 in the other group. Among the former one presented with an hemiplegia of two years' duration, another with hemiplegia and visual field changes of recent onset (mixed case), a third showed a unilateral tremor of nine month's duration, a fourth with bilateral tremor, and a fifth patient who died shortly afterwards, a possible extensor plantar response. Among the 6 patients in the other group one showed variable pyramidal signs and a visual field defect (mixed case), one transient loss of consciousness together with bilateral tremor thought to be of arteriosclerotic origin, two suffered from paralysis agitans and two showed unilateral extensor plantar responses without other gross physical signs. Finally, we noted the frequency of *dementia*, by which is meant a chronic progressive disorganization of personality and intellect, and which by the criteria used could have occurred only among the mixed cases. Four patients were found with this condition; one of these suffered from chronic mania which rendered the assessment of dementia somewhat uncertain; there was also a history of alcoholism. Two other patients had suffered depressive attacks before the age of 60 (at 36 and 55 years of age) and both exhibited atypical features. No patient exhibited the characteristic picture of uncomplicated senile dementia.

Summary. In the whole material 21 per cent. of cases show "organic signs", there being a slight preponderance in the late onset group. Exclusion of the mixed cases reduces this difference almost to zero and the incidence falls to 14 per cent. This figure includes cases with mild memory impairment and transient confusion only, which are compatible with severe affective disturbance *per se*, an interpretation which is supported by the results of the follow-up (q.v.). When mixed cases and those in whom the presence of a neurological lesion was uncertain are omitted from consideration, only 6 cases are left

showing unequivocal neurological signs, and they are divided equally between
the two groups (one with an old hemiplegia, one with unilateral tremor, and one
with bilateral tremor, in the early onset group; two with paralysis agitans, and
one with bilateral tremor and transient losses of consciousness in the late onset
group).

2. *Mental Test Performance* (Table IV)

The tests used were those described by Roth and Hopkins (1953), and
Hopkins and Roth (1953). They consisted of an Information and Memory test,
a Vocabulary test (Wechsler), and the Progressive Matrices (Raven), and were
given before therapy was begun. Table IV gives the results for the groups of
affective disorder proper (the mixed cases are excluded). One hundred and three

TABLE IV

*Performance (Mean Scores) on 3 Mental Tests by Two Groups Aged 60 and Over with
Affective Disorder. The Differences are not Significant. "Mixed" (Organic) Cases are
not Shown (see Text)*

	Groups With	
	Early Onset	Late Onset
Mental Tests:		
Information Test	16·0	17·0
Matrices	19·0	19·4
Vocabulary (weighted scores)	11·2	9·8
Number doing all 3 tests	33	37
Mean Ages	66·8	70·4
Total Tested	48	55

patients were tested of whom 71 had all three tests; the remainder were omitted
on one or more tests, either because their psychiatric condition or specific
defects made testing impracticable, or through factors beyond the psychologist's
control. The differences between the groups are not significant (P=>·05).
This is of special interest for the following reason: it is not uncommon when
examining elderly patients with affective disorder to find signs such as mild
memory impairment, some decrease in mental agility, or a reduced capacity for
abstraction, which may be attributed to degenerative changes in the brain;
these changes may then be held to be of aetiological significance for the disorder,
and to influence its prognosis adversely. But the question arises whether signs of
this kind, particularly when exhibited in a setting of affective disturbance, do in
fact commonly herald the onset of an organic psychosis proper, or whether they
fall within the normal range of decline in mental performance characteristic of
growing old. Now, in the group with early onset normal degenerative changes no
doubt occur but dementia is probably rare; the failure of our tests to show
differences suggests that the degenerative changes in the late onset group, among
the patients tested, also fell within the normal range.

If all individual performances are examined, *i.e.* including those of patients
who did fewer than all three tests, five are found to fall within the senile psychotic
range, as described by Hopkins and Roth (1953), in one or more of the tests. It
is of interest to examine the clinical states of these patients. One of the two
patients who belonged to the early onset group was "confused" and aurally
hallucinated on admission. She performed poorly on the Matrices, which was
unfinished and therefore regarded as unreliable. She has repeatedly relapsed,
but shows no clinical evidence of organic disease. The other patient obtained
very good scores on the Information and Vocabulary tests, and her difficulty on
the Matrices suggested a perceptual rather than a generalized intellectual im-
pairment; when re-tested after E.C.T. her score improved and she has remained

well for 18 months. Of the 3 patients in the late onset group whose performances fell within the senile psychotic range, one was severely depressed and "confused" and obtained very low scores on the Information and Vocabulary tests; after E.C.T. her performance improved, but her Vocabulary test score suggested high grade mental defect, which was not contraverted by the social history. She relapsed after discharge but has shown no clinical evidence of dementia. Another patient was confused in a setting of mania when tested; a few weeks later he had a series of fits attributed to cerebrovascular disease. The remaining patient was severely agitated; shortly after testing, during a course of E.C.T., she became aphasic and is now suffering from a mild arteriosclerotic dementia (see also section on Outcome, Cases 2 and 3). In the last case mentioned, agitation on admission was severe to the point of inaccessibility, and manic excitement with confusion made assessment difficult in the previous one. Thus, scores within the senile psychotic range were obtained either in cases in which complicating factors were present to influence the interpretation of test results, or in which symptoms probably due to cerebral arteriosclerosis made their appearance within a short time.

Mixed Cases. Only 7 of the 14 cases did all three tests and the results therefore are too few to tabulate. Five fell within and 4 just above the senile psychotic range on one or more of the tests.

Organic Groups. Of 71 patients with senile and arteriosclerotic psychoses tested during the same period, some have already been described by Hopkins and Roth (1953) and the performances of the remainder have been found to confirm these findings (Hopkins and Roth, to be published). About 4 patients out of 5 fell within the senile psychotic range in contrast to the affective groups.

In conclusion, a comparison of the symptomatology and mental test performance in two groups of affective disorder shows that they do not differ in the frequency of signs of cerebral involvement, but that both groups do differ significantly from the organic psychoses, to which the mixed cases tend to conform.

Outcome

The follow-up was conducted until 31 December, 1953. The mean period of observation was 20·5 months for both affective groups. Cases of organic psychosis admitted between the same dates were followed for a similar period. The outcome was assessed in two ways: (1) By allotting patients to one of the categories, Dead, In-patient, Discharged, in order to compare the broad pattern of outcome of the late onset group of affective disorders with the other affective and the organic groups; (2) By tracing the subsequent history of each patient and assessing his/her actual psychiatric condition at the time of contact (which was made by letter or by visit from the Psychiatric Social Worker) to record the occurrence of physical or mental deterioration, or relapse of affective disorder. Co-operation was good and only two patients are untraced.

(1) *Dead, In-patient, Discharged.* The outcome according to these categories is shown in Figure 1 at 6 months after admission and Table V after 9–27 months. It will be clear that the pattern of outcome in the two affective groups is *broadly similar* and is in sharp contrast to that in the organic psychoses. In view of the high mortality associated with the latter it would seem unlikely that cerebral disease could often be a cause of affective disorder in the group of late onset. A more detailed analysis reveals the following facts:

(i) *Deaths*. After a follow-up period of 9–27 months 21 patients (22 per cent.) of the late onset group are dead compared with 7 (8 per cent.) of the other affective group. The difference is significant at the 1 per cent. level of chance. However, after excluding mixed cases the figures become 15 and 8 per cent. respectively. When correction is made for differences in age this difference fails to reach statistical significance. There is therefore unlikely to be any factor peculiar to the late onset group which adversely influences the chances of survival to an important degree. There are nevertheless some observations to suggest that the small difference in mortality may be a real one. But it is not due to cerebral disease. Evidence has been obtained (to be presented in the next paper) that physical illness is much more common among the late onset group, and that the difference cannot be accounted for in terms of the greater mean age of the patients in it. Moreover, analysis of the relevant case records reveals that a specific somatic illness was the cause of death in every case in the late onset group; in no case among the affective groups proper was a macroscopic lesion found in the brain at autopsy.

TABLE V

Outcome on 31 December, 1953 (Mean Period of Observation 20·5 Months) in Two Groups with Affective Disorder and in Group with Senile and Arteriosclerotic Psychoses

	Affective Group with: Early Onset			Affective Group with: Late Onset			Senile and Arteriosclerotic Psychoses
	Affective	"Mixed"	Total	Affective	"Mixed"	Total	
Dead ..	7	0	7	14	7	21	50
In-Patient	13	4	17	11	1	12	17
Discharged	66	1	67	64	1	65	7
Total ..	86	5	91	89	9	98	74

(ii) The in-patient and discharged categories in the two groups are similar (Table III).

Mixed cases. Among 14 mixed cases only two are discharged and seven dead, an outcome markedly different from the remainder of the material.

Influence of the "organic signs" on the prognosis. After excluding the mixed (organic) cases it is found that local or chronic central nervous system disease and doubtful signs of cerebral degeneration (mild degrees of memory defect and transient confusion, see Section on Symptomatology) do not influence the prognosis materially for the worse. In particular, clouding of consciousness which is often held to indicate an organic cerebral factor in psychiatric disorder does not alone justify a poor prognosis. When it is considered that acute confusion can reasonably be expected on account of restlessness, lack of sleep and inanition alone, to be associated with a higher mortality or a more chronic course, our results make it unlikely that the confusion shown by many of these cases arose from senile or arteriosclerotic degenerative disease. Only when there is evidence of other kinds that such disease exists is the outlook worse than in uncomplicated affective disturbance.

(2) *Psychiatric Assessment of Cases at Time of Follow-up.* The actual psychiatric condition at the time of follow-up contact irrespective of in- or out-patient status provides further information. Psychiatric illness was considered to exist if there was: (i) affective disturbance or hypochondriasis; (ii) confusional episodes, a chronic amnestic syndrome or dementia. Using these criteria, 29 per cent. were found to be ill, 18 per cent. to have recovered after

relapsing once or more often, and 38 per cent. of the whole material to have remained well after treatment.

Affective disturbance or hypochondriasis was present in 50 cases of whom 32 were suffering from chronic depression or mania (4 cases), and 18 had had periods of remission lasting for several months. These patients were equally distributed between the two groups.
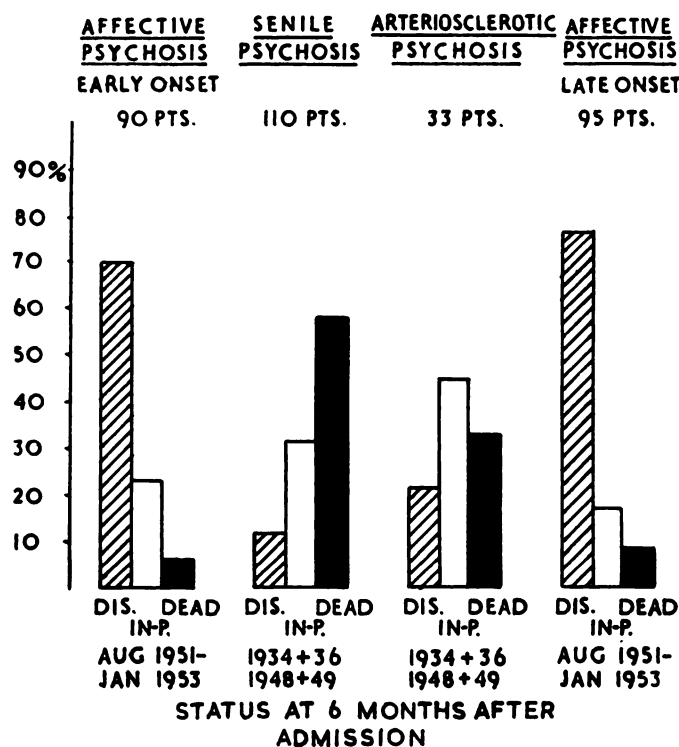

FIG. 1*

Organic psychoses were found in 8 patients out of the whole material (including the original mixed cases). Of these 8 cases, however, 2 had not previously been regarded as "organic" and therefore represent new cases:

Case 1. A woman of 75, was admitted in a state of severe agitated depression, and treated with E.C.T. during which she developed aphasia of a mixed type. She has remained aphasic and, in addition, has become euphoric and somewhat childish, but not grossly demented. (In-patient.)

Case 2. A man aged 86 was admitted with multiple somatic complaints of a few years' duration, and two months' depression with suicidal thoughts. He was in fair physical health, correctly orientated, and performed well on mental tests. He was discharged "recovered" after conservative treatment. Sixteen months later he was admitted to a general hospital with giddiness, unsteady gait, and urinary incontinence. There was generalized tremulousness, but no localizing signs in the nervous system. B.P. not raised. Physically he gradually deteriorated, and had to be spoon-fed. Mentally he was said to be occasionally confused at night; mood showed extreme dejection and anxiety about lack of progress, and fear of never being able to leave hospital. He was not demented. (In-patient, General Hospital.)

The first of these two cases was one to whom reference has previously been made in the section on intellectual tests. Her performance fell within the senile

* In this figure four "mixed cases" have been inadvertently excluded, one from the early and three from the late onset groups of affective psychosis.

psychotic range; she was exceedingly agitated on admission, became pale and shocked following each of two successive electroconvulsive treatments, and her aphasia and mild dementia were observed after her recovery from the last. The dysphasia has undergone improvement and the dementia has shown no tendency to progress during two and a half years' observation. The status of this patient is not certain but she has been classed as a case of cerebrovascular disease with mild dementia.

The second patient was not demented but his occasional nocturnal confusion was probably due to early arteriosclerotic psychosis.

A note was also kept of any cases that developed fresh symptoms or signs indicative of cerebrovascular disease, even where features of an organic psychosis were absent or uncertain:

Case 1. A man of 67 suffered from hypochondriasis, with mild depression, associated with a chronic sinusitis; B.P. on admission 200/115; 6 months later he had the first of several epileptiform fits. He did not develop focal signs or any impairment of memory or of habits. (In-patient.)

Case 2. A man of 71 was admitted in a manic state of sudden onset and was regarded as "confused"; he performed poorly on mental tests, and 3 weeks later he had several fits associated with transitory focal changes in the EEG. There is slight deterioration of habits in a setting of grandiose and overactive behaviour. The psychiatric picture is accountable in terms of mania.

There are thus four new patients with fresh organic features; in three of them focal neurological symptoms or signs have appeared while two show the early stages of an organic psychosis. The cause is probably cerebral arteriosclerosis in each case and all four belong to the late onset group. The significance of this finding will be discussed at a later stage.

Relapse and Recovery. Examination of the relapse rate among those regarded as well on the 31 December, 1953, shows an interesting difference between the early and late onset groups. In the whole material of 189 patients 35 had relapsed once or more often and subsequently recovered, and 25 of these belonged to the early onset group. In 28 of the 35 cases the relapse had been severe enough to require re-admission to hospital. The early onset group, in fact, because of their higher relapse rate, spent in all rather longer in hospital during the observation period than the other group. Of the 72 patients *remaining well* after discharge (39 per cent. of the whole material) 30 per cent. belonged to the early and 43 per cent. to the late onset group. Of the mixed cases only one was considered to be well 16 months after admission.

DISCUSSION

1. *Affective Disorder of Late and Early Onset, and Cerebral Disease.* The comparison between the late and early onset groups reveals no difference between them in respect of clinical signs and symptoms indicative of cerebral disease at the time of admission to hospital. In psychological performance the two groups were likewise closely similar. But four new cases of cerebrovascular disease, two of them with organic features in the psychiatric picture, came to light during follow-up; all were of the group of late onset. This finding requires evaluation as also the presence of cerebrovascular or local neurological signs in a small proportion of cases in each group and the existence of a mixed group in which some cases begin with a typical affective psychosis.

With regard to the two new cases of organic psychosis this development is not peculiar to affective disorder of late life. In a previous study (Roth, 1955) two out of four cases in whom an organic dementia supervened have had typical

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depressive psychoses in early life (34 and 41 years). In the present series the two "mixed" cases with dementia have had a depressive illness when aged 36 and 55 respectively. Nor are neurological complications of cerebrovascular disease without mental changes confined to the late onset group. The fact that all four new cases of cerebrovascular disease came from the late onset group may therefore be due to its exposure to a greater risk of developing this complication
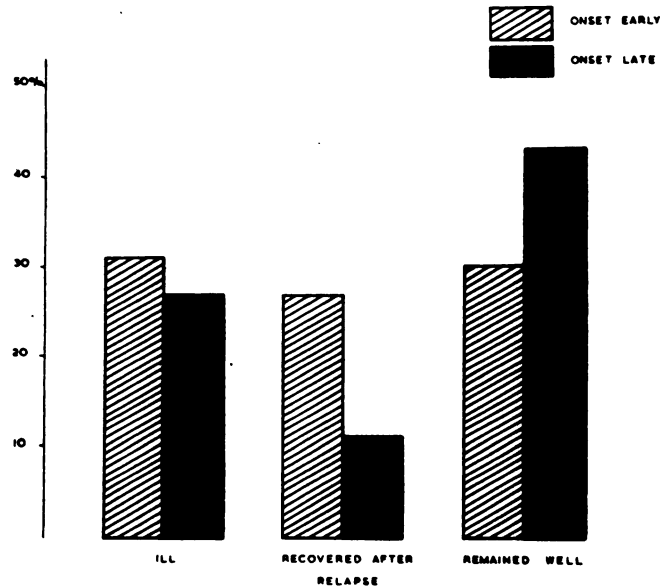
PSYCHIATRIC CONDITION IN TWO GROUPS WITH AFFECTIVE DISORDER
9-27 MONTHS AFTER ADMISSION
FIG. 2

owing to its higher mean age. That the association between affective psychosis and cerebrovascular disease may be a fortuitous one is suggested in particular by the histories of those mixed organic cases that commenced with an affective psychosis in early life.

Case 1. A woman aged 67 was admitted with a five-month history of an illness that initially showed depressive and paranoid features. She presented on admission with a fatuous mood, marked memory impairment and disorientation in time, bizarre paranoid delusions and deterioration of habits. She had had a depressive illness at the age of 47 from which she had made a complete recovery. Her first relapse had not appeared until 8 years later.

Case 2. A man aged 70 was admitted with one year's history of forgetfulness, disorientation, and recent incontinence; there had been several outbreaks of violence and he had attempted to commit suicide by climbing out of the window. He had had an attack of depression at the age of 58 following a physical illness. His first relapse did not occur until 11 to 12 years later.

Case 3. A woman aged 68 was admitted with progressive dementia of some three years' duration. There had been rapid deterioration and marked memory impairment in recent months. There was a history that she had "never been the same since the age of 22 when the first child was born". At 55 she was treated in a private mental hospital for a depressive illness. Following this she worked as a secretary for ten years.

It would seem unlikely that the affective psychosis in these cases could have been due to cerebrovascular disease which had remained dormant until the

appearance many years later of an organic psychosis. In such cases the aetio-
logical independence of the two conditions seems particularly clear. It may be
that the situation is not really different in affective disorder of late onset except
that postponement of the age of manifestation creates a spurious impression of
causal relationship with any cerebral degenerative process that may happen to
be coincident.

However even if there is no direct aetiological relationship between cerebro-
vascular disease and affective disorder of late onset there is evidently some slight
hazard of cerebrovascular disease developing in affective psychosis whether this
commences early in life or in old age. We cannot assume that the association is
wholly fortuitous unless there is evidence to suggest that it is of an order
accountable in terms of chance expectation. Such evidence does in fact exist.
In a study of a random sample of normal old people whose age composition was
similar to that of our total affective group (except that 65 was the lower age
limit for males), Sheldon (1948) found 4·4 per cent. of cases with neurological
lesions due to cerebrovascular disease. There were in addition 2·1 per cent. of
cases with a severe tremor. The incidence both of cerebrovascular disease and
total neurological disorder is therefore slightly in excess of that in our affective
groups even if all mixed cases are reckoned. Sheldon also reports "severe mental
deterioration" in 3·8 per cent. of his sample as well as 11 per cent. with a slight
impairment of mental faculties. Here comparison is more difficult owing to
ambiguities attaching to the standards of classification. But with this reservation
in mind his figure of 3·8 per cent. may be compared with an incidence of 4–5
per cent. of cases with organic psychiatric symptoms indicative of cerebral
disease in our material when all cases are reckoned except those of the mixed
group that were unequivocally organic from the beginning of the illness. The
affective psychoses proper showed on follow-up an incidence of only 1·1 per
cent. with organic psychoses and periods of observation as long as 5 years do
not increase this beyond 2·5 per cent. (Roth and Collins, 1954).

Now, it has been suggested on the basis of rather inconclusive evidence that
the pyknic or eurymorph build is associated not only with manic-depressive
psychosis but also with cerebrovascular disease (as well as diabetes, nephritis,
dropsy, alimentary disease, etc.) (Cohen, 1940). In a previous study (Roth,
1955) a relatively high incidence of affective symptoms in cases of arterio-
sclerotic psychosis (30 per cent.) was found and one of the possible explana-
tions suggested was some degree of association between the predispositions to
cerebral arteriosclerosis and affective disorder. The results of the present study
speak against any such association. Some alternative explanations for the
combination of clinical features suggest themselves. It may be that the loosely
knit and fleeting affective symptoms commonly found in arteriosclerotic
psychosis have little to do with the specific predisposition that probably underlies
affective psychoses proper (Slater, 1936); or that the greater likelihood of mixed
cases coming under observation explains the association observed.

Both these explanations may be relevant, but they are not entirely satis-
factory. It is not clear for example why arteriosclerotic dementia rather than
senile psychosis, a common disease, tends to complicate a small proportion of
affective disorders of old age. The association of these last two conditions is very
uncommon; thus it is rare to find any affective colouring or a previous history
of depressive illness in senile psychosis. One reason for this may be that since
arteriosclerotic psychosis is a condition of rather earlier onset, cases of affective
disorder are exposed to the risk of developing it rather sooner than to the hazard
of senile psychosis. Now, we know that the mortality of affective psychosis is

significantly higher than that of the normal population (Alström, 1942; Stenstedt, 1952). It is possible therefore that far fewer cases survive to the age of maximum risk for senile psychosis than are alive to suffer the hazard of cerebrovascular disease. But these are evidently matters for further investigation.

2. *Pattern of Outcome*. Despite its slightly higher mortality and the small excess of cases with cerebrovascular disease, the comparison of the general pattern of outcome in the two groups is considerably to the advantage of the group of late onset. The patients in it relapse less often, they spend a shorter time in hospital and a higher proportion remain well. If, therefore, it were reasonable to assume that the pattern of outcome for the group of early onset represented the fate of cases of affective disorders of largely functional aetiology the other group would *a fortiori* deserve to be regarded as of similarly benign causation. However, it was evidently necessary to check this assumption by a further analysis of data. This was done by comparing the outcome of those in the early onset group, whose first attack had occurred before 45 years, with those who fell ill after this age. The pattern was very similar in the two groups with the majority discharged and very few dead; a comparison by the χ^2 test was consistent with the hypothesis that they came from a homogeneous population. Nor could any significant difference be found in the incidence of organic signs or in performance in psychological tests.

The data about outcome may, therefore, be interpreted as arguing strongly against any important contribution by cerebral degeneration to the causation of late life affective disorders. It is true that affective symptoms, even when connected with indubitable cerebral disease, may remit spontaneously or improve with electroconvulsive therapy, a fact which has led certain authors (Gallinek, 1947, 1948) to suggest that the presence of organic cerebral lesions in association with affective disorders is no obstacle to sustained recovery with E.C.T. This is probably an over-optimistic view of the position. In the first place stricter diagnostic criteria would probably have led to a diagnosis of senile or arteriosclerotic psychosis in only a proportion of the cases reported. The remainder would appear to have been affective disorders in old age with extensive peripheral and retinal arteriosclerosis, and these are not a reliable indication that degenerative changes are proceeding in the brain itself. In our own experience, as already described, the small proportion of cases in which indubitable signs of a progressive cerebral degenerative process are associated with an affective symptom-complex show a high mortality, and even when they survive for a period rarely sustain any improvement; for although their affective symptoms may be temporarily relieved by E.C.T., the negative symptoms arising from degeneration are not. The affective symptoms tend to show a less sustained response than in ordinary cases of affective disorder.

In fact, while the findings underline the benign character of affective disorder in late life, they also make it necessary to emphasize the importance of making the distinction between these cases and the small group of mixed conditions in which affective symptoms are seen in the setting of an organic psychosis, nearly always associated with cerebrovascular disease. Whereas confusion in the acute stage, some degree of memory impairment and local neurological signs do not seem to affect the prognosis adversely, prolonged or fluctuating confusion, an amnestic syndrome or dementia associated with affective symptoms carry a very high mortality. Treatment in these cases is attended with hazards of a quite different order from these associated with

affective psychosis proper in old age, and may call for decisions of considerable difficulty.

The great majority of patients with an affective symptom-complex in old age are free from the features associated with the mixed group; and the high proportion of patients well on follow-up and the relatively low incidence of relapse in this general run of affective cases make it unlikely that the contribution of cerebral degeneration to their aetiology can be of much importance. This view is reinforced when it is borne in mind that affective disorder in fortuitous association with some cerebral degeneration which aggravates the disability may be more likely than uncomplicated affective illness to present for admission to a mental hospital.

When the evidence that has been obtained here is integrated with other data we have obtained about late life affective disorder a consistent picture emerges. Thus, other investigations have shown that the group of early onset have a greater loading with neurotic symptoms and a significantly higher proportion of relatives with neurosis than the late onset group, although the incidence of specific psychotic illness among first degree relatives of the two groups is similar. This suggestion that the latter are a less vulnerable and better integrated group of individuals is confirmed by the greater stability that attaches to their recoveries. These facts suggest that the existence of the group of late onset is due to postponement of the age of manifestation of a predisposition to mental illness similar to that possessed by members of the other group. In other words appearance of affective disorder for the first time in old age is a measure of resistance or, from the point of view of the genetic contribution to causation, diminished penetrance of the responsible gene, rather than an indication of organic disease of the brain. Finally the factor that has been identified as an exogenous cause of breakdown in those who have avoided illness in early life is physical illness. These data will be presented in the succeeding papers of this series.

SUMMARY

1. The association of cerebral degeneration with affective disorder arising for the first time in the senium has been examined by comparing two groups of patients, (a) those who had fallen ill for the first time before 60, and (b) those in whom the first attack had occurred at the age of 60 or later.

2. The two groups showed a similar incidence of signs indicative of or liable to be attributed to cerebral disease. Nor is there any difference between the two groups in respect of mental test performance. Cases of affective disorder of both early and late onset are exposed to some risk of suffering from cerebrovascular disease in old age. A review of the relevant evidence suggests that this is probably no greater than the risk in the normal population; the slight excess of cases with cerebrovascular symptoms found in follow-up of the group with late onset is likely to be due to its greater mean age. But further investigations into a possible association between cerebrovascular disease and affective symptoms are indicated.

3. The pattern of outcome of the two groups is closely similar with high discharge and low mortality rates, which sharply differentiate them from the organic groups proper. But attention is drawn to a small group of "mixed" cases which carry a far worse prognosis.

4. There is reason to believe that the slightly greater mortality of the group of late onset represents a real difference though it is not significant. It is linked with the higher incidence of physical illness of this group; the aetiological role of this is examined in another paper.

5. The conclusion is reached that cerebral degeneration of the kind found in the senile and arteriosclerotic psychoses is unlikely to be an aetiological factor of any importance in the causation of affective psychosis in late life, whether or not this appeared in the senium for the first time. Depressive or manic psychosis of late onset may be regarded together with affective disorders of earlier life as forming a nosological entity distinct from psychoses with cerebral degeneration.

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