A STUDY OF THE DEMENTIA PRÆCOX GROUP IN THE LIGHT OF CERTAIN CASES SHOWING ANOMALIES OR SCLEROSES IN PARTICULAR BRAIN-REGIONS.*

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I. The Schism over Dementia Præcox.

When it became apparent that the psychiatric world must needs split over the genesis of dementia præcox, one party describing it as a species of intoxication with brain damage and the other as a dissociative mental disease without structural damage to the brain, one found one's mind almost wholly open in the matter. Perhaps, at the outset, one was not quite ready to admit dementia præcox (Kraepelin's disease) among such relatively immortal entities as general paresis and hysteria, for example. The dissociation hypothesis possibly seemed the wider of the two, permitting each case to be a law unto itself in such wise that a proper diagnosis really turned into a fairly full katamnesis.

In any event it was gratuitous to hypothecate a toxine *toto coelo* and much more innocent to assume dissociations, especially if one could give precise descriptions of these for a number of typical cases. To be sure, some workers asserted characteristic satellitoses and other evidence of neuronic disease in the lower cortex-layers of the cerebrum; but these findings were perhaps inconstant, probably shared by other types of disease, possibly secondary either to the disease or to something else, and certainly incapable of affording any explanation of the mechanism of dementia præcox.

If one scanned the situation in neuropathology, the outlook was not bright. Restricting oneself to the cerebral cortex alone, cytopathology appeared to have fallen on evil days. Nissl had given up his specific nerve-cell intoxication pictures. Alzheimer's methods for split products of nerve-cell metabolism had not been developed or fully applied. And, in any case, the effects of terminal complicating disease (intestinal, pulmonary, bladder, and the like) with a variety of intercurrent infections and intoxicatons seemed to render dubious the outcome of almost any strictly cytopathological study, at least such as would contemplate symptomatic correlations. To conceive a " katatonic storm " sweeping through the cortex and leaving behind it a characteristic trail was within reason, but surely difficult of proof in the midst of so many cortical storms about the point of death.

Stratigraphic considerations were more hopeful. In fact, ever since Alzheimer's brief paragraph in 1897—*Ebenso findet sich ganz zweifellos bei der Katatonic eine pathologische Gliafaserbildung in der Rinde, anscheinend auf gewisse Rindenschichten (und die Markleiste) beschränkt*[1]—there has been an ever recurrent assertion that satellitosis and correspondent nerve-cell disorder of the inner cortex-layers are characteristic of dementia præcox, or at least of its katatonic form. In fact these findings were supposed to draw together the two diseases, dementia præcox and general paresis, since both showed the same changes, complicated in the latter by a multitude of other stratigraphic changes as well as by exudation.

Such opinions are not confined to Germany. Thus, in France, Klippel and Lhermitte, 1908,[2] consider dementia præcox to be due to a progressive atrophy of the association neurones. The lesions of dementia præcox, they say, are all essentially neuroepithelial, *i. e.*, confined to nerve-cells and neuroglia, and never essentially vasculoconjunctive, or, as we should express it, ectodermal, never mesodermal. The fundamental lesion is " a regressive atrophy of the nerve-cells of the deep cortical layers and disappearance of the interconnecting processes," with neuroglia proliferation running *pari passu* with the atrophic process. Meningovascular lesions, miliary hemorrhages, congenital malformations, terminal lesions due to cachexia or infection, are frequent, but are not indispensably found. Even cerebellar atrophy, and various instances

of visceral hypoplasia, are simply signs of frail organisms, which either precede without causing dementia præcox or are purely incidental effects thereof. Klippel, in discussion, admitted that similar neuroepitheliæ (ectodermal) lesions were found in other chronic mental diseases.

Perhaps no work has been more widely quoted in this direction than that of Sioli, done partly at Munich under Alzheimer and partly at Bonn and summarily reported in 1909. Sioli's statements refer, however, only in part to stratigraphic considerations.

Sioli in his brief *Autoreferat,* 1909,[3] states that he found *in all parts examined* of 20 cases of dementia præcox certain evidences of destruction of nerve tissue. A portion of Sioli's data is cytopathological (nerve-cell disease with increase of Scharlach-stainable lipoids), but he indicates that the process may lead to atrophy or disappearance of cells, amounting in places to distinct stratigraphic disorder. Degenerative products were found accumulated in clear non-cellular spaces about the vessels, and protagonoid and Scharlach-stainable substances were found in tissues and in adventitial cells *en route* to the vessels. Inflammatory exudation was quite lacking. Perivascular and periganglionic glia-cell proliferation, fibrillary gliosis in the subpial zone, in deep cortex-layers, and in the white matter, alterations of glia-cell cytoplasm, amœboid neuroglia in the white matter occurred. The severest cases, especially those with their perivascular spaces packed with degeneration products, are thought to correspond with acute katatonic exacerbations.

Alzheimer, in his masterly statement concerning split products of nerve-cell and fibre metabolism, 1910,[4] maintains that much new light has been thrown, by his new methods and adaptations of old ones, upon such conditions as status epilepticus, severe paralytic attacks, deliria, and katatonic excitements, and he believes that anyone using these methods will be convinced that dementia præcox and epilepsy are severe organic diseases. Alzheimer would almost risk differentiating histologically between a katatonic excitement and a mania, because the katatonic case will show characteristic amœboid glia-cells, whereas the mania will not. For the purpose of this differentiation, severe disease of the other viscera must not step in to complicate the picture since such disease may bring out the amœboid glia-cells in the nervous

system. Again, a severe toxic delirium at its height and a severe katatonic excitement at its height will exhibit similar changes (just as the posterior columns of a tabes and a spinal transsection might be confused under certain circumstances from the granule-cell content of both). The fact seems to be that "organic" changes can now be demonstrated in a number of conditions formerly termed "functional." The differentiation of katatonia remains difficult, however, on account of precisely the conditions mentioned by Alzheimer, toxic delirium and severe bodily disease, which may produce somewhat the same pictures.

One remarkable case of sudden death in a stuporous katatonic who had no demonstrable physical disease is mentioned by Alzheimer to show that, without loss of any nerve-cell or degeneration of a single axis-cylinder, a true *Hirntod* may occur due tc changes demonstrable by methods for the split products.

Unfortunately for the neuropathologist, such cases of pure *Hirntod* are rare. In the Danvers State Hospital material, infection at the time of death is almost the rule. Exact experiences with the cultivation of the more easily growing organisms from the blood and cerebrospinal fluid in 150 unselected cases have been communicated by Gay, Canavan, and myself.[8,9] Cerebrospinal fluids are particularly prone at death to show organisms. This experience, as well as an inspection of the great members of tuberculous and acute infections in our material, caused us to discount in advance the cytopathological change *per se* and to hold somewhat in doubt the acute or recent neuroglia change as indicating mental disease. The asserted stratigraphical changes (cell-atrophies and losses in lower cortex-layers and correspondent satellitosis) seemed more trustworthy, but obviously less differential (seen also in general paresis and in some senile cases).

The status of the dementia præcox question may be summed up as follows:

One body of workers prefers to describe dementia præcox in such terms as *dementia sejunctiva* (Gross[7]), *Missverhältniss zwischen Affekt und Vorstellung* (Kölpin[6]), *dysphrenia* (Wolff[9]), *dementia dissecans* (Zweig[10]), *schizophrenia* (*Zerreissung oder Spaltung der psychischen Funktionen*) (Bleuler[11]), *Apraxia ideatrix* (Dromard[12]), emphasizing in general the dissociative factors which emerge upon psychological analysis of the more clearly cut

cases. "Disruptions of judgment," "specific factors in individual cases," "unpsychological reactions," "intrapsychic ataxia" or more specifically "noothymopsychic ataxia," "intrapsychic inhibition," "psychogenic conflicts," "psychological dispositions," "psychic causos," "psychic trauma," are phrases picked almost at random from certain modern discussions.[13 14 16]

Other workers pin their faith to the supposed "organic" character of this disease. The ground of this belief is often scarcely more than that the disease is essentially deteriorative on the mental side and hence *must* be "organic" on the cerebral side. Others set much store by autointoxication and believe that the effects of autointoxication must be registered in the cerebral cortex, could we but read it aright. Proceeding from the dictum that insanity and, therefore, dementia præcox are brain diseases, these workers argue that dementia præcox is presumably a destructive disease of the cerebral cortex, after the manner of general paresis.

A few workers accord significance to both the functional psychic features and the organic cortical features. There is, however, a general tendency to take sides, with the almost universal feeling that the histologists have not satisfactorily proved the "organic" nature of the disease.

I was instigated to the analysis of my own material by the conviction that, though the histopathologists had not proved their point beyond peradventure, the functionalists were in the same plight. I had been engaged upon an analysis of cases of mental disease with onset after the fiftieth year,[16 17] and had there come upon so many instances of satellitosis in the deeper layers of the cortex without distinct katatonic features clinically that I had been disposed to discount the differential character of deep-layer gliosis for any type of mental disease. This reaction, in brief, appeared to be a necessary and natural result of destructive processes involving these layers, and the deposition or increase of neuroglia cells in this locus did not assume to my mind the differential character of such findings, as, *e. g.*, the plasma cell exudate of general paresis. Even the plasma cell, as all will admit, is not *sensu strictiori* pathognomonic for general paresis (witness trypanosomiasis, not to mention tuberculous and frankly luetic processes). Gliosis of the deep layers of the cortex is obviously

far less differential than plasma cell exudation, if only because normally we find neuroglia and satellite cells in this region.

Feeling a deal of uncertainty about the differential value of stratigraphic alterations and especially of satellitosis, I was also not disposed to believe that dementia præcox would turn out to be a diffuse cell disease. All that Alzheimer maintains, if I understand him aright, is that anyone who chooses to examine dementia præcox material by certain methods can convince himself that it is invariably an "organic" disease.[18] It would be a much longer step to assert that the changes invariably found are differential changes. Indeed, deliria and severe physical disease are consistent with the same changes.

Neither stratigraphic changes nor cytopathological changes, taken as exhibited *throughout a brain,* appealed to me as likely to throw much light on the immediate mechanism of dementia præcox. Indeed these changes bring up more new problems than they solve old ones in the wide field of neurobiology.

The *topographic idea* then occurred to me. In making, some years ago, an analysis of the first 1250 autopsies of the Danvers State Hospital and collecting the lesions of different parts of the brain in card-catalogue form, I had been much struck with the preponderance of brain lesions in certain areas. The frontal incidence was particularly high, and this, I took to be due to the greater liability of the frontal tissues (on the stock evolutionary grounds). Having no convenient opportunity to correlate these findings with clinical data (a want now happily supplied by the index of clinical symptoms which Dr. Page has had constructed), I did not further work up these relations.

In connection, however, with work on encephalitis,[19] on gliosis,[20,21] and especially on the "soft brain," [22] I had begun to gather unusually careful data concerning focal and general variations in consistence of brains. I had, therefore, some hope that my series would prove unusually suitable for topographic study.

Upon analysis, as the sequel will prove, not merely focal scleroses, but also easily identifiable macroscopic atrophies (or aplasias) were found in a surprisingly large number of cases. My topographic data depend, therefore, only in part upon the palpable mild scleroses which I had been especially studying.

On the basis of the anatomical data and without necessarily any reference to microscopic studies (which have been carried out more or less thoroughly in the series), I wish to commend the topographic idea concerning lesions in dementia præcox to neuropathologists. Whether a superior frontal atrophy or a postcentral aplasia is or is not superior to a psychic scar or ataxia, as really explanatory of the mechanism of dementia præcox, I will not pretend to say. In any event, the brains of all dementia præcox cases should be carefully examined.

II. Material, with Statistical Analysis.

The autopsy material of the Danvers State Hospital Laboratory from May, 1902, to January, 1910 (including the services of Drs. A. M. Barrett, E. E. Southard, and a portion of Dr. H. M. Adler's), consists of 647 cases. Sixty-three of these have been chosen, on clinical grounds, as probable or possible examples of dementia præcox. The 10 per cent thus chosen constitute the maximum rather than the minimum number of possible cases, since it was thought best to include certain doubtful cases for purposes of comparison. As will presently appear, several of the cases are so clouded by other factors, such as certain congenital features, alcoholism, or attacks suggestive of manic-depressive insanity, that the diagnosis of dementia præcox may appear extremely doubtful. It was felt that histological features might serve to extract the true cases.

As it is extremely desirable not to confuse phenomena of a normally aging brain with possible findings based on mental disease, the age of the subjects at death is important. The series is quite representative.

TABLE I.

Classified by decades according to age at death, the material shows:

11	cases	dying	in	the	third	decade	(21-30)=	8	male,	3	female
19	"	"	"	"	fourth	"	(31-40)=	7	"	12	"
12	"	"	"	"	fifth	"	(41-50)=	3	"	9	"
11	"	"	"	"	sixth	"	(51-60)=	6	"	5	"
8	"	"	"	"	seventh	"	(61-70)=	7	"	1	"
2	"	"	"	"	eighth	"	(71-80)=	2	"	0	"
63							(21-80)=	33	"	30	"

It is also necessary to secure a representative series from the standpoint of age at onset. The series even includes two cases with strongly congenital coloring.

TABLE II.

Classified by decades according to age at onset, the material shows:

2	cases	with	congenital	features	(possibly	imbecile)	=	2	male,	0	female
6	"	"	onset	in	the	second	decade	(11-20)	=	6	"	0	"
28	"	"	"	"	"	third	"	(21-30)	=	13	"	15	"
20	"	"	"	"	"	fourth	"	(31-40)	=	9	"	11	"
7	"	"	"	"	"	fifth	"	(41-50)	=	3	"	4	"
63										33	"	30	"

It is essential to know how long the morbid process may be supposed to have lasted. Although many of these cases are not at all progressive, yet in many others slow transitions in clinical disease-type are exhibited. The total durations are given in

TABLE III.

Classified by duration of symptoms in hemidecade periods, the material shows:

18	cases	under	5	years	in	duration.....			8	male,	10	female
11	"	between	6	and	10	years	in	duration,	5	"	6	"
10	"	"	11	"	15	"	"	"	3	"	7	"
3	"	"	16	"	20	"	"	"	2	"	1	"
7	"	"	21	"	25	"	"	"	4	"	3	"
4	"	"	26	"	30	"	"	"	2	"	2	"
3	"	"	31	"	35	"	"	"	3	"	0	"
3	"	"	36	"	40	"	"	"	2	"	1	"
1	"	"	41	"	45	"	"	"	1	"	0	"
2	"	"	46	"	50	"	"	"	2	"	0	"
1	"	"	61	"	65	"	"	"	1	"	0	"
63									33		30	

Although it is well known that various clinical phenomena are rather thoroughly commingled in this disease, making the older distinctions hard to maintain and more or less justifying Kraepelin in his union of types under a single caption, yet certain features do particularly characterize some cases, and the following table presents the impressions which these cases made, so to say, in the rough, before intensive analysis.

TABLE IV.

SUPERFICIAL ANALYSIS OF CASES.

Hebephrenic	5	cases,	2	male,	3	female
Katatonic	17	"	9	"	8	"
Paranoid	30	"	18	"	12	"
Dementia-præcox-like:						
Imbecile	1	"	1	"	0	"
Alcoholic	1	"	1	"	0	"
Manic-depressive, involutional and unclassified	9	"	3	"	6	"
	63	"	34	"	29	"

There was such an admixture of symptoms in several of the cases, or symptoms of doubtful import, that possibly the katatonic cases should number 20, and the paranoid cases, 32. Imbecile traits came in question in seven cases in all, though possibly not to obscure the eventual diagnosis in more than three. Alcoholism can, with difficulty, be disengaged from the clinical picture of five cases. The at times doubtful, or eventually unclassified cases, which have been chosen to study with this group, number 15; but of these perhaps eight only can be fairly claimed as not instances of dementia præcox; and, if a somewhat liberal definition be admitted, all these cases will warrant consideration. As Table IV indicates 52 cases (29 male, 23 female) probably belong in the group with some certainty on clinical grounds.

In the process of anatomical analysis, much may be gained from the weight correlations of certain organs. If the brain weights stand up well, we at least have indication that no such conditions as those underlying general paresis or cerebral atrophy are present. The brain weights in this series correspond well with the normal, though they show a slight tendency to reduction (2 per cent).

TABLE V.

BRAIN WEIGHTS BY SEX.

Male (26 cases)	1336	dementia	præcox,	1357	normal	(Vierordt)
Female (29 cases)	1218	"	"	1235	"	"
Differences	118	"	"	122	"	"
Percentages:						
Male	98%	"	"	100%	"	"
Female	98%	"	"	100%	"	"

An analysis of the brain weights according to age at death yields

by no means so even a curve, doubtless because the numbers are too small for this particular purpose. The results are as follows:

TABLE VI.

BRAIN WEIGHTS BY DECADES IN WHICH DEATH OCCURRED.

Male	21-30,	6 cases.....	1333	dementia	præcox,	1358	normal	(Boyd)
Female	21-30,	3 "	1278	"	"	1239	"	"
Male	31-40,	5 "	1476	"	"	1366	"	"
Female	31-40,	11 "	1194	"	"	1222	"	"
Male	41-50,	3 "	1350	"	"	1348	"	"
Female	41-50,	9 "	1237	"	"	1214	"	"
Male	51-60,	6 "	1353	"	"	1345	"	"
Female	51-60,	5 "	1222	"	"	1225	"	"
Male	61-70,	5 "	1364	"	"	1315	"	"
Female	61-70,	1 "	1100	"	"	1210	"	"
Male	71-80,	1 "	1390	"	"	1290	"	"

It might be suspected that the different forms of dementia præcox would lead to different degrees of brain-weight reduction. The weights in the hebephrenic, katatonic, and paranoid cases, in accordance with the clinical analysis of Table IV, have been arranged:

TABLE VII.

Hebephrenic,	male	2 cases.....	1338	1357	normal	(Vierordt)
	female	3 "	1168	1235	"	"
Katatonic,	male	9 "	1329	1357	"	"
	female	8 "	1193	1235	"	"
Paranoid,	male	12 "	1309	1357	"	"
	female	11 "	1240	1235	"	"

The differences are all less than 70 grams, and the weights are consequently within five per cent of the assigned normals.

Since the duration of the disease, though it certainly does not vary with the duration of any active process in all cases, might be supposed to bear some relation with the extent of any destructive process, the weights have been arranged according to duration:

TABLE VIII.

Cases with duration under 10 years:				
Male	1331	1357	normal	(Vierordt)
Female 16 cases.....	1223	1235	"	"
Cases with duration 11-20 years:				
Male 5 cases.....	1261	1357	"	"
Female 7 "	1243	1235	"	"
Cases with duration over 20 years:				
Male 10 cases.....	1375	1357	"	"
Female 6 "	1173	1235	"	"

Obviously these figures produce no even curve; but, should they be confirmed by other material, the interference could certainly be drawn that these brains stand wear and tear particularly well.

If such figures tend to show that no coarse katabolic effects evince themselves in the brains of this group, it is interesting to inquire whether any evidence of such disorder can be traced in other organs by this method.

TABLE IX.

HEART WEIGHTS.

Male 31 cases	281	
minus 3 hypertrophies (500 + g.)	244	313 normal (Vierordt)
Female 27 cases	264	
minus 1 hypertrophy	253	310 " "

TABLE X.

LIVER WEIGHTS.

Male 30 cases	1369	1579 normal (Vierordt)
Female 28 "	1257	1526 " "

TABLE XI.

SPLEEN WEIGHTS.

Male 30 cases	160	
minus 1 case wt. 870	132	149 normal (Vierordt)
Female 27 cases	106	180 " "

TABLE XII.

COMBINED KIDNEY WEIGHTS.

Male 31 cases	280	277 normal (Vierordt)
Female 29 "	255	264 " "

Tables IX to XII appear to show that certain organs of the trunk are more disposed to evince losses in weight than is the brain in dementia præcox. The kidney weights, however, stand up well. The weight of the spleen, as always, showed marked variations, and these variations largely depend probably on certain terminal conditions independent of mental disease.

Reductions in average weights of heart and liver reach a little over eight per cent, for both males and females in both series. It is hard to draw a significant conclusion therefrom.

To sum up the data of this section, we learn from a fairly representative series of cases of dementia præcox and similar diseases that a reduction in brain weight of two per cent is perhaps to

be expected in the total group, that the reductions in brain weight of five per cent occur in certain forms (here a larger number of cases is required for deductions), that the brain weights do not undergo progressive reduction with the duration of the disease, and that the hearts and livers of the series show in general a reduction of eight per cent in weight. Since the weights of the trunk viscera probably vary rather uncontrollably in the present state of knowledge (the factors of muscular activity and of nutrition in these patients come particularly in question), it is plain that more stress must be laid on brain conditions. The brains must be approached, therefore, with the premonition that changes, if any, will be fine changes, and possibly qualitative and transformatory rather than destructive.

III. Gross Anatomical Analysis of the Brain Findings.

As it is our object to show *either,* first, that there are no characteristic brain findings in this series of cases *or,* secondly, that there are characteristic findings common to the series, it is obviously necessary to exclude cases with certain features which we are sure are not characteristically allied with dementia præcox. Such complicating features are *coarse cerebral atrophy* and *regionary arteriosclerosis.* These features complicate and sometimes influence the course of dementia præcox; but it is certain that arteriosclerosis and highly probable that coarse cerebral atrophy are not characteristically associated with the disease.

As is well known, the question, whether brain atrophy exists, cannot be safely answered from the brain weight alone, since apparently high weights are consistent with atrophy of originally large brains, and apparently low weights may mean simply that the original weights were low. Qualitative data are safer guides here.

Five brains gave the qualitative impression of *generalized atrophy.* All these cases were of long total duration (11 years or more).

TABLE XIII.

Autopsy Number.	Clinical Number.	Sex.	Age.	Disease-Type.	Duration.	Terminal Disease.	Brain Weight.
752.	9888.	F.	64.	hebephrenic,	9y.	pneumonia, 7d.	1100.
958.	10738.	F.	37.	paranoid,	11y.	exhaustion, 1m.	1210.
1266.	7559.	F.	58.	paranoid,	13 ++ y.	dysentery, some weeks.	1250.
1274.	11027.	M.	56.	katatonic,	31y.	hemiplegia, 1m.	1365.
1297.	7511.	F.	47.	paranoid,	19y.	cancer of uterus, 2 + m.	1390.

It seems safe to eliminate this group from prior consideration, despite the fact that the gliosis shown may be more or less closely related with dementia præcox.

One of the best indices of damaging local arteriosclerosis is afforded by *cysts of softening,* which were found in three cases, 1274 and 1297 of Table XIII, and 1171 (5986, F., 43, paranoid, 17+(30?) y., brain weight 1115g.), also excluded from prior consideration.

Also it may be safer at first to exclude seven cases (1099, 13180, M., 67; 1121, 13398, F., 56; 1174, 9769, F., 48; 1258, 2, M., 64; 1270, 617, M., 68; 1337, 15017, F., 45; and 1368, 12120, M., 56) on the score of *marked sclerosis of vessels of the circle of Willis.* It is certain that this sclerosis has no direct effect upon the mental life; but there is at least a suspicion of vascular disease in the finer branches in such cases (only two of which in this series, viz., 1337 and 1174, are under 56 years of age).

It is noteworthy that we are required to exclude on these grounds (grounds, namely, of complicating "organic" brain-disease) only about 20 per cent of our series. This confirms the impression gained from our statistical analysis of the brain weights.

There is another general condition, frequently found in cases of all descriptions (both sane and insane), which might be considered to have some bearing especially upon the histology of the superficial layers—*chronic leptomeningitis of diffuse distribution* (to the focal distributions we shall return in a moment). Eleven cases (842, 904, 913, 943, 958, 1014, 1025, 1027, 1093, 1234, 1338) may be excluded on this ground. These 11 and four others (already excluded) yield another perhaps surprisingly small percentage (about 22 per cent) of cases showing diffuse chronic leptomeningitis.

For completeness are also presented the data concerning

TABLE XIV.

DURAL AND CALVARIAL CONDITIONS.

Arachnoidal villi unusually developed	3	cases
Thickening of dura mater (not included under adhesions)	4	"
Chronic internal hemorrhagic pachymeningitis	3	"
Dense calvarium	9	"
Thick calvarium	6	"
Thick and dense calvarium	2	"
Thin calvarium	3	"
Calvarial adhesions of the dura mater	25	"

If we rely upon the statistical analysis of Section II, we cannot be so sure that mild *focal lesions of an atrophic or sclerotic nature* have nothing to do with processes in dementia præcox, since these lesions will not appreciably influence brain weights. It is, of course, *à priori* unlikely that such circumscribed foci, which are doubtless in the vast majority of instances due to some degree of local tissue destruction, can correspond with the extended series of vital reactions which we term dementia præcox. Nevertheless, it is wise to examine our series carefully for foci of a slightly destructive or perhaps purely irritative character which might bear on the course of certain cases.

Consequently, excluding as diffusely atrophic five cases, as markedly arteriosclerotic (cysts of softening or basal cerebral arteriosclerosis) eight cases, as showing diffuse chronic pial changes 11 cases, we remain with a material of 39 cases, which deserve primary consideration from the standpoint of *possibly significant focal brain lesions.* Obviously the results of the search in these 39 cases (two of which must be excluded through inadequate protocols) may be applied, with due caution, to the remainder.

A group of 14 cases amongst these 37 "non-organic" cases showed certain *minor lesions* made out in the gross, but *not frankly destructive, some possibly congenital in origin.* A summary view of these cases is presented in

TABLE XV.

MINOR MACROSCOPIC BRAIN LESIONS IN DEMENTIA PRÆCOX.

I. Pre-Rolandic Lesions.

Autopsy Number.	Clinical Number.	Sex.	Age.	Disease-Type.	Duration.	Frontal Lobe Lesions.
840.	11211.	F.	38.	katatonic,	3y.	Atrophy and gliosis of frontal lobes.
1062.	7987.	F.	38.	paranoid (alcoholic)	11 + y.	Gliosis of superior frontal, prefrontal, and orbital gyri.
1143.	8823.	F.	47.	paranoid or katatonic,	10y.	Gliosis of frontal, including orbital, gyri (v. also cerebellum).
1294.	10862.	F.	37.	paranoid,	6y.	Frontal lobe gliosis (v. also post-Rolandic and cerebellar groups).
1310.	13582.	F.	28.	hebephrenic mannerisms,	4y.	Frontal lobe gliosis (v. postcentral group).
1358.	10580.	M.	24.	katatonic,	10y.	Gliosis of left inferior frontal lobe.
1360.	10168.	M.	51.	suicidal,	10y.	Atrophy of prefrontal gyri.

II. Post-Rolandic Lesions.

						Occipital Region Gliosis.
1137.	6531.	M.	35.	paranoid, later katatonic,	15y.	Right superior parietal microgyria (atrophia?).
1168.	11863.	F.	24.	hebephrenic paranoid?,	3½y.	Bilateral aplasia of postcentral gyri.
1298.	14591.	F.	36.	katatonic,	10m	Right postcentral atrophy (v. discussion).
1310.	.....	See Frontal Group.		.....		Left postcentral aplasia or atrophy.
1149.	11641.	M.	57.	paranoid,	32y.	Occipital region gliosis.
1294.	.....	See Frontal Group.		.....		Occipital region gliosis.
1317.	12143.	F.	44.	paranoid,	21y.	Occipital microgyria.

III. Infra-Sylvian Group.

						Cerebellar Lesions.
1319.	14597.	F.	31.	paranoid, (imbecile)	8y.	Superior temporal anomaly.

IV. Cerebellar Lesions.

1034.	12756.	M.	35.	first paranoid later katatonic,	2y.	Sclerosis of dentate nuclei of cerebellum.
1143.	.....	See Frontal Group.		.....		Sclerosis of right dentate nucleus, culmena, and clivi of cerebellum. Pons and olives firm.
1168.	.....	See Post-Rolandic Group.		.....		Sclerosis of right dentate nucleus, cacumena, and clivi of cerebellum. Sclerosis of olives.

A somewhat similar small group of four cases has shown certain appearances in the spinal cord, indicating abnormality of quite doubtful interpretation.

TABLE XVI.

GROSS LESIONS OF THE SPINAL CORD.

Autopsy Number.	Clinical Number.	Sex.	Age.	Disease-Type.	Duration.	Gross Lesions of the Spinal Cord.
1317.	.....	See Post-Rolandic Group.		.....		Cervical portion abnormally firm.
1319.	.....	See Infra-Sylvian Group.		.....		Cervical cord abnormally large.
1335.	.....	See Table XVII.		.....		Cord abnormally small.
1350.	4820.	M.	62.	katatonic,	35 + y.	Gliosis of lumbar spinal cord.

Here then, as indicated in Tables XV and XVI, is a group of 15 cases showing certain minor chronic lesions (or evidences of aplasia) in the central nervous system of quite doubtful, though

certainly very varied, origin. Adding four more cases of *generalized cerebral sclerosis* of a mild form, not associated with gross atrophy, viz.

TABLE XVII.

Autopsy Number.	Clinical Number.	Sex.	Age.	Disease-Type.	Duration.	
991.	11047.	M.	35.	paranoid,	11y.	Brain weight 1170 grams.
1135.	11296.	F.	28.	katatonic,	6y.	Brain weight 1430 grams.
1303.	11624.	F.	55.	hebephrenic,	25y.	Brain weight 1220 grams.
1335.	13648.	M.	32.	katatonic (alcoholic)	20y.	Brain weight 985 grams.

we obtain a total of *19 cases of slightly, though macroscopically, abnormal central nervous system in a series of 37 cases, selected as not showing coarse complicating features like brain atrophy, intracranial arteriosclerosis, cysts of softening, and the like.*

These 19 cases, or at all events a certain number of them, demand attention as a group of dementia præcox cases with lesions of doubtful interpretation, but not readily set aside as non-significant.

If we should group our cases up to this point, we should obtain (1) *complicated cases,* showing gross lesions certainly not related with dementia præcox, 40 per cent, (2) *cases with minor lesions* having a doubtful relation to dementia præcox, 31 per cent, and (3) a residuum of *cases without observed gross lesions,* 29 per cent.

It will be wise at this point to analyze the cases of groups (2) and (3), *i. e.,* the non-complicated cases from a clinical point of view. The 37 cases are distributed as follows:

TABLE XVIII.

Hebephrenic	4	2 male,	2	female	
Katatonic	12	5 "	7	"	
Paranoid	13	7 "	6	"	
Alcoholic	1	1 "	0	"	
Doubtful	7	3 "	4	"	

If we eliminate the alcoholic (1240, no gross lesions) and doubtful cases (819, 939, 1151, no gross lesions; 1143, 1360, frontal lobe lesions; 1350, spinal cord lesion; 1135, generalized gliosis, Compare Tables XV-XVII) for the time being, we obtain 52 per cent of our group (now reduced to 29 cases) showing minor lesions.

A microscopic analysis of the 15 cases showing minor lesions may indicate what type of lesion to look for in those cases which failed to show gross lesions. Lesions of this sort should be demonstrable by any method which displays cells and nuclei well.

In case the lesions should prove non-stratigraphical, *i. e.*, not ideally demonstrable by complete cell-counting, the task will be more difficult. The qualitative intracellular or special extracellular properties which this latter search would entail will require material very seldom obtained, material free from terminal complications. Cases hitherto reported have suffered perhaps from such terminal disease. Tuberculosis is a special offender in this direction. Tuberculosis occurred in our series as follows:

TABLE XV.

TUBERCULOSIS IN 63 CASES OF DEMENTIA PRÆCOX.

Active forms	21	cases
Healed and chronic forms	16	"
All forms	37	"

TUBERCULOSIS IN 39 CHOSEN CASES.

Active forms	16	cases
Healed and chronic forms	7	"
All forms	23	"

In both series there is 58 per cent of tuberculosis, counting all forms. One case in three of the whole series either died with or showed an active form of tuberculosis, whereas about two cases in five of our chosen "non-organic" series showed similar active tuberculosis.

Whereas it has never perhaps been convincingly shown that active tuberculosis outside the nervous system can produce important non-exudative lesions within the nervous system, it is probably a sound policy to exclude such cases from a list *sans reproche*, especially if intracellular conditions are to be studied. This process would leave us with *23 cases free from coarse destructive brain lesions and from active tuberculosis.*

Nine cases showing *decubitus*, 10 cases of soft brain" (only one of which occurred in the non-organic series), and three cases of *edema of brain substance* might also offer obstacles to finer

cytological analysis. For this purpose a list of 21 cases is available; but clinical doubts and difficulties remove eight cases, leaving 13 cytologically appropriate cases (840, 884, 891, 944, 1006 (typhoid fever), 1034, 1081, 1298, 1303, 1317 (carcinomatosis), 1350, 1358, 1360).

To sum up, we have divided our cases upon anatomical grounds into three groups, (1) cases complicated by gross destructive brain lesions (40 per cent), (2) cases having certain minor anomalies or mildly destructive or irritative lesions (31 per cent), and (3) cases without observed gross lesions (29 per cent). After excluding cases unsuitable for analysis on various grounds, we obtained a group of 29 cases, 15 of which (52 per cent) showed the minor anomalies and mild lesions just mentioned. It will be the task of the next section to study these 15 cases intensively to see whether they evince any common features. Later studies may then apply these observations to the rest of the series, in which significant lesions may well occur hidden among complications.

IV. Clinical and Anatomical Analysis of Fifteen Cases of Dementia Præcox Selected as Showing Certain Minor Gross Lesions of the Nervous System.

At this point it seems pertinent to inquire whether, upon a closer analysis of the cases which show minor gross lesions or anomalies, any hint of correlation between these lesions and individual clinical phenomena can detected. It must be pointed out forthwith that no very close correlation can be hoped for, since we deal with far less constant phenomena than, *e g.*, those of epilepsy. The histories, presented below in as condensed form as deemed advisable to offer a sound basis for clinical diagnosis, obviously betray far greater variations in course and qualitatively more complex features than would a similar number of histories of epileptics. But clinical and anatomical correlations even in epilepsy are difficult, despite the firm establishment of the "uncinate" group on an anatomical basis. In view of the clinical variety of the dementia præcox group, or even of the group of cases characterized by katatonic symptoms, it is at the outset doubtful whether a "frontal lobe group," a "postcentral group,"

a "cerebellar group" can be firmly established for dementia præcox. Obviously such a grouping should be earnestly essayed.

The *condensed histories,* drawn from the records of numerous workers (among whom may be mentioned Drs. H. W. Mitchell, H. A. Cotton, H. M. Swift, and Charles Ricksher, who have been at the heads of the various services during the major part of the time covered by these reports) and the *summarized autopsy protocols* (for which the pathologists, bacteriologists and assistant physicians named below have been responsible) are here presented.

CASE I.—S. M., D. S. H., No. 12211, Path. No. 840. Female, 37, single, school-teacher. Born in Cambridge, Mass., of Irish parentage. Was a case of dementia præcox, katatonic type, of three years duration.

Heredity.—Negative.

Previous History.—Patient taught school from 22-35. In August, 1901, after a period of over-work, the patient became depressed ("had lost her soul"); her mind dwelt on suicide. Patient remained unoccupied; two weeks after onset of depression was committed to McLean Hospital, where she showed languor, slow movements, little spontaneous talk, a general effect of emotional gloom and certain somatic delusions ("bowels gone"). A brief attack of excitement followed, with confusion and resistiveness. Short periods of excitement followed with later increasing inertia, and little spontaneous talk. Seven weeks after commitment she began to show increase of muscular tension and had to be tube-fed.

Patient was transferred to Danvers Hospital April 1, 1903, and then showed a flushed face, clammy skin, and considerable acne. Pulse slow and weak, respirations shallow.

The katatonic signs consisted of an evenly distributed increase of muscular tension. Patient lay constantly in bed, on one side, with arms loosely adducted, hands clenched, legs flexed, chin and knees drawn together, eye-lids tightly closed, a fixed facial expression, with lips protruded.

At first patient would take food from a cup, but tube-feeding was later constantly resorted to.

Patient would flinch slightly to pin pricks, but would not move limb even if pin was deeply thrust. Risus sardonicus appeared at times. Occasionally, the eye-lids were kept half closed, and the eye-balls rolled upward.

Within six weeks, a slight physical failure was noted. Patient would occasionally speak at night. Later, talking spells occasionally appeared, such as "Go away," "Stop that," "Oh, what shall I do? I can't read. Oh, a thousand times. It is nothing at all"; or again, "I shall have to stop in this bed forever. God Almighty in Heaven, here I am talking, and I have no head. I am as empty as space. There is nothing in this bed, and I have no head. I have fixed everything wrong. It is terrible. Look, I am talking without a head. It is impossible. Is it not? An empty bed.

I am a skeleton bitch. This is a frightful impossibility." Looking at her hands she said, "These are not hands. How can I do this talking without a head? God help me. It is all wrong. I simply imagine that I see them. There is nobody here, the bed is empty. I don't know what I am doing."

Emaciation became rapid late in 1903, and patient died after a period of continued fever.

ANATOMICAL DIAGNOSIS (A. M. Barrett).

Cause of Death.—Phthisis pulmonalis.

Chronic Conditions.—Poor musculature. Malnutrition. Bilateral chronic adhesive (apical and posterior) pleuritis. Tuberculous cavity of apex of left lung. Cavitation and disseminated tuberculosis of upper lobes of both lungs. Enlarged bronchial lymph nodes. Bronchitis. Chronic fibrous ("milk patch") pericarditis.

Recent Conditions.—(Possibly bronchitis and bronchial lymphnoditis). Fatty liver (microscopic evidence). Fatty kidney (microscopic evidence, slight).

Nervous System.—Brain weight 1090 grams. Generalized increase of consistence of brain. Slight visible atrophy of gyri of both frontal regions. Cerebral cortex unusually dark in color, but without puncta cruenta.

CASE II.—P. F., D. S. H., No. 10147, Path. No. 991. Male, 35, married, carpenter. Born in Nova Scotia of Nova Scotian parents. Was a case of dementia præcox, paranoid type.

Heredity.—Negative.

Previous History.—Masturbation; sexual excess. At 21 years married; five children. At 31 years "nervousness," loss of confidence, somatopsychic delusions ("heart gone," "insides working"). In hospital quiet, apathetic, hypochondriacal. Discharged at 35 and next year recommitted. Diagnosis, hypochondriacal paranoia. The diagnosis was later changed to chronic melancholia. Emaciation and suspicion of phthisis at 38 years. Signs of phthisis upon recommitment at D. S. H., October 25, 1902. Extremities blue, teeth poor. At first refused food. Groaning and complaints of pain and abnormal sensations. Disorientation (lack of interest?) for time and place.

"I can't speak because it pulls down and pulls up, and is wound around me." At no time katatonic signs, except mutism (possibly paranoidal origin).

ANATOMICAL DIAGNOSIS (A. M. Barrett).

Cause of Death.—Phthisis pulmonalis.

Chronic Condition.—Malnutrition. Poor musculature. Chronic obliterative pleuritis, bilateral. Phthisis pulmonalis, with cavitation and fibrosis. Chronic persplenitis. Chronic interstitial nephritis. Exostosis on inner surface of frontal bone. Adherent dura.

Acute Condition.—Acute fibrinous pericarditis (organism of colon group).

Nervous System.—Brain weight 1360 grams. Slight generalized cerebral gliosis.

CASE III.—R. O., D. S. H., Nos. 11871, 12756, Path. No. 1034. Male, 35, single, shoe-factory operative. Born in Italy. Was a case of dementia præcox, at first paranoid, later katatonic, of two years duration.

Facts concerning heredity unknown.

Previous History.—Emigrated from Italy at about 23. Shoe-factory operative of average capacity. Easily affected by alcohol (some beer and whiskey daily). In March, 1904, stated that anarchists and socialists wished to kill him; that he heard men talking and singing in the next room; thought that people were going to "do him," and ceased to work steadily. In the course of five or six weeks patient began to feel that his friends had turned against him, and when a man borrowed his mandolin and returned it minus one string, patient reasoned that he was being hypnotized. At that time, the diagnosis lay between dementia præcox and alcoholic insanity, the former preferred.

Patient was committed to Danvers Hospital April 27, 1904. Undersized, unusually hirsute. There was slight swaying in the Romberg position. The knee-jerks were exaggerated. Patient was reticent. At one time said, "There is going to be something this side and then on the other side," making signs with his fingers around his head. Once asked to play cards, snatched the cards from the table and refused to give them up. Dulness and inactivity increased, with a tendency to stupor, interspersed with brighter intervals. Nine months after admission, periods with marked echopraxia and some cerea flexibilitas, with diminished response to peripheral stimuli, set in. Patient became reluctant to eat.

Discharged February 2, 1905, to go to Italy. Patient was readmitted October 5, 1905, with mutism, cerea flexibilitas, slight resistiveness on being roused, fixed facial expression, staring eyes and pouting lips. Slight albuminuria was now demonstrated for the first time. Automatism shortly developed, with prompt obedience to commands, such as protrusion of the tongue for incision. Patient habitually sat for hours with hands spread over knees, staring at the floor. Saliva was held in mouth for hours. Symptoms of pulmonary gangrene set in and patient died a week later, January 23, 1906.

ANATOMICAL DIAGNOSIS (E. E. Southard).

Cause of Death.—Gangrene of right lung.

Chronic Conditions.—Emaciation. Unequal pupils. Irregularity of right pupils (iris narrow above). Slight mitral valvular sclerosis. Small heart (150 grams, but left ventricle 1.5 cm. thick), and small aorta (5 cm. in circumference).

Acute Conditions.—Gangrene of posterior portion of right upper lobe of lung (culture, streptococcus pyogenes and diphtheroid organisms), with acute fibrinous pleuritis, bronchial edema, and swelling of bronchial lymph nodes. Septicemia (determined on culture, streptococcus pyogenes and diphtheroid organisms). Unusual hirsuteness.

Nervous System.—Brain weight 1410 grams. Dentate nuclei abnormally firm and yellowish.

CASE IV.—D. R., D. S. H., No. 7987, Path. No. 1062. Female, 38, married. Born in Nova Scotia of Irish parentage. Was a case of dementia præcox, paranoid type, of eleven years duration.

Facts of heredity unknown.

Previous History.—At the age of 28, about a month before commitment to D. S. H., patient had been depressed and suicidal, with delusions that she was being killed, had been partially buried, had seen spirits, had had two hearts and was immortal. It appeared that the patient had been lately deserted by her husband and much over-worked. She had had three children, one living.

Shortly after admission, August 31, 1895, she was given the diagnosis of primary delusional insanity. She showed râles in both apices and edema of ankles. Patient worked in the laundry. Was occasionally reticent, but at other times freely stated her delusions. Tooth-aches and neuralgic pains she attributed to external influences. Was at times abusive, noisy and obscene. At other times would show no evidence of mental disorder for several weeks. In the course of two or three years, physical inertia increased, delusions could be still elicited, with somewhat less coherent explanations. Sample of conversation: "I was referring if you thought I felt well and if it was for your purpose to ask these questions. I proved it whether I am worthy of my home. There are two police stations and if you are acquainted with medical things you will see the church about me." Active auditory hallucinations appeared at times. The tuberculosis probable at admission became definite 10 years later. Patient died after a terminal disease of about four months. This patient apparently never showed well-defined katatonic signs, unless occasional reticence with physicians and a single period of mutism can be so interpreted.

ANATOMICAL DIAGNOSIS (E. E. Southard).

Cause of Death.—Phthisis pulmonalis.

Chronic Conditions.—Poor musculature. Malnutrition. Poor teeth. Lineæ atrophicæ of abdominal skin. Chronic obliterative pleuritis (right), and extensive adhesions of left pleura. Extensive bilateral tuberculosis with cavitation of lungs and bronchitis. Enlargement and induration of bronchial lymph nodes (tuberculosis, microscopically). Aortic, common iliac, internal iliac (slight), renal (microscopic), and (slight) coronary arteriosclerosis. Fatty liver with (microscopically) slight portal cirrhosis. Genitalia atrophic. Thyroid small (aberrant thyroid above bifurcation of trachea, right anterior, 2 x 1.5 x 0.5 cm.). Marrow of right femur red.

Nervous System.—Brain weight 1260 grams. Gliosis of superior frontal, prefrontal and orbital gyri. Brain (except gliotic areas and occipital gyri) and spinal cord (especially lumbar) reduced in consistence. Cerebellar cortex darker than cerebral cortex.

CASE V.—M. R., D. S. H., No. 6531, Path. No. 1137. Male, 35, single. Shoe-factory operative. Born in Lynn, Mass., of Irish parentage. Was a case of dementia præcox, at first paranoid, later at times katatonic, and finally demented; of about 15 years total duration.

Heredity of insanity denied. Father possibly alcoholic. A brother died of tuberculosis.

Previous History.—September 1, 1891, patient developed a delusion that persons in an electric light plant opposite his shop were putting currents on him. Insomnia, constipation, lack of appetite, pains in the head and confusion of mind followed, and patient was committed to D. S. H., October 2, 1891, with exaggerated knee-jerks and little or no physical disorder. Apparent dementia increased. Unusual motions and gestures could not be explained by patient. At first he worked well in the brush shop, but later ceased work, became mute, and sat still in one place, smiling. The attendant could get patient to walk up and down the ward. Limbs were habitually blue and cold. In taking exercise, a certain number of steps were always taken and a certain crack in the floor was followed. When seated, the limbs were held fixed and the mouth open. At times the patient would sit gesticulating for long periods at a time. Later, the gestures and peculiar attitudes ceased, but mutism persisted. Once, in 1903, the patient whispered a few words. There was never any refusal of food during the Danvers stay. Death January 19, 1906.

ANATOMICAL DIAGNOSIS (E. E. Southard).

Cause of Death.—Phthisis pulmonalis.

Chronic Conditions.—Malnutrition. Chronic adhesive pleuritis of left upper lobe and right apex. Mitral valvular sclerosis. Brown atrophy of heart muscle. Small heart (170 grams, but left ventricle 1.3 cm. thick) and small aorta. Chronic interstitial nephritis. Dilatation of stomach. Right testis fibrotic.

Recent Conditions.—Tuberculous pneumonia of left lung, with acute fibrinous pleuritis. Bronchopneumonia of posterior portion of right lung. Early enterocolitis (?) with large, soft mesenteric lymph nodes. Acute splenitis. Fatty liver and kidney (both slight).

Nervous System.—Brain weight 1465 grams. Superficial asymmetry in minor sulci of cerebrum. Microgyria of right superior parietal lobule (no certain evidence of atrophy, but more flaring sulci; in particular the right parieto-occipital fissure is 1 cm. deeper and much wider than the left). Focal chronic fibrous leptomeningitis of right parieto-occipital fissure. Consistence of brain diminished (anterior poles least and lower surface of cerebellum less than upper surface).

Chemistry.—The water-content of three portions of the brain was determined in the chemical laboratory of the Harvard Medical School by Mr. J. B. Ayer, Jr., who found the following percentages: frontal region, 75 per cent; parietal, 77 per cent; cerebellum 82 per cent water. These findings parallel the consistence noted with the finger. The anterior poles were the least softened. The low percentage of water possibly indicates relatively high neuroglia content.

CASE VI.—G. B., D. S. H., Nos. 11641, 3238, Path. No. 1149. Male, 57, single, carpenter. Born in Salem, Mass., of American stock. Was a case of dementia præcox, paranoid type, of perhaps 32 years duration.

Heredity.—Facts not known.

Previous History.—Was perhaps not "just right" from boyhood. Had certain delusions and may possibly have been suicidal early in life, but was shortly transferred after his first stay at Danvers to the Salem Almshouse, where he was quiet and industrious. Patient showed insomnia at times and had sensations of "sparks of fire" dropping on his head.

Readmitted January 1, 1904, with signs suggesting tuberculosis at both apices. A coarse tremor of extended tongue, a moderately fine tremor of extended fingers, and markedly exaggerated knee-jerks. Examination by Dr. H. W. Mitchell showed that the knee-jerks are usually followed by momentary clonus or tonic spasm of the leg followed by general body spasm, which does not seem to be always the same. The different movements depend upon the different postures of the body at the time the knee-jerk is obtained. Often the same body spasm can be gotten by a feint to strike the quadriceps tendon. Achilles reflex is prompt, but not much increased. It is followed, however, by various spasms of the legs, the most common being a tonic spasm of the muscles of the leg and thigh, often accompanied by irregular spasms of muscles of the trunk. *Triceps* and *biceps* prompt and lively and followed by irregular body spasms. *Cremasteric* and abdominal slight. *Plantar* very much increased, followed by tonic or clonic leg spasms. Usually no lifting of right toe. Rarely a suggestion of Babinsky reflex. The only physical stigma consisted in poorly-formed lobules.

Auditory hallucinations had been frequent for many years, always in the tones of attendants or other bystanders. There was one episode of visual, olfactory and gustatory hallucinations of an unpleasant character.

Very characteristic were patient's description of peculiar spiritualistic phenomena, with "forerunners and communications." Patient would often communicate with God, assuming a rigid position, gazing into space, and saying, "God, our Heavenly Father, I would like to communicate, if convenient, don't discommode yourself!" He pauses a few moments and then says, "Is that you? Is that you really, Heavenly Father? Please come as an apparition, as strong as you can." Then in a faint voice, "That's pretty good, pretty good. Can you come a little stronger, I wish you would if you could; that pretty good, that's good. God, Heavenly Father, is it safe to show the forerunner in the face of Dr. Mitchell? Are you sure, perfectly sure? All right." He would then make a peculiar movement of the hands which he alleges is a forerunner, and has the power of destroying life. Asked to forecast the future, he calls up God as previously, and says, "I wish to ask a question in regard to Dr. Mitchell's success in the future? Is your time precious, God? Can you spare it?" He turns to the examiner and says, "He is gone now to examine. He examines by astronomy." In the meantime, patient converses pleasantly about the weather until God calls, and later assures examiner that his success is to be unlimited, and that he has received communication. Result of these communications were, as a rule, optimistic.

Patient made characteristic, elaborative, decorative drawing, ostensibly

for certain Masonic lodges. In 1905 certain slight mannerisms appeared, which later grew more frequent. He would wet his hands frequently, repeat certain muscular movements, shake his body, and make peculiar noises in his throat.

The patient died March 1, 1907, having been taken the day previously with vomiting and severe abdominal pains.

ANATOMICAL DIAGNOSIS (H. W. Mitchell and F. P. Gay).

Cause of Death.—Tuberculous enterocolitis with ulceration and perforation with localized peritonitis. Bacillus coli communis in heart's blood at autopsy.

Chronic Conditions.—Emaciation. Chronic fibrous pericarditis. Slight tricuspid valvular sclerosis. Chronic obliterative pleuritis (left) and chronic apical adhesive pleuritis (right). Disseminated tuberculosis of both lungs. Caseating mesenteric lymph nodes. Chronic pericholecystitis. Hepatic atrophy (especially left half of right lobe and all of left lobe). Chronic splenitis (marked).

Acute Conditions.—See cause of death. Acute nephritis.

Nervous System.—Brain weight 1490 grams. Generalized cerebral sclerosis (without visible atrophy). Occipital lobes firmer than rest of brain. Chronic fibrous leptomeningitis, confined to the superior frontal gyri. Cerebellum and spinal cord soft. Slight chronic external adhesive pachymeningitis.

CASE VII.—R. S., D. S. H., No. 11863, Path. No. 1168. Female, 24, single, a weaver by occupation. Born in Canada of French-Canadian parentage. Was a case of dementia præcox, hebephrenic type, of four years duration.

Heredity.—An aunt insane.

Previous History.—Of normal early development. Four years a weaver in Massachusetts. Deserted by lover at 20. Indifference and melancholy, auditory hallucinations, delusions of persecution, subjective sensations of heat. Occasional attacks of violence and refusal to be dressed followed.

Upon commitment, April 22, 1904, a slight tremor of tongue, slight albuminuria, and semi-adherent lobules were noted. Patient was quiet, usually mute, indifferent, occasionally irritable, and resistive. Patient lay in bed with clothes pulled over her head and would start up suddenly, rocking back and forth.

There was an apparent amnesia for recent and remote events. Auditory hallucinations, ill-defined delusions of persecution, a silly apathetic attitude persisted. Mutism developed later.

About a year after admission, signs of tuberculosis and physical failure set in, and 17 months after admission, signs of tuberculosis were detected and tubercle bacilli were found. Thereafter patient grew brighter and would occasionally sing, but would not talk and had to be tube-fed. The knee-jerks, normal on admission, were later lost (September, 1906).

The patient died May 4, 1907, about 14 months after onset of physical failure.

ANATOMICAL DIAGNOSIS (E. E. Southard).

Cause of Death.—Thrombosis of left common iliac vein and vena cava (unidentified organisms).

Chronic Conditions.—Malnutrition. Ascites. Hypertrophic cirrhosis of liver (2260 grams). Chronic adhesive pleuritis (both upper lobes). Bilateral phthisis pulmonalis. Bronchial lymph node tuberculosis. Brown atrophy of heart muscle. Slight mitral valvular sclerosis. Coronary arteriosclerosis. Chronic gastritis. Slight enlargement of right lobe of thyroid gland.

Recent Conditions.—See cause of death. Edema of left leg. Fatty changes in liver and kidney. Acute perisplenitis (extension from pleural process).

Nervous System.—"Brain weight 1105 grams. The cerebral hemispheres show no variety in consistence and suggest a slight softening of post-mortem origin. The convolutions are everywhere of the usual richness and appearance except that the upper two-thirds of the postcentral gyri appear narrower than normal, being scarce two-thirds the width of the precentral gyri. It is impossible to make out on section that the underlying white matter is firmer in the postcentral than the precentral gyri. The limits of this lesion cannot be made out exactly, and the lesion probably represents an anomaly of the postcentral gyri. Basal ganglia not remarkable. Weight of cerebellum, bulb and pons, 145 grams. The olives have the consistence of those of a normal brain. The right dentate nucleus is firmer than usual. There is a suggestion of thinning out of the laminæ in the clival and cacuminal regions.

Middle Ears.—Normal.

Spinal Cord.—Shows an increase of consistence in the lumbar region, and several segments at various points seem to show a thinning out of the anterior halves without, however, demonstrable diminution in the area of cross-section."

CASE VIII.—J. O., D. S. H., No. 10862, Path. No. 1294. Female, 37, married, housewife. Born in Lynn, Mass., of Irish parentage. Was a case of mental disease, possibly dementia præcox, paranoid type, of six years duration.

Heredity.—Facts not known.

Previous History.—Patient was married at 23 and had four children, three girls and a boy. Nineteen days after the birth of the last child, which took place normally, except that both legs had been swollen, patient became noisy, thought she was dying and asked for the priest. She was carried to Lynn Hospital and was there excited and had auditory hallucinations. The left leg had swollen much worse 10 days after birth of child.

Upon commitment to D. S. H. June 5, 1902, this leg was still swollen and the skin scaling. The patient was confused and suspicious, at first tractable, later resistant, occasionally listening to imaginary voices, stating "they seem to speak from my hand." Delusions were sometimes somatic. When

asked what was the trouble wth her, "It is like little bits of formed children. It makes me nervous." Pointing to the physician's note-book, she said, "That is not saints' work." Periods of violence with biting, kicking and scratching would alternate with quiet and agreeable periods. Food was refused. Ten days later the patient had become somewhat better and developed some insight, and about a month after admission was apparently recovered from hallucinations. Removed upon a visit by her husband, the patient again became depressed, apprehensive and confused. Heard "rappings" at night. Patient stated, "These things I am telling you are all lies, but I have got to say them, because I have that feeling and cannot explain. I feel as though someone was compelling me to go through with it. This person has a grudge against me." There was considerable variation in the development of hallucinations. Patient spoke of queer doings going on at the hospital and talked about seeing "four generations" walking out of the dining-room. Exceedingly active hallucinations developed again in November, 1902, and patient broke glass to reach her husband, who was being crucified. Patient became resistive, violent, profane; would then relapse into depression and confusion. Food was refused as unnecessary. In February, 1903, patient had become dull, would talk little, was occasionally resistive.

March 9, 1903, said, "When the sandbags came on the ward for the old lady with the fracture, the Lord said even the sandbag liked her because she had sandbags at the Lynn Hospital, and she used to go to the beaches too." Occasionally talked in a grandiose way about being St. Johanna. Occasionally struck patients without provocation, and would frequently run the length of the ward for no apparent reason. Patient often spoke of herself in the third person and often knelt in an attitude of prayer. While walking attempted to touch every tree. Patient began to refuse to dress and take care of her room. Conversation became loose and contained many meaningless phrases: "Why did you come here? You hear me and you know my reports as a queen. Yes, I am the queen of England. I was known as Mrs. Page in the hospital. The carriages and horses are all in my name. Do you deny it, Johnnie? Who do you mean? Nothing new. I have all my money invested. I have my own rights and places up there."

In 1907 the patient was transferred to the tuberculosis ward and there died December 14, 1908. Toward the close of life, knee-jerks had been exaggerated. There was apparent amnesia, and only partial orientation could be demonstrated.

ANATOMICAL DIAGNOSIS (A. H. Peabody and M. M. Canavan).

Cause of Death.—Phthisis pulmonalis and tuberculous enteritis with ulceration.

Chronic Conditions.—Malnutrition. Slight ascites, hydrothorax, and edema of ankles. Hydropericardium. Slight chronic fibrous endocarditis. Chronic obliterative pleuritis (right). Chronic apical pleuritis (left). Ovarian atrophy. Erosion of cervix. Tuberculous ulceraton of colon. Enlarged lymph nodes near cecum and along aorta. Cavitation of left

upper lobe. Disseminated tuberculosis of right lung. Enlarged bronchial lymph nodes. Calvarium dense. Slight chronic external adhesive pachymeningitis.

Acute Conditions.—Acute nephritis.

Nervous System.—Slight chronic leptomeningitis with adhesions at frontal and temporal tips. Brain weight 1120 grams. Generalized increase of consistence of cerebrum (especially frontal and occipital), pons, and cerebellum.

CASE IX.—J. W., D. S. H., No. 14591, Path. No. 1298. Female, 36, married, housewife. Born in Dracut, Mass., of Irish parentage. Was a case of dementia præcox, katatonic type, of about nine months duration.

Heredity.—Negative. One brother and one sister died of tuberculosis.

Previous History.—Healthy as a child. A good student, disposed to quick temper. Married at 25. Miscarriage at five months, followed by three boys and a girl. Became nervous and run down at 34 years.

Present Illness.—Onset of pain in right side about April 1, 1908. Several weeks later patient dropped her work complaining of "physical incapacity and pain in the chest." Insomnia and brooding followed and in June patient complained of having tuberculosis, but said she could not get well. After a vacation she began in August to worry more. She was once disposed to jump out of a window and several times stated that relatives were trying to cut her up. She feared poison in her food. There were spells of looseness of bowels followed by constipation.

Patient was committed to D. S. H. October 6, 1908. Partially adherent lobules of ears. Slight hypertrichosis of upper lip. Gothic palate. Teeth in poor condition. Atrophy of breasts. Expansion of right lung less than that of right. Slight resistance of passive movements. Upon admission patient chiefly lay in bed as a rule with her eyes full of tears, moved very slowly and expressed the idea that every one was trying to hurt her. Patient's emotional reactions were very slight, although stating that deep palpation of the abdomen hurt her. Her expression gave no signs of pain. Although describing fear of being hurt, she gave no further evidence of fear. At first appeared depressed and retarded, she later improved. Had a spell of untidiness, became more active, gave irrelevant replies, and showed inertia suggesting dementia præcox. The diagnosis of manic depressive insanity, depressed phase, was first made, largely based on retardation in conversation and movements. In the middle of December, 1908, patient again became untidy and sat on floor; showed certain physical failure. Her conversation was limited largely to "I want to go home." Without definite proof of tuberculosis, she was placed in the building for tuberculosis, and there showed restlessness, negativism, a tendency to pulling bed clothes from other patients and untidiness. There were several slight rises of temperature. January 7, 1909, patient had a severe generalized convulsion, after which time she lost weight, became unable to speak and to swallow easily. She mentioned slight headache in the last few days of her life. Death January 16, 1909.

ANATOMICAL DIAGNOSIS (M. M. Canavan and C. G. McGaffin.)

Cause of Death.—Ileocolitis with ileac ulceration. Infection of cerebrospinal fluid with organism resembling bacillus of fowl-cholera.

Chronic Conditions.—Malnutrition. Sacral and trochanteric decubitus. Teeth poor. Gastroptosis. Chronic perisplenitis. Chronic periappendicitis. Chronic adhesive apical pleuritis. Slight chronic parietal endocarditis. Mitral valvular sclerosis. Small vegetation of aortic valve. Slight aortic sclerosis. Tuberculosis of apices. Slight cirrhosis of liver with fatty change. Chronic purulent cholecystitis. Laceration of cervix. Chronic external adhesive pachymeningitis over vortex.

Acute Conditions.—Tumor of left kidney. Acute nephritis (pyelo nephritis?). Acute endocervicitis. Thrombus of left internal iliac artery. Uulcers of ileum. Injection of jejunum, ileum, colon and rectum.

Nervous System.—Pia faintly injected and adherent to dura over left middle frontal in an area 1 x 1 cm. in diameter, 16 cm. from tip of pole. Pia is raised from the brain by a clear fluid over the vertex region. Pia slightly cloudy over vessels, but strips from cortex smoothly. Hemispheres equal in size and in general slightly firmer than normal. The left second temporal convolution is more prominent than others of its side or the opposite temporal convolutions. The left precentral gyrus measures on mesial aspect 2 cm., left postcentral 1.5 cm. The right precentral measures on mesial aspect 5 cm.; the right postcentral 1 cm. Sulci around right postcentral gaping. Cut sections show the postcentrals to have faint and thin grey matter and their white matter shrinks from the knife. The ventricles are smooth. Ganglia normal. Basal vessels not notable. Sections of the brain show no further gross lesions.

Brain weight 1300 grams. Pons and cerebellum 190 grams.

Middle Ears.—Gasserian ganglia and cord not notable.

CASE X.—M. M., D. S. H., Nos. 2874, 11624, Path. No. 1303. Female, single, 55, compositor. Born in Peabody, Mass., of American parentage. Was a case of dementia præcox, observed in a terminal stage.

Heredity.—An uncle insane at D. S. H.

Previous History.—Patient was admitted to D. S. H. with diagnosis of chronic mania (duration six months) June 6, 1883, and was discharged unimproved to Salem Almshouse August 28, 1885. At 29 believed she was a clairvoyant; apparently had auditory hallucinations. Complained of pains in throat and constantly spitting blood. "Could feel other people's injuries." Excitement on admission; assumption of absurd attitudes and declamation. Disconnection on talk. Made mysterious mention of Masonic signs. More active delusions brought out by menstruation. Her delusions dealt chiefly with injuries brought upon others which she could feel. At Salem Almshouse the dementia advanced. She had a vagrant tendency and was resistive.

Upon second admission to D. S. H. January 4, 1904, patient showed a heavy growth of hair on chin and upper lip; a narrow high palate and slight arcus senilis. Exaggerated knee-jerks, continuous tremor of lips,

slight lingual tremor, inconstant tremor of hands, slight peripheral arteriosclerosis, and signs of aortic valve sclerosis. Mentally, patient talked disconnectedly in answer to questions. Failed to occupy herself in any way; wore an unchanging facial expression. Claimed to have been dead and reborn many times. Persistently stated that she bore another name than her own and showed an apparent defect of memory for both recent and remote impressions. Was unable to make her way about the ward. Sample of conversation: "We don't know whether it is Heaven or earth we are sitting in. The house feels such a move. It moved right along this morning like a train. You were marked when you came in." Do you hear voices sometimes? "I hear the occupants of another world." Do you have any thoughts? "When I read books." Do you read books? "Sometimes. I believe I am a baby with all these attacks." What attacks? "The attacks, points, and scoops." Are you out of your mind? "You have got to pray to God to get out of this building. My father told me I would be the Lord's wife. He told me to obey my husband and my Lord." How long have you been married? "I can't tell, a number of years. I have been a baby since I have been married."

Again, Why were you sent here? "Because I pushed the bed back and a bullet came through the wall. I was chewed and born and clambered and went through shambles." Why were you sent here? "Because there were so many thieves around." What did you do? "I started my nun work and read my Bible in my room, thank God and all God."

Patient at Middleton Colony restless and vagrant. In last few months the patient grew careless of dress and showed mannerisms, stereotyped movements, resistiveness and severe Bright's disease. Death February 16, 1909.

Anatomical Diagnosis (A. H. Peabody and C. G. McGaffin).

Cause of Death.—Chronic diffuse nephritis and acute bronchitis.

Chronic Conditions.—Malnutrition. Slight sacral decubitus. Aortic valvular sclerosis (foci of calcification). Slight aortic sclerosis. Coronary arteriosclerosis. Dilated stomach. Chronic diffuse nephritis. Chronic perisplenitis. Mural and subperitoneal fibromyomata of uterus. Atrophy of ovaries. Calvarium dense. Exostosis of frontal bone. Adherent dura. Chronic tympanitis auris. Calcification in falx cerebri.

Acute Conditions.—Acute bronchitis. Slight enlargement of mesenteric lymph nodes. Abrasions of forehead and left hand.

Nervous System.—Brain weight 1220 grams. Chronic fibrous leptomeningitis of vertex, along sulci at base of brain and over cerebellar cisterna. Generalized increase of consistence of brain. Pigmentation of cerebral grey matter.

Case XI.—E. F., D. S. H., No. 13582, Path. No. 1310. Female, 28, single, mill operative. Born at Manchester, N. H., of Scotch-Irish parentage. Was a case of dementia præcox probably of hebephrenic type, possibly, originally imbecile. The total duration of the dementia præcox features was perhaps four years.

Heredity.—Facts unknown. Insanity in family denied.

Previous History—Patient always of subnormal mental capacity. "Peculiar, stupid, and ugly." Dull and backward at school. Worked steadily in a mill, but never saved money. Was sullen and cranky. At 24 years irritability, indolence, untidiness, aimless wandering and increasing silliness set in. A tendency to gluttony. The police often picked her up on the street at night.

Patient was admitted to D. S. H. April 5, 1907. Adherent ear lobules. High arching palate. Acne eruption. Gait peculiar, at times normal, at times patient swings one foot in front of the other and totters back and forth (mannerism?). Occasionally turns and twists her fingers about in a stereotyped way, touching objects with finger tips. Knee-jerks exaggerated. Patient smiled and grinned, was untidy, and habitually lay in bed with clothes over her head. Patient mute except on repeated questioning, when an occasional "yes" or "no" could be elicited. Later patient became more tidy and again untidy. Patient was apparently not oriented while in hospital and showed amnesia and defective impressibility.

Developing fever in November, 1908, she was transferred to the tuberculosis building, where she grew weaker and died March 22, 1909.

ANATOMICAL DIAGNOSIS (C. G. McGaffin and N. B. Burns).

Cause of Death.—Phthisis pulmonalis.

Chronic Conditions.—Malnutrition. Unequal pupils. Asymmetry of thorax. Marked mitral sclerosis. Hypertrophy of left ventricle. Hydropericardium. Chronic adhesive pleuritis of anterior portion of left lung. Tuberculosis, with cavitation of left lung, and slightly of right lung. Enlarged bronchial lymph nodes. Chronic passive congestion of liver. Dextroflexion of uterus. Thyroid gland small. Cyst of left Fallopian tube.

Acute Conditions.—Thrombosis of left auricle, staphylococcus septicemia.

Nervous System.—Gliosis of both frontal regions. Atrophy (or aplasia?) of left postcentral gyrus. Left precentral gyrus broader than right. Brain weight 1300 grams.

CASE XII.—M. C., D. S. H., No. 12143, Path. No. 1317. Female, 44, single, mill operative. Born in Ireland; father English, mother Irish. Was a case of dementia præcox of paranoid type of 21 years standing.

Heredity.—Father intemperate.

Previous History.—Patient a woman of ordinary mental capacity. Limited education; of melancholy and reserved tendency. Attack began at 23 with insomnia and anorexia, followed later by auditory hallucinations, fear, desire to become a nun, and wandering tendency.

On admission to D. S. H., October 25, 1897, the diagnosis of primary dementia was made. Patient was resistive, repeating, "Oh, my God protect me." Had auditory hallucinations and various delusions, sometimes religious. Mutism, refused to eat, restlessness, later increased stupidity, untidiness, and troublesome activity. In 1890 patient was able to work in the laundry, but in 1893 became quarrelsome and violent, often laughed in

meaningless fashion and could not be prevailed upon to answer questions. Removed to Lawrence Almshouse June, 1893.

Recommitted to D. S. H. August 31, 1904. Patient sat about idly talking to herself or laughing in a silly manner and if permitted would wear four or five aprons. Her speech was peculiar and babyish and many replies were in whispers. Disorientation was apparently complete. Memory for recent and remote events was poorly preserved. Grimaces and various mannerisms. Patient would for long periods sit about listlessly and then become talkative. At times patient became quarrelsome; noisy at night and resistive.

Cancer of left breast was noted in July, 1908. Operation November 30, 1908. Had no effect on mental state. Death from metastases May 19, 1909.

ANATOMICAL DIAGNOSIS (A. H. Peabody and M. M. Canavan).

Cause of Death.—Multiple metastatic carcinomatosis.

Chronic Conditions.—Inequality of pupils. Edema of ankles. Brown atrophy heart muscle. Slight coronary arteriosclerosis. Chronic periappendicitis. Chronic adhesive pleuritis. Lateral misplacement of uterus. Chronic gastritis. Surgical removal of left breast (carcinoma). Carcinoma of axillary lymph nodes, left lungs, bronchial lymph nodes, and liver.

Acute Conditions.—Icterus. Hemorrhagic conjunctivitis. Hemorrhagic endometritis. Acute nephritis. Hypostatic pneumonia.

Nervous System.—Adherent dura. Chronic fibrous leptomeningitis, along sulci. Cervical spinal cord firm. Brain weight 1210 grams.

CASE XIII.—M. K., D. S. H., No. 14597, Path. No. 1319. Female, 31, married, mill operative. Born in Ireland. Was a case of dementia præcox of the paranoid type (possibly imbecile) of eight years duration.

Heredity.—Sister epileptic.

Previous History.—Poor scholar and truant in convent school in Ireland. House work and mill work after coming to America at 15. Married at 18; three children, followed by separation. Illegitimate child at 23. An attempt at suicide is asserted at 23-24. History before commitment is limited. Insomnia and street-walking are reported.

Commitment to D. S. H. October 10, 1908. Slight coarse tremor of fingers and tongue. Patient dull and apathetic. Lay quietly in bed looking at one point on ceiling as if hallucinated. Orientation imperfect. School knowledge and calculating ability deficient. Memory somewhat impaired for remote events; still more impaired for recent events. It later transpired that she could see the Virgin Mary at any time. Patient at times sang religious strains. Muscular movements were in general slow and languid. She was apt to assume attitudes suggesting those of saints in religious pictures. Once she betrayed a fear that men were after her. In January, 1909, she had become at times resistive and fearful. She was tube-fed several times. At times patient stated that she had a bad taste in her mouth.

Died May 28, 1909, of colitis.

ANATOMICAL DIAGNOSIS (A. H. Peabody and M. M. Canavan).

Cause of Death.—Acute follicular colitis.

Chronic Conditions.—Malnutrition. Inequality of pupils. Edema of ankles. Ascites. Chronic adhesive pleuritis, left. Chronic fibrous pericarditis. Chronic fibrous endocarditis. Aortic sclerosis. Tuberculosis of left apex. Chronic perisplenitis. Renal arteriosclerosis. Chronic diffuse nephritis. Slight cirrhosis of liver. Chronic endocervicitis. Calvarium dense.

Acute Conditions.—Acute nephritis. Acute jejunitis, ileitis and colitis. Acute proctitis. Acute vaginitis.

Nervous System.—Cervical spinal cord large. Slight chronic leptomeningitis especially basal. Brain weight 1250 grams.

CASE XIV.—F. O., D. S. H., Nos. 8471, 13648, Path. No. 1335. Male, 32, single, shoemaker, born in Lynn, Mass. Father born in Massachusetts; mother born in Nova Scotia. Was a case of dementia præcox, katatonic type, of 20 years duration.

Heredity.—Paternal grandfather alcoholic.

Previous History.—At 12 years an attack of confusion and more or less unconsciousness lasting two weeks. Pains in back and head at intervals for years. At 18 years spells of laughter and boisterousness, delusions of being mesmerized, elation and depression spells, insomnia, threats of violence and suicide.

On commitment to D. S. H., October 23, 1896, patient was talkative and expressed numerous delusions and pseudoscientific theories. "The moon is the blind eye of some animal. There is a change every thousand years, so the men of a thousand years ago are now women, and *vice versa*. The reason why the Egyptians are so small is because he put vitriol into them a thousand years ago, and it is all described in the inscriptions. He has the shoulders of an Egyptian, the head of Napoleon or an Italian, and his limbs are French. We are all being continually acted upon by minerals, herbs, electricity, and magnetism, and one person's brain acts directly upon another's."

The physical condition was well maintained. There was a progressive apathy, with occasional noisy spells and unprovoked assaults on patients. In 1898 assigned historic parts to officers: head supervisor was Mrs. Grover Cleveland, superintendent was Napoleon, the pathologist was Daniel Webster, etc. Much profane, obscene and foolish talk.

Later, patient was habitually found mumbling and laughing foolishly on a settee. Eczema of buttocks and scrotum from dribbling of urine. Dysentery in September, 1904. The urine then began to show albumin.

Patient's apathy occasionally gave place to excitement, denudative spells, and the expression of extravagant delusions.

Transferred to Foxboro State Hospital March 5, 1907. Readmitted to D. S. H. May 10, 1907. Untidy, manneristic, with tendency to hold fixed positions. Placed in tuberculosis building in 1908, where he had spells of noise-making. Diarrhœa set in in July, 1909, but there was no blood or

mucus in the stools. Toward the close, patient could not keep a straight line in walking. Patient's characteristic position was similar, lying, standing, and walking, and consisted in a curled-up stoop with arms folded over abdomen.

Death suddenly, after a gradual exhaustion, August 21, 1909.

ANATOMICAL DIAGNOSIS (M. M. Canavan and A. A. Hornor).

Cause of Death.—Phthisis pulmonalis. Intestinal obstruction.

Chronic Conditions.—Malnutrition. Dilatation of pupils, oval from above downwards. Scaling and pigmentation of skin. Chronic focal adhesive peritonitis. Chronic adhesive apical pleuritis (left). Hydrothorax (right). Heart small (145 grams). Slight chronic fibrous endocarditis (left ventricle). Tuberculosis of apex of left lung. Tuberculosis with cavitation of right lung. Liver weight 940 grams. Cystitis and prostatitis. Slightly adherent dura. Chronic tympanitis auris (left).

Acute and Recent Conditions.—Intestinal obstruction. Acute jejunitis and ileitis. Mesenteric lymphnoditis. Acute nephritis.

Nervous System.—Spinal cord small. Chronic leptomeningitis along sulci of vertex, in Sylvian fissures, and at base of brain. Thrombi of superior longitudinal and left lateral sinuses.

CASE XV.—M. D., D. S. H., Nos. 10098, 10580, Path. No. 1358. Male, 24, single, shoemaker. Born in New Brunswick of Irish-Canadian parentage. Was a case of dementia præcox, katatonic type, of 10 years duration.

Heredity.—Unknown. Orphan.

Previous History.—Two years before commitment, malaria with refusal to talk (patient's statement). Normal to 15 years, of average school capacity. Ten days before commitment patient had spells of crying, jumping, shouting, and incoherent talk, with refusal of food for about a week. Patient believed he had appendicitis. Urine was drawn with catheter four or five days before commitment. Headache during two nights before commitment.

Commitment D. S. H. September 15, 1900. Nose asymmetrical. Malnutrition. Depression explained by patient as due to lack of sleep, having no mother and lack of appetite. Patient was dazed and bewildered, refused food, was at times normal, later mute, untidy, resistive. The katatonic symptoms then diminished, and patient could be got to take food. Periods of mutism and fixed attitudes alternated with brighter and more responsive periods. Late in 1900 he had become apathetic, but worked in the dining-room, occasionally noisy and mischievous. Tonsillitis in March, 1901. Weight and physique had in general much improved. Active symptoms then almost wholly ceased, and patient was discharged April 1, 1901.

After discharge, patient worked well in shoe shop and drove team acceptably to employers. On being taken to learn a trade in Boston, August, 1901, he stayed but two weeks, and returned erratic, boastful, profane, threatening, and was recommitted October 12, 1901, in approximately perfect physical health.

As a rule surly and profane, patient was sometimes tractable (November

1901; February to July, 1902; September to January, 1903). Occasionally untidy. Often restless, sleepless, and annoying to helpless patients. A second attack of follicular tonsillitis September, 1902.

April, 1904, confusion, peculiar way of putting on clothes, swaggering about, mutism or incoherent responses to questions, facial grimaces, twitching of facial muscles. November and December, 1904, orderly and tractable, though apathetic, correspondent with an attack somewhat suggestive of typhoid fever (positive Widal reaction in second week).

During 1905 and 1906, patient was apathetic, idle, properly oriented, and had very good memory.

In the spring of 1906 patient grew depressed and unwilling to eat, became untidy, mumbling, and disoriented, and during July and August became restless, excited, given to running about making peculiar movements and assaulting helpless patients. A period of quiet dulness followed.

Patient's weight increased; he was given parole privileges.

In February, 1909, patient grew despondent and untidy, often refused food, and took to continual praying. In August dysentery set in, with persistent diarrhœa; mutism and occasional prayers.

Sudden collapse set in on November 18, 1909. Death. Patient mumbled a few words to physician on day of death.

ANATOMICAL DIAGNOSIS (H. M. Adler and M. M. Canavan).

Cause of Death.—Acute ulcerative ileocolitis (bacillary dysentery).

Chronic Conditions.—Malnutrition. Unequal pupils. Trochanteric decubitus. Chronic appendicitis. Chronic obliterative pleuritis (right). Obsolete tuberculosis of left apex. Chronic perisplenitis. Chronic gastritis. Cystitis (thickened wall). Calcification of lymph node near pancreas. Calvarium thick. Slightly adherent dura mater.

Acute Conditions.—Acute ileocitis. Enlargement of mesenteric lymph nodes. Acute bronchitis (right). Acute splenitis. Fatty changes of liver and (slight) kidneys.

Nervous System.—Sclerosis of left inferior frontal gyrus. Brain weight 1200 grams. Slight chronic fibrous leptomeningitis. Lumbar spinal cord soft.

In seeking for correlations in these data, let us first inquire how many of the lesions described can safely or probably be regarded as congenital anomalies or lesions acquired long prior to mental change. For a proper judgment here we shall need to take into account not merely the lesions in question, but the total clinical and anatomical impression presented by each case.

I, 840. A woman of Irish extraction, a capable school-teacher for 13 years, developed at 35 after over-work, a depressed, delusive, languid state, upon which typical katatonic symptoms shortly supervened, and died of phthisis at 37. Possibly the brain was somewhat atrophied, but not visibly so, save in the frontal regions. Although visible generalized atrophy cannot be asserted, there was a palpable generalized gliosis. (*Acquired.*)

II, 991. A Nova Scotian carpenter, given to frequent masturbation and later to excess in venery, developed a mental disease at 24 variously diagnosed in different State hospitals as "hypochondriacal paranoia," "chronic melancholia," "neurasthenia," is said to have threatened suicide, complained of pain, abnormal sensations ("brain and legs whirling round"; "I can't speak, because it pulls down and up and wound around me"—making motions from abdomen to neck), was hypochondriacal, eventually answered only in monosyllables, developed tuberculosis and died at 35. Slight generalized cerebral gliosis, without visible atrophy. (*Acquired.*)

III, 1034. An Italian immigrant, for 10 years a shoe operative of average capacity, somewhat easily affected by alcohol, developed at 33 auditory hallucinations and persecutory delusions, later grew dull, reticent, given to impulsive acts, and then showed echopraxia, cerea flexibilitas, mutism, at times automatism; died of pulmonary gangrene at 35. A kind of simian hirsuteness and hypoplasia of heart and aorta perhaps suggest "degeneracy." The pupils also were unequal and one was oval. The brain of this case was of good weight, and the solitary lesion it showed was a sclerosis and pigmentation of the dentate nuclei of the cerebellum. (*Acquired.*)

IV, 1062. An Irish housewife, who had borne three children, was deserted by her husband and developed at 28 somatic delusions, depression, and suicidal tendencies. On commitment signs of tuberculosis of both apices were discovered, which tuberculosis was fatal 10 years later. Full of delusions, abusive, noisy, obscene, the woman never showed katatonic signs unless reticence and a single period of mutism can be so interpreted. The brain of this case was of proper weight and showed palpable gliosis (without visible atrophy) of the superior frontal, prefrontal, and orbital gyri. At death (38 years) the genitalia were already atrophic. There was an aberrant thyroid. (*Acquired.*)

V, 1137. An Irish shoe operative (father possibly alcoholic) developed loose delusions of influence and a little later peculiar motions and gestures, mutism, stereotyped movements. All these symptoms, except mutism, ceased in later years. The total process lasted 15 years and the man died at 35. As in Case II, both heart and aorta were small. One testis was atrophied. The brain weighed 1465 grams and showed a striking microgyria of the right parietal lobule. Whether this lesion is acquired or aplastic would be hard to decide on anatomical grounds, but there was a focus of chronic pial change in the adjacent parieto-occipital fissure. There is a suggestion of sclerotic changes in the frontal regions and the lower surface of the cerebellum. (*Acquired? Congenital??*)

VI, 1149. A carpenter, hyper-religious, and given to spiritualism, perhaps never "just right," has episodes of auditory, visual, olfactory, and gustatory hallucination (possibly also tactile), but during a quiet course of 32 years eventually settles into habitual, apparently voluntary, "communications" with God. Certain tremors, of doubtful interpretation, partly voluntary, were at one time evident in reflex tests. Characteristic mannerisms were

late in appearing (55 years) and were then slight. Death at 57. The brain showed a generalized increase in consistence (without visible atrophy) and especially firm occipital regions. There was no palpable sclerosis of the frontal regions, but there was a regionary chronic leptomeningitis. (*Acquired.*)

VII, 1168. A French-Canadian woman, of normal development and a weaver for four years, after desertion by lover, developed auditory hallucinations, persecutory delusions, certain subjective sensations, and resistivism, later apathy, mutism and less of knee-jerks. Death four years after onset, at 24 years. The brain weighed 1105 grams and showed an atrophy (or aplasia) of both post-central gyri, a mild sclerosis of the right dentate nucleus, and possibly other slight chronic cerebellar lesions. (*Acquired, Congenital?*)

VIII, 1294. An Irish housewife, who had borne four children, developed swelling of both legs at her fourth confinement and 19 days after birth of child became boisterous, fearful of death, and had auditory hallucinations—thrombosis of left leg had set in. Auditory hallucinations, delusions of suspicion, and periods of violence gave place to virtual recovery. At home recurrence of hallucinations, followed in the hospital by violence, resistiveness, refusal of food, later apathy. Impulsive movements, frequent genuflexion, employment of third for first person, stereotyped movements. Death after six years at 37. Generalized slight cerebral sclerosis, especially frontal and occipital. Slight focal leptomeningitis, frontal poles and tips of temporal lobes. Atrophy of ovaries. (*Acquired.*)

IX, 1298. An Irish housewife, who had borne four children, developed pains, insomnia, ideas of suicide, fear of tuberculosis, delusions of poisoning. On commitment, hypertrichosis of upper lip and atrophy of breasts had set in. The palate was Gothic. The symptoms first suggested the depressed phase of manic-depressive insanity. Apathy, negativism, untidiness, followed a severe generalized convulsion nine days before death (nine weeks after onset, 36 years). Brain of proper weight. Atrophy (or aplasia?) of postcentral gyri. Gliosis of left second temporal gyrus. (*Acquired? Congenital.*)

X, 1303. A woman compositor of New England parentage (uncle insane) believed at 29 that she was clairvoyant and apparently had auditory hallucinations as well as somatopsychic delusions, possibly based on hallucinations. Apathy, peculiar autopsychic delusions toward death, carelessness in dress, mannerisms, stereotypy, resistiveness. Course of 25 years. Death at 55. Generalized increase of consistence of brain, with pigmentation and a chronic leptomeningitis of the vertex, along sulci, at the base, and over cisterna cerebellaris. (*Acquired.*)

XI, 1310. A Scotch-Irish mill-worker, a woman always of subnormal mental capacity, developed at 24 a pronounced change of character with hebephrenic features. In hospital mannerisms or peculiarities of gait, certain mannerisms of finger movements, and virtual mutism. Unequal

pupils. High palate. Asymmetry of thorax. Death at 28. Small thyroid gland. Frontal lobe gliosis. Atrophy or (aplasia?) of left postcentral gyrus. (*Acquired, conegnital?*)

XII, 1317. Woman, mill-worker (father alcoholic), at 23 had insomnia, followed by auditory hallucinations, fear, religiosity, vagrancy. In hospital, resistive, hallucinated, delusive, mute, refusing to eat; later violence. Finally apathy, with manneristic speech and grimaces. Death from carcinomatosis, 21 years after onset. Occipital microgyria. Chronic leptomeningitis along sulci. Cervical spinal cord firm. (*Acquired.*)

XIII, 1319. High-grade imbecile. Irish mill operative. Sister epileptic. Mother of three children and a fourth illegitimate. One attempt at suicide. Eight years' course with onset at 23. Religiosity. Could see Virgin Mary at any time (hallucination rather than delusion). Imitation of saints' attitudes as seen in pictures. Possibly gustatory hallucinations. Death at 31. Unequal pupils. Cervical spinal cord unusually large. Slight leptomeningitis, especially basal. (*Acquired and congenital.*)

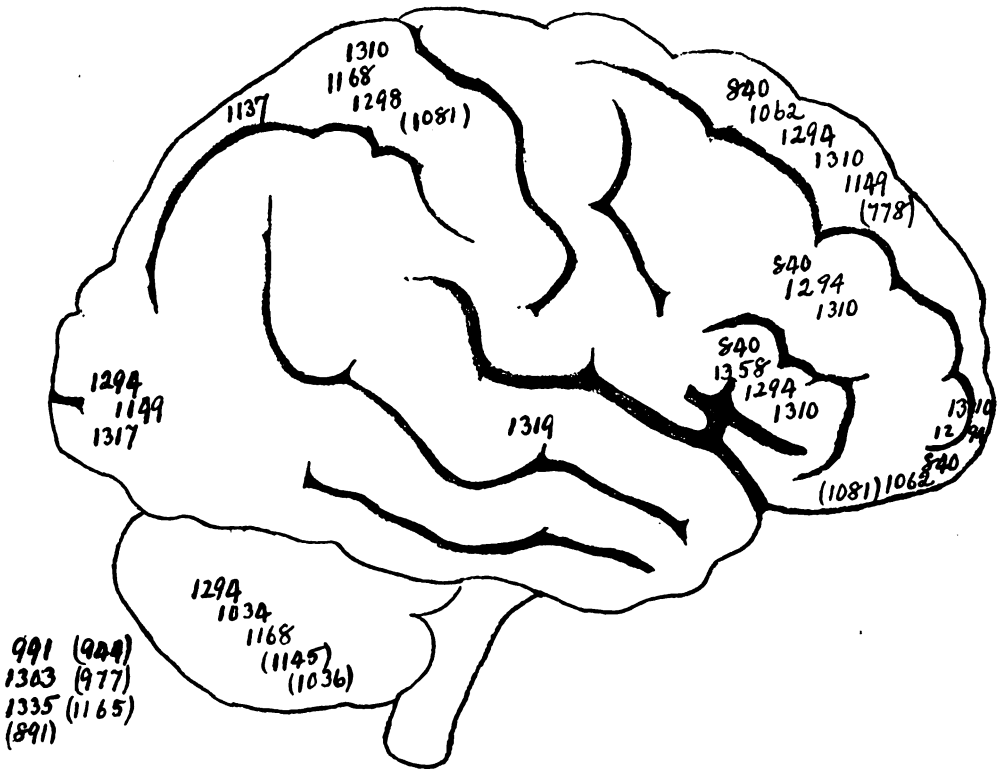
XIV, 1335. Shoe operative. Attack of doubtful character at 12 years. Paranoid symptoms began at 18. Katatonic symptoms gradually supplanted the paranoid. Death at 32. Spinal cord unusually small. Brain weighed 985 grams, but was apparently not to any great degree atrophied. Heart (145 grams) and liver (945 grams) also small. (*Congenital.*)

XV, 1358. Irish-Canadian, shoe operative. Onset at 15. Katatonic, later apathetic, then apparently recovered (seven months after onset). Recurrence four months later. Remarkably periodic course. Death at 24. Palpable sclerosis of the left inferior frontal gyrus. Slight chronic fibrous leptomeningitis. (*Acquired.*)

One's superficial judgment, therefore, concerning the origin of the lesions in question is that they took rise in the adult brain in 840, 991, 1034, 1062, 1149, 1168 (at least in part), 1294, 1303, 1310 (at least in part), 1317, 1319 (in part), 1358=12 cases, possibly also in 1137, 1298=maximum of 14 cases. So far as 1335 is concerned (Case XIV), it might well be doubted whether the hypoplastic nervous system formed more than a nidus for the mental process; perhaps this case should be put in the macroscopically normal group.

It is but fair to insist, on the other hand, upon the congenital features. Besides 1335, 1137, 1168, 1298, 1310, 1319, gave rise to a suspicion of congenital features in the nervous system alone =6 cases. And, if we add anatomical features outside the nervous system, then 1034 (hirsuteness, hypoplasia of heart and aorta) 1062 (aberrant thyroid) might be added=a maximum of eight cases probably or possibly in part provided with congenital features.

It appears, accordingly, that, although congenital features are not absent from our group, there is strong color for the provisional judgment that numerous acquired lesions of the nervous system exist in our series.



FOCAL ATROPHIES, APLASIAS, OR SCLEROSES IN DEMENTIA PRÆCOX.
() indicate microscopic evidence only.

THE PRE-ROLANDIC GROUP.

The frontal region was specially marked out for injury (whether acquired or congenital is for the moment not considered) in cases 840, 1062 and 1358; was prominently injured also in 1294 and 1310; and obviously shared to some degree in the generalized mild injury which was macroscopically made out in 991, 1135, 1303, and in 1335 (unless this brain be regarded as showing hypoplasia of congenital origin), *i. e.*, in at most nine cases.

Consider first the three cases in which the macroscopic lesions specially affected the frontal region. 840 was at first paranoid, then shortly katatonic. 1062 was paranoid, perhaps never katatonic. 1358 was a katatonic case with remarkable remissions. At first sight it seems hopeless to seek clinical correlations in these cases. But, bearing in mind the conclusions of Campbell and Brodmann concerning the histological differentiation of the so-called frontal region into subdivisions, it is clear that we cannot demand close clinical correlations here.

As a matter of fact, the lesions of 840 (the case with paranoid-katatonic course) involved, so far as eye and finger could determine, the *whole* of both frontal regions, and the whole brain itself showed a generalized increase of consistence. Whatever the relation of the patient's brain disease to her symptoms, there is not the slightest doubt that the patient had been subject to a sclerosing brain disease of mild but generalized character during the last years before death (assigned duration three years). Microscopically, the gliosis of this case was generalized and not demonstrably severer in the infrastellate layers.

But, though the changes of 840 are too severe and wide-spread and the symptoms too mixed for correlation, the same is not true of 1062 (paranoid, perhaps never katatonic). A woman of the same age as 840, but with a much longer assigned duration of symptoms (11 years or more) and with alcoholism clouding the issue, 1062 had maintained proper brain weight and showed gliosis confined (so far as macroscopic examination could determine) to the superior frontal, prefrontal, and orbital gyri, *i. e.*, to a continuous area probably containing but two histologically separate cortex-types. It is perfectly true that microscopic examination shows a degree of the same process (gliosis, satellitosis) in other regions, so that here again the brain cannot be freed from the suspicion of a generalized change. Still both macroscopic and microscopic examinations seem to prove that the superior frontal and prefontal cortex is subject to the most severe and possibly to the oldest process of injury. It becomes, therefore, at least a working hypothesis for this case to consider the paranoid symptoms as related with lesions in the superior frontal and prefrontal regions.

But what kind of interpretation is left open for the purely kata-

tonic case, 1358? The analysis of this case is still far from complete. The greater part of both frontal regions was, as a matter of fact, wholly spared from macroscopic lesion. Only the left inferior frontal gyrus was affected, presenting an induration of an isolated and distinct, though mild, character in the midst of an otherwise apparently normal brain (slight general leptomeningitis). What relation, if any, this particular lesion bears to the katatonia of this (clinically somewhat unusual) case, is impossible to say; but it is certain that the data of 1358 do not controvert in any respect the correlations suspected for 1062 (the practically pure paranoid case) or even for 840 (a clinically more rapidly progressive and mixed case), as the macroscopic distribution of the lesions indicates.

The other frontal lobe cases deserve brief mention. The distribution of the lesions in 1294 is in consonance with the progressive paranoid-to-katatonic character of the disease: the case resembles in some respects 840 (just considered); but its duration is longer (six years) and the katatonic symptoms were much delayed in their development. The brain had undergone a mild generalized sclerotic process (widely distributed gliosis microscopically) which had especially affected the frontal and occipital parts of the brain and included the cerebellar cortex and even the pons. The frontal tips actually showed a few pial adhesions (a rare event outside of general paresis and other exudative or post-exudative lesions). The extent of this prefrontal process again recalls 840; but the whole case is obviously too complex, progressive, and longstanding to permit more than a suspicion of the course of cortical events.

1310 is best considered below among complications of the post-Rolandic group: it showed both delusions and katatonic symptoms, but was at first pronouncedly hebephrenic.

The group of generalized glioses (without defined gross atrophy) here considered numbers three. One of these (991) was practically paranoidal throughout its 11-year course, and, as a matter of fact, microscopically showed a marked superior frontal lobe gliosis (with satellitosis); but the case is clinically not too clear, and no deductions need be risked therefrom.

Another generalized gliosis, 1303, was apparently the end-stage of a hebephrenic, with a disease of 25 years' duration. Cor-

relations are impossible. Histologically, there were marked gliosis and satellitosis, especially of deeper layers.

1335, the last of this group, is very possibly an instance of hypoplasia or of arrested development of the brain. The brain at autopsy weighed but 985 grams (heart 140 grams, liver 940 grams). Correlations here also are difficult.

Before dismissing the pre-Rolandic group, 1149 may be considered in this connection. I have placed 1149 provisionally in the post-Rolandic group largely on the basis of the well-defined occipital gliosis; but the brain showed a generalized sclerosis (microscopically marked, with some degree of satellitosis in places). The reason for possibly including it, more especially, in the frontal group is the occurrence of chronic fibrous lepromeningitis, confined to the superior frontal gyri. The case was clinically a supreme example of a paranoid dementia præcox of 32 or more years' duration, and with certain katatonic symptoms appearing very late in life.

The above sketch of the features of the pre-Rolandic group leaves us with the suspicion that paranoid cases begin with lesions striking especially the frontal tips and the superior frontal gyri. Cases with katatonia supervening later and with a progressive course of greater duration show involvement of other regions or even of the whole brain.

The Post-Rolandic Group.

(a) Cases 1137, 1168, 1298 and 1310 (also frontal) form a sub-group which might, perhaps, be termed sensory-perceptual. (b) Cases 1149 and 1317 are cases of occipital lesion, 1319 of superior temporal lesion.

(a) The postcentral-superior-parietal or sensory-perceptual group of cases claim attention as exhibiting lesions in a region doubtless of great importance in interpretation of sensory impulses. All four of the cases were alike in developing katatonic symptoms.

1137 began, it is true, with a delusion, but a peculiar one (electrification), possibly due to sensory misinterpretation: thereafter the patient developed katatonia, demented seriously, and died (15 years' duration). The visible atrophy (or aplasia) in the right superior parietal region, accompanied by microgyria and a dense

local deposit of fibrous tissue, formed a striking local lesion. At the time of death, however, gliotic changes with satellitosis had become widespread. Purposely I avoid discussing whether the focal lesion is acquired or congenital and what its pathogenesis may be, since for the time being the topographic distribution of such lesions is the important consideration.

1168 showed at autopsy what looked like a bilateral anomaly—a hypoplasia of both postcentral gyri in their upper two-thirds. The onset in this woman occurred at 20 after desertion, and katatonic symptoms were admixed with persecutory delusions and subjective heat-sensations almost at the start. The course was katatonic thereafter.

1298 pursued an acute course of katatonic character with death after nine months. The brain showed, besides double postcentral gliosis in the white matter and visible atrophy of the right postcentral gyrus, a peculiar focus of duropial adhesions over the left middle frontal gyrus. This case was at one time diagnosed as depressed phase of manic-depressive insanity.

1310 appears clinically to show a marked imbecilic strain. Perhaps the left postcentral atrophy and the precentral inequalities are largely of congenital derivation. The frontal gliosis is consistent with the imbecilic or hebephrenic cast of the case. Numerous katatonic features developed.

The sensory-perceptual sub-group, as represented by these cases, shows lesions which lead to the suspicion, if not the proof, of congenital anomalies. Symptomatically these cases have katatonic symptoms in common.

Post-Rolandic group (b). 1149 and 1317, as well as 1294 (discussed with the pre-Rolandic cases), belong to an occipital group.

1149 was briefly mentioned in the frontal connection above, because the prominence of the frontal region (which could not be differentiated on palpation from the remainder of the sclerotic brain) was emphasized by a local frontal leptomeningitis. In point of fact the occipital regions were more markedly sclerotic than the rest of the brain. The case might be asserted to present a beautiful instance of anatomoclinical correlation, were we to insist on the relation between the occipital gliosis and the well-defined, constantly recurring, voluntarily executed visual episodes

("communications with God"). Obviously, such a superfine correlation would mean running a good horse too hard. Those "communications" must have involved numerous cortical events outside the occipital region. It seems safe to maintain, however, that, granting some agency exerting a mildly destructive or irritative effect upon the occipital region, a useless mental habit like these "communications" would probably assume a visual coloring. The existence of disease in a given brain-region may well be conceived to determine the course of events in the intact remainder. The histological examination of this case is incomplete, but I conclude from available sections that the calcarine cortex-type is relatively intact, whereas the common occipital cortex-type exhibits much more marked gliosis and satellitosis. In this early phase of our problem, it seems best to rely upon coarse and well-defined qualitative distinctions rather than the cell-enumerations which later work will demand. I judge from recent comments on cortex-architecture that the occipitocalcarine relations will be the most vulnerable point of attack in this direction.

1294, which has been discussed above, also exhibited similar histologically demonstrable variations in the intensity of lesions in the calcarine and occipital regions (common occipital type more markedly affected in the infrastellate layers). As a matter of fact, however, in 1294 the hallucinations shown were auditory rather than visual (though the patient once broke glass to reach her husband being crucified). The brain showed frontal, cerebellar, and pontine gliosis, in addition to the occipital. No temporal gliosis was made out macroscopically, but there were foci of leptomeningitis, both at temporal and at frontal tips.

1317 again breaks down in anatomoclinical correlation much as does 1294, since, despite the occipital microgyria, the hallucinations, so far as was made out clinically, were auditory. There were some religious delusions.

With respect to relative developments of paranoidal and katatonic features in this occipital sub-group, it has been pointed out that 1149 was a classical paranoid case with a few katatonic symptoms toward the close of life (32 years' duration). 1317 was more doubtful but probably can be interpreted as mainly paranoidal; katatonic symptoms developed late in a course of 21 years. 1294 was paranoidal.

If we compare the sensory-perceptual group (a) cases 1137, 1168, 1298 and 1310 with the occipital group (b) 1149, 1317 (1294), we cannot but be struck with the predominantly katatonic character of group (a). The physiological correlations between katatonic symptoms and the sensory-perceptual field are briefly mentioned in Chapter V.

Infra-Sylvian Group.

I have provisionally placed but one case, 1319, in this group, a paranoidal case, probably upon an imbecilic basis. There are no striking anatomoclinical correlations in the case. This group will undoubtedly grow with further experience. 1294, *e. g.*, showed focal leptomeningitis of the temporal tips.

Cerebellar Group.

It is noteworthy that the cases which we procure at autopsy in dementia præcox are provided as a rule with multiple lesions. This is particularly true in the advanced cases, where interpretation may be difficult by reason of the fact that gliosis has overtaken the brain as a whole. This difficulty reappears in the cerebellar cases.

1034, however, is a macroscopically pure case of sclerosis of the dentate nuclei of the cerebellum. Clinically 1034 was a classical example of *cerea flexibilitas,* in an Italian of 35 years, who began with paranoid symptoms (feared anarchists), and in less than six weeks became typically katatonic. Microscopic examination shows in various areas of the brain a gliosis which had escaped palpation in the gross. Some of the areas of intracortical alteration were undoubtedly far too small to attract attention macroscopically. There was a slight satellitosis of the frontal region. The case appeared then, like many other cases of this series, microscopically not so definite as the data of palpation had indicated.

1168 is a case which has been briefly mentioned in the sensory-perceptual sub-group of the post-Rolandic cases as showing a hypoplasia of both postcentral gyri in their upper two-thirds. In addition thereto there was a sclerosis of the olives, of the right dentate nucleus of the cerebellum, and of the cacuminal and clival portions of the cerebellum. This case was classified as hebephrenic, but mutism, resistivism, assumption of fixed attitudes and

impulsive rocking movements give rise to the suspicion that katatonic features cannot be excluded. A congenital element is also very possible from both history and brain findings.

A third case, 1143, showing almost the same findings in the brain has been excluded from the group of typical dementia præcox cases but might be included upon a more liberal interpretation of symptoms.

Other cases would have to be added to this group on the score of serious microscopic alterations, which were made out in the face of protocols to the effect that the cerebella were macroscopically normal. The group is, therefore, actually much larger than the two cases (1034 and 1168) would indicate.

Provisional Grouping of 14 Cases without Recorded Gross Lesions.

I have analyzed in some detail the cases with recorded minor gross lesions and anomalies to the number of 15. There are 14 outstanding cases having a clear clinical title to the diagnosis of dementia præcox, but in which no gross lesions were recorded. It is of interest to learn what light a microscopic examination will throw upon these cases and whether any cases are subject to a tentative topographic grouping.

There are several cases about which there is no doubt that they actually belong in the gross lesion group. Thus 1145 should, perhaps have been excluded altogether from this study since the protocols were mislaid. Ample block material exists, however, which microscopically shows characteristic satellitosis of the deep cortex-layers and a marked gliosis of the dentate nuclei (more marked left than right). This case might well be placed in Table XVII above, as well as in the cerebellar group.

1145. 10705. F. 37. paranoid. 6y. Brain wt. 1185.
(Pregnancy at origin.)

I am sure also that with increasing experience, case 1036 would have become an accession to the gross list in the cerebellar group. A sketch of this case was presented by the writer in 1907 in his study of the granule layer of the cerebellum.[28] 1036, 11317, M. 28, hebephrenic, 6y; cardiorenal, renal 6+y; brain 1175g.

778, a paranoid case upon an imbecilic basis, I should desire to place (with some trepidation) in the superior frontal group. The

reason for this is that the superior frontal gyri, far more than other regions examined, gave evidence of a sclerotic process: considerable gliosis of the underlying white matter, superficial gliosis of rather focal character, and perhaps a slight generalized gliosis of the whole gyri, with infrastellate satellitosis. That the process was not confined to this region is true, and neuroglia cell mitosis was a curious finding in the right precentral gyrus. The paranoid features had come on two years before death at 41 in this imbecile. Very possibly the case scarcely belongs with dementia præcox as usually conceived; but it seems certain that a similar process has begun in the tissues.

1081, a suicide, can with some confidence be placed in the postcentral sub-group, if only by the evidence of the stained sections which demonstrate a marked inequality in the two postcentral gyri. After considerable search, a focus of gliosis and satellitosis was found in one of the orbital regions. This case, a good instance of a hebephrenic with onset at 18 and suicide at 45, shows how a minor lesion—anomaly or acquired lesion, it would not be safe to say which—can be overlooked at autopsy. Had not the postcentral gyri been sectioned in coordinate places and had not the orbital gyri been sectioned, this brain might well have passed into the "normal" group both macroscopically and microscopically.

1208 is a case described by Ayer and the writer in 1908,* in which the gross findings are so altered by the effects of a suicidal attempt and by terminal metastatic brain abscesses that a judgment concerning essential lesions of dementia præcox is difficult. The case should perhaps be excluded from the whole series on the ground of complications.

So excluding 1208, we arrive at the judgment that 15 cases in which gross lesions were actually described, together with four cases in which (in all conscience and with greater experience) gross lesions *should* have been observed, our total of gross lesion cases would run to 19 in 28 (the chosen uncomplicated 29 cases minus case 1208). This result would mean that gross lesions—focal atrophies and aplasias, and a few focal and diffuse glioses without visible atrophy—are found in 68 per cent of a series of typical dementia præcox cases, from which have purposely been previously excluded all instances of frank arteriosclerotic and coarsely wasting processes.

It seems strange that such a high percentage of visible and tangible lesions should have escaped attention, if this Danvers series is at all typical of dementia præcox in general. I am sure that in many laboratories the brains of autopsied cases fail to get intensive study until after long immersion in formaldehyde solution, which obliterates (or by distortion perhaps conceals) minor size-differences in gyri. Moreover, anatomists, familiar with sculpture anomalies of such relatively plastic organs as the liver, kidney and spleen, are inclined to dismiss cerebral anomalies of sculpture as of the same minor order of interest. Again, the careful palpation of the cerebrum and of the cerebellum is not duly practiced in all laboratories, nor are blocks for microscopic examination chosen on the basis of such intensive inspection and palpation of the brain as careful work demands.

Our own experience has shown how difficult it may be to keep one's house in order for intensive work. Eight cases are outstanding in which notes of gross lesions are missing. Of these eight, four show in certain regions characteristic gliosis and satellitosis (891, 944, 977, 1165). The other four (794, 806, 873, 1006) have so far proved refractory to our efforts to show stratigraphic alterations.

The result is that 24 out of the chosen 28 cases show either gross and microscopic lesions or microscopic lesions alone, *i. e.*, 86 per cent.

V. The Topographic Idea in the Study of Dementia Præcox and Allied Conditions.

The eternal hope of the neuropathologist is the hope of showing visible "changes" in the nervous system in the functional psychoses, and not only *in* them but *of* them. All insanity, we hear on every hand, is really nothing but brain disease, and, if our technique were only better, we should be able to point out the particular brain-changes which are responsible for insanity. I was assured by an enthusiastic psychopathologist that these brain-changes are actually so certain to exist that we should not waste our time looking for them.

There are reasons which make this equation:

Insanity = brain-disease

really erroneous. In the first place, certain psychiatrists to the

contrary notwithstanding, modern work has shown that the equation should better read

Insanities = brain-diseases,

and in the particular form

Some insanities = brain-diseases

perhaps we should be inclined to accept at least the spirit of the statement.

Ever since the doctrines of Flourens were overthrown, from the days of Hughlings Jackson and Hitzig down to the era of the topographers (Campbell and Brodmann, for example), it has been known that the brain is a complex of organs. The brain has parts. Yet those authors who assert that insanities are diseases of the brain are as a rule quite silent as to the brain-*parts* involved. The brain as an organ of mental disease is for these authors really the old Flourens brain, having interchangeable parts like a liver or a kidney.

The only justification for this view of which I am aware is the sound idea that the brain, although its parts are not homogeneous and interchangeable, still works in a certain integrated, organized way, and, when disorder and disorganized workings of brain-elements supervene, then mental diseases appear. Thus Wernicke supposes that

insanity = disease of the association elements of the brain.

This is a definite advance upon older conceptions, at all events in clearness. I suppose no one doubts the conceivableness of a mental disease based upon such transcortical lesions of association fibers as Wernicke supposes. But few would be so bold as to generalize the transcortical-injury idea[35] to cover the great bulk of mental diseases.

Even in the field of aphasia, one observes with recent writers a tendency to replace the focal-destruction theory with some theory more consonant with modern ideas as to the tremendous breadth, and complexity of the cortical areas subtending speech. From the psychological and logical side comes a vigorous plea from Wundt[36] against the fashionable focalizing of the speech functions in specified areas.

Thus a curious situation develops. On the one hand, the topographers, both physiological and histological, are demonstrating

more and more the extreme delicacy of subdivision which exists in the brain-cortex, as elsewhere in the nervous system, so that one gains the idea that perhaps no parts of the brain are functionally interchangeable, save by re-education. On the other hand, logicians and critical workers are calling a halt upon the focalizers and denying some of the most classical and approved localizations. These latter objections are brought with the more force against the localization of a complex function like speech, which savors of the old faculty-psychology and contains a *soupçon* of phrenology.

I believe we should be even more critical concerning the structural foundations of mental disease. Suppose we grant that any mental symptoms you please, *e. g.,* delusions, hallucinations, negativism, *cerea flexibilitas,* have a cerebral origin, is it necessary to suppose likewise a cerebral disease, as a basis therefor? Yes, some would reply, a cerebral disease, but not necessarily structural, perhaps functional only. Even the latter escape I should be tempted to forbid.

Consider diabetes mellitus. The glycosuria has in one sense a renal origin. But it would be a mistake to consider diabetes mellitus a renal disease, structural or functional. I believe that the brain permits certain mental symptoms to develop and purveys these symptoms, much as the kidney of a diabetic permits and purveys glycosuria.

Similar considerations hold with respect to the purveying of convulsions by the brain, an account of which I presented in a paper on the mechanism of gliosis in epilepsy. Neither a convulsion nor a katatonic impulsive movement nor the clenched fist of a thug is adequately explained by lesions of the muscles involved, by lesions of the motor nerves or spinal cord, by activities in the precentral gyrus, or even necessarily by any post-Rolandic or pre-Rolandic brain mechanism or combination of mechanisms. Perhaps, indeed, the reason lodges back of the central nervous system: the convulsion might have been a phenomenon of reflex epilepsy due to intestinal worms, even the katatonic movement might conceivably prove a normal and proper reaction to some received stimulus, and the thug's brain might have been quite "normal" while engaged in permitting asocial acts for whose source one should seek far afield.

On such grounds it has not seemed certain to me that mental disease is necessarily brain disease or that, were we able to inspect thoroughly all brain-parts, we should necessarily discover "changes" therein in mental disease. Perhaps the thyroid or the pituitary glands might induce mental symptoms without inducing brain "changes," over and above the proper physiological changes going on in any brain-part during the execution of its normal function. We might be forced to look into the thyroid for the cause of some mental diseases, just as into the pancreas for that of a diabetes mellitus.

A priori, therefore, it has not seemed to me at all necessary that diseases like manic-depressive insanity or dementia præcox (to use Kraepelin's nomenclature) should exhibit, even theoretically, brain-changes. One was especially disposed not to conceive brain-changes of a universal character, such as the universal liver changes in phosphorus poisoning, as underlying these diseases. No doubt there are instances of such universal brain-change and no doubt mental symptoms occur as a consequence. Hyperpyrexia might serve as an example. General paresis, however, our paradigm in this field, despite the severe and widespread brain changes which characterize it, is still an example of a disease of focal character. From its protean and progressive character, a theoretically similar focality for brain lesions in dementia præcox was thought probable. The mild, irritative and persistently complex character of many symptoms in dementia præcox seemed to argue very mildly destructive or irritative lesions, such that an occasional definite cure or disappearance of a given symptom or set of symptoms could be effected by removal of irritating factors or by advancing destruction of the offending elements.

If these contentions were sound, it became clear that no random block of brain tissue could demonstrate the nature of dementia præcox, as a particular block of lung tissue might demonstrate that of pneumonia. Neither would all the cells be equally or peculiarly affected nor would the cells of certain strata do more than demonstrate the effects of disease in those strata.

But, if the cells or strata of no random block of brain tissue could serve as a test of dementia præcox, would not particular and happily chosen blocks, or even ideally possible total-brain

sections suitable for cytopathology, solve the problem. I suppose all would agree that such work might solve the problems at least of localization and possibly of pathogenesis in dementia præcox, provided that the disease is really a brain disease.

I therefore began to study all cases of dementia præcox accessible to me (the protocols and prepared sections from the Danvers collection made in Prof. Barrett's service and my own), to get a general view of the subject. As will be seen, I at first included with type cases also cases only doubtfully belonging in dementia præcox, and these I have excluded from the conclusions of this report, although many exhibited lesions which might well serve, if we were surer of our conditions, to bring the cases back into the group.

The histopathology, although studied in connection with many of the lesions, has been left in the background to avoid involvement in a tangle of discussion concerning intracortical reflex-arcs.

Conclusions.

1. Existent evidence for the organic nature of dementia præcox is not wholly convincing, since (a) the cytological changes described are found also in cases of toxic deliria and in cases complicated by severe visceral disease, and (b) the stratigraphic changes described are found also in certain senile cases without characteristic symptoms of dementia præcox.

2. Resort must, therefore, be had to the topographic idea, for the adequate exploitation of which total-brain sections, with cytological exploration of *all* areas, are ideally necessary.

3. Random blocks of brain tissue with demonstration of satellitosis, infrastellate gliosis, or disintegration products of cell disorder will throw little light on the mechanism of dementia præcox.

4. The data of the functionalists (dissociation, sejunction, intrapsychic ataxia, and the like) are of the utmost importance as indicating the essential focality of the pathogenic process and the focal variations in its severity.

5. The curability of certain cases, the remissive character of some cases, the speedy disappearance of particular symptoms, the persistent complexity of reaction in some instances, the absence of characteristic severe projection-system symptoms, all indicate

that the process is histopathologically mild and that the focal changes found will be but slightly destructive or even irritative (in the sense of slight injuries readily repaired or compensated for).

6. Grossly destructive lesions of a transcortical character in Wernicke's sense might conceivably effect, *e. g.*, a permanent katatonic complex and doubtless will be found to do so occasionally; but the protean and progressive character of dementia præcox will exclude such transcortical injuries from playing a large part in the pathogenesis.

7. The focal lesions to be sought for will doubtless escape macroscopic notice in many instances, since the volume of apparatus engaged in effecting very prominent symptoms is often slight and spread very thin in numerous areas.

8. Studies of the "soft brain" and of gliosis in epilepsy have proved, however, that even comparatively slight degrees of cortical gliosis can often be palpated at autopsy.

9. Palpable glioses of a focal or variable character, combined in numerous instances with visible atrophy and microgyria, have been found in over half the series under examination, in cases regarded as clinically above reproach and *not* subject to coarse wasting processes, focal encephalomalacia, cortical arteriosclerosis, or diffuse chronic pial changes.

10. The frequent co-existence of several foci of sclerosis or atrophy in the same brain and the microscopic observation of milder degrees of nerve-cell disorder and gliosis in regions without gross lesions tend to the conception that the agent is more general and diffuse in its action than would seem at first sight, so that future research may well demonstrate that certain instances of coarse brain wasting and even of diffuse chronic leptomeningitis belong in the group (microscopic corroboration necessary for assigning values to focal variations).

11. The microscopic examination of the residue of cases in which gross lesions or anomalies were not described shows the same tendency to gliosis and satellitosis in numerous instances and the same tendency to focal variations from gyrus to gyrus exhibited by the gross lesion group. These findings suggest that the minor gross lesions and anomalies of several cases actually escaped notice (the protocols, though drawn up with a certain

system, are by various hands) at autopsy, so that the probable actual proportion of gross lesions is 68 per cent. If microscopic evidence is resorted to, the "organic" proportion in our series rises to 86 per cent.

12. Several groups of cases were classified from the distribution of macroscopic lesions, although the focal purity of these cases can often be brought in question from the results of microscopic examination (infrastellate gliosis and satellitosis also in macroscopically "normal" areas).

I. Pre-Rolandic group, including a superior frontal-prefrontal sub-group of paranoidal trend (*cf., e. g.,* case 1062).

II. Post-Rolandic group, including (a) postcentral-superior-parietal (sensory-perceptual) sub-group in which katatonic features are the common factors (*cf., e. g.,* case 1298); (b) occipital sub-group (*cf.* case 1149).

III. Infra-sylvian group (too small for clinical correlations).

IV. Cerebellar group (katatonic features).

13. If these data find general confirmation, they will doubtless go far to unify discussion, since mild, variable and progressive intracortical lesions, proceeding at different rates in different parts of the apparatus, and having the peculiar distributions indicated above, would explain adequately some of the contentions of the dissociationists, while remaining not wholly inconsistent with Kraepelinian ideas.

14. The frontal-paranoid correlation is in line with modern physiological ideas, but it must be granted that the occipital and temporal regions, as elaborating important long-distance impulses, may well play a part also in paranoid states.

15. The cerebellar-katatonic correlation is doubtless in line with some contentions of the Wernicke school, and obvious comments might be made in conection with the proprioceptive functions of the cerebellum (Sherrington).

16. The postcentral-superior-parietal relations to katatonic symptoms are perhaps theoretically the most novel suggestion from the work, but here again the results are not inconsistent with modern physiology.

17. The topographic study of dementia præcox brains, both gross and microscopic, is commended as likely to shed new light on the pathogenesis of certain symptoms, notably paranoidal and katatonic symptoms.

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