ANATOMICAL FINDINGS IN SENILE DEMENTIA: A DIAGNOSTIC STUDY BEARING ESPECIALLY ON THE GROUP OF CEREBRAL ATROPHIES.*

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I have lately possessed the unusual advantage of reviewing a considerable collection of autopsies (247) upon cases of mental disease introduced at various times in the years 1904-1908 at the daily clinics of the Danvers State Hospital, Massachusetts. The cases introduced in these clinics are of particular value, because the often divergent opinions of several diagnosticians, from three to eight or more, are recorded in each instance. The staff has varied from time to time, but has at all times contained members familiar in our recent American psychiatric literature, such as Prof. A. M. Barrett (now of Ann Arbor), Dr. H. A. Cotton (now of Trenton, New Jersey), Dr. H. W. Mitchell (now of the Eastern Maine Hospital for the Insane), Dr. H. M. Swift, and Dr. Charles Ricksher, as well as the moderator, Superintendent Charles W. Page. The clinical diagnoses which I have considered have not been those chosen for the statistical records required for the Board of Insanity, but *all* the diagnoses rendered for each case.

For more minute examination I have naturally resorted to those cases in which all the staff agreed, holding the opinion that uniformity in diagnosis by several men is of more value than that induced by a single chief of clinic.

To establish the degree of accuracy in diagnosis at these clinics, I may mention (what I have dealt with more specifically before the American Neurological Association) the 85 per cent accurate diagnoses where all agreed to general paresis. Only 6 out of 41 cases *unanimously* diagnosed general paresis turned out to be cases of

something else. The reasons for these 6 incorrect diagnoses I shall present *in extenso* elsewhere,¹ but they do not militate against the general accuracy of diagnosis in the Danvers daily clinics.

I was the more astonished to find that, on accepted anatomical criteria, our success in the diagnosis of senile dementia at these clinics was not at all comparable with our surprisingly good results in general paresis. On the hypothesis that cerebral atrophy is a necessary feature in senile dementia, our diagnoses turned out to be only 38 per cent correct. On the hypothesis that cortical arteriosclerosis is a necessary feature in senile dementia, our diagnoses were but 48 per cent correct. And, in fact, 14 of the 42 cases in which the diagnosis of uncomplicated senile dementia was rendered, viz., 33 per cent, proved to show neither sclerosis of terminal arteries nor cerebral atrophy, so that *our general percentage of accuracy, as established by the finding of either cerebral atrophy or cortical arteriosclerosis (or both), was 66 per cent for senile dementia.*

The general analysis of this material may be presented in the following table, which deals with the data of 42 uncomplicated cases in a total of 71 cases of probable senile dementia in a grand total of 247 cases of various types of mental disease subject to anatomical review:

DIAGNOSIS OF SENILE DEMENTIA.

Clinically uncomplicated	42
Brains underweight	29
Males under 1358 G.....	10
Females under 1235 G.....	19
Brain atrophic	11
At least one-sixth loss in weight.	
Brains atrophic	16
All data considered.	
Sclerosis of cerebral end-arteries.....	20
Atrophic, not arteriosclerotic	8
Not atrophic, not arteriosclerotic.....	14

These 42 cases have been subjected to closer analysis with the object of determining the necessary features in a case of senile dementia.

It does not appear that the anatomical and histological characters of senile dementia are as clear-cut and ready of diagnosis

as the post-mortem characters of general paresis. But there is a widely current opinion that the brains of senile demented show well-marked *cerebral atrophy*. Other descriptions give equal prominence to *arteriosclerotic lesions*. Frequently the literary student gains the impression that both kinds of disease characterize the brains of senile demented, or even obtains a thinly-veiled conception that the brain atrophy is somehow due to arteriosclerosis.

CEREBRAL ATROPHY.

With respect to cerebral atrophy, it appears that there is actually no standard by which to determine the amount of loss in weight which shall signify atrophy. Thirteen of the brains in the 42 uncomplicated cases of senile dementia, remarkably enough, yielded weights above the averages ordinarily assigned for male (1358 grams) and female (1235) grams. Thus, unless some of these 13 cases possessed unusually large brains at the outset (of which there is no evidence otherwise), we need consider only 29 cases as belonging possibly in the cerebral atrophy group.

There is, however, no warrant for the diagnosis of cerebral atrophy in every case which is somewhat underweight with respect to the assigned averages of the books, since we must take into account initial differences in brain weight (variations according to race, body weight, stature, age). Thus brain weights ranging from 1461 to 1265 have been assigned to average normal males, and weights from 1341 to 1112 to average normal females.²

It is obvious, therefore, that the degree of loss which is to warrant the diagnosis "atrophy" is hard to determine. Perhaps, in the last resort, we should be dissatisfied with any result which did not depend on an obviously impossible calculation—namely, the degree of loss from the original weight in the given case.

If in this series we adopt the arbitrary standard sometimes advocated—namely, a conceived loss of one-sixth the original weight³—and take the ordinarily assigned averages as original weights, we at once reduce the cases showing brain atrophy to 11. Thus only 26 per cent of 42 cases diagnosed as senile dementia would show atrophic brains.

Perhaps it is better to trust the qualitative data with respect to the diagnosis, cerebral atrophy. Upon collation of the qualitative findings, paying attention to the occurrence of both diffuse and

focal atrophies of convolutions, the same result as before recorded (on the criterion of weights) was registered for the incidence of brain atrophy. There were 13 cases which could not be regarded as atrophic and 29 which showed either diffuse or focal convolutional atrophy. The distribution of these classes was almost the same as the distribution of the weight classes. Two cases were carried over from the larger class (29) to the smaller (13). (The first on the score of focal atrophy of one frontal region, the second on the score of a focal lesion (possibly aplasia) of the frontal lobes). And two cases were carried in the reverse direction from the smaller class (13) to the larger (29) on the basis of exact gross descriptions, suggesting approximate normality of convolutions.

But the atrophies which were employed to separate these two classes were not all diffuse atrophies such as we have in mind in the current definitions of senile dementia. Only 20 of these cases showed an obvious diffuse cerebral atrophy, and of these four showed a slight or a questionable atrophy. Thus, if the gross qualitative differentiae are adopted, 16 out of 42 cases of senile dementia (or 38 per cent) showed cerebral atrophy of a convincing character.

CORTICAL ARTERIOSCLEROSIS.

A review of the gross and microscopic findings indicates that we cannot safely exclude cerebral arteriosclerosis of greater or less degree in any single case of this series of 42 cases. (Four cases in which no specific note was made of cerebral arteriosclerosis yield other data, gross or microscopic, from which some degree of such change can be assumed.) Similar statements probably hold good of many brains in the non-insane in advanced age.

But it is evident that there are important theoretical differences between cases which show sclerosis of the larger anastomosing arteries and those which show sclerosis of terminal arteries. Sclerosis of the terminal arteries of the brain, whether leading to infarctions or not, obviously means much more from the standpoint of the integrity of the cerebral functions. In fact it would seem difficult to exclude with certainty cases of extensive small-branch arteriosclerosis from the group of organic dementia.

Twenty out of 42 cases diagnosed senile dementia proved to

show a significant arterial disease—sclerosis of terminal cerebral arteries, leading to gross or microscopic infarctions in 16 instances. Although the other 22 of the series showed arteriosclerosis also, this sclerosis was confined to the circle of Willis or to the proximal portions of the primary branches of the circle, so that the changes were deemed of no special psychiatric importance, beyond that which may attach to sclerosis of the pipe arteries throughout the body. Although it may be scarcely justifiable to transfer these 20 cases of small-branch arteriosclerosis bodily over to the group of organic dementia, since many of the symptoms shown may have been due to quite other causes than the arteriosclerosis shown, still it is manifestly unwise to study such cases from the standpoint of a critical symptomatology under the impression that they are pure instances of senile (not organic) dementia.

CASES WITHOUT SCLEROSIS OF CEREBRAL END-ARTERIES.

An analysis of this residuum of 22 cases not showing significant cortical arteriosclerosis (either focal encephalomalacia or other evidence of sclerosis of terminal cerebral arteries) shows that eight belong frankly in the atrophic series, whereas 14 stand out as cases in which neither diffuse cerebral atrophy nor sclerosis of terminal cerebral arteries can be ascribed to the brains.

Should this prove an adequate analysis of the anatomy of these cases, it is plain that, in the histories of the eight simple atrophic cases, we might find data corresponding to our conception of senile dementia (providing cerebral atrophy is a necessary feature of this disease). And in the histories of the outstanding 14 we might expect a variety of data in which the characteristic features of senile dementia are lacking.

That somewhat similar results might be expected in a large series of cases, at least in so far as the exclusion of arteriosclerotic cases as "organic" is concerned, is seen from the following table compiled from writers, mentioned again below:

FOCAL LESIONS IN "SENILE DEMENTIA."

Nötzli, 1895	19	13	32
Meyer, 1896	11	13	24
Appeldorn, 1908	18	14	32
Southard, 1910	20	22	42
	68	62	130

CASES OF CEREBRAL ATROPHY.

The following pages are devoted to brief clinical summaries of the eight supposedly pure brain atrophy cases, together with the main anatomical diagnoses in each case.

The special features of the different brains are discussed together on a later page.

CASE I.—D. I. H., 11801, Path. Lab. 872. Woman, born 1823. *Heredity*: Father and two brothers died of senile dementia. Mother died of asthma. *Personal history*: Normal in girlhood. Taught school. Married 1843; 9 children (four living in 1904); one miscarriage. Of a melancholy turn. Delirious during a fever, 1874. Fractured thigh, 1897, after which came mental change; amnesia, fabrications, apathy. Cut up clothes. Numerous dreams. Fearful, often said she was dying.

Committed to D. I. H., 1904. Emaciation, anemia, senile skin, teeth absent, feet blue, muscles flabby and weak, arcus senilis. Double cataract, blind, pupils non-reactive, somewhat deaf, tongue and face muscles finely tremulous, too weak to walk or stand, slight paraphasia (?), cannot write, radials and brachials thick and tortuous, pulse thready, irregular, and faint (90 to 100), organic reflexes altered.

Disorientation for time, place, and persons. Amnesia for recent and remote events. Impressibility poor. Multiplies as far as 3×5 , and adds 2 and 2, but does no further tests. Resistive, restless.

Death 15 days after admission.

The autopsy showed *chronic conditions*:

Malnutrition.

Marked general arteriosclerosis, with calcification and ulceration of aorta, extensive coronary sclerosis, and moderate involvement of bases cerebral arteries.

Bilateral generalized pleural adhesions.

Scar of right apex.

Chronic diffuse nephritis.

Brown atrophy of heart muscle.

Slight chronic passive congestion of liver.

Slight chronic localized peritonitis (omental).

Diffuse cerebral atrophy.

And much evidence of *acute disease*:

Acute sphenoidal, ethmoidal, and occipital sinusitis.

Bilateral bronchopneumonia, with acute bronchitis and tracheitis (without lymphnoditis).

Edema of left side of rima glottidis.

Lung cultures yielded staphylococci, streptococci, pneumococci, and a bacillus of the pseudodiphtheria group.

Culture from the ethmoidal sinus yielded *S. p. aureus*, but culture from sphenoidal sinus remained sterile.

The *cause of death* was undoubtedly bronchopneumonia.

CASE II.—D. I. H., 11716, Path. Lab. 849. Woman, born 1818. *Heredity* and much of *personal history* unknown. Onset said to be in 1900 after a fall. (Gall-stones and chronic fibrous peritonitis at autopsy.) Widow.

Committed to D. I. H., 1904. Malnutrition, senile skin, arcus senilis, teeth absent, musculature poor, right eye blind, right pupil fails to react to direct light, hearing somewhat defective, left knee-jerk, elbow and forearm reflexes exaggerated, tremor of tongue, labial tremor when talking, right leg weaker than left and kept flexed, incoordination in movements of feet, muscular sense in legs diminished, radials and brachials thickened and tortuous, pulse full, regular, 96.

Excited and resistive on admission. Disorientation for time, place, and persons. General amnesia. Fabricates (assigning wrong names).

The autopsy showed *chronic conditions*:

Obesity.

Aortic sclerosis with ulceration.

Mitral sclerosis.

(Coronary arteries normal.)

Diffuse and focal sclerosis of basal cerebral vessels.

Chronic fibrous endocarditis.

Chronic adhesive pleuritis, left.

Calcified and caseous nodule in central part of left lower lobe.

Scar of right apex.

Chronic nodular perisplenitis.

Cholelithiasis.

Moderate chronic passive congestion of liver.

Fatty liver.

Chronic diffuse nephritis.

Chronic localized peritonitis.

Chronic external adhesive pachymeningitis.

Diffuse cerebral atrophy.

Acute conditions:

Edema of left leg (thrombosis?, not proved).

No cultures were taken from this case and the cause of death is doubtful.

CASE III.—D. I. H., 11881, Path. Lab., 1050. Woman, born 1834. Alms-house transfer to D. I. H., 1904. Nutrition and musculature fair. Senile facies and skin. Arcus senilis. Varicose veins. Teeth almost all absent. Radial arteries not palpably sclerotic. Vision and hearing impaired.

Pleasant, garrulous, Irishwoman, speaking mixture of English and Gaelic. Knew month and day of week, but not the year. Repeated Lord's Prayer. Counted from 1-20, performed a few of the simplest problems. Amnesia for remote events, not so marked for recent events. Cannot write or read. Death in 1906.

The autopsy showed *chronic conditions*:

Cardiac hypertrophy.

Coronary, splenic, and renal arteriosclerosis.

Brown atrophy of heart.
Chronic passive congestion of lungs.
Slight portal cirrhosis of liver.
Chronic diffuse nephritis.
Chronic perisplenitis.
Chronic splenitis.

Acute conditions:

None noted.
No cultures taken.

CASE IV.—D. I. H., 12162, Path. Lab. 1058. Woman, born 1834 (assigned date). Almshouse transfer. Delusions ("holy water taken away"), suspicious, visual hallucinations (talks to supposed faces), violence at night for unknown period before transfer. Committed August 31, 1904.

Malnutrition, teeth absent, edema of feet and lower legs, weakness of muscles, gait unsteady, slight tremor of hands, rather coarse tremor of tongue, vision defective, knee-jerks and Achilles jerks diminished, wrist and triceps brisk.

Disorientation for time (except month). Amnesia complete (could, however, repeat Lord's Prayer). Later complete disorientation.

Death April 24, 1906.

The autopsy showed *chronic conditions*:

Cardiac hypertrophy.
Chronic diffuse nephritis.
Sclerosis with calcification of aortic valve.
Mitral sclerosis.
Aortic sclerosis.
Coronary, basilar, and vertebral arteriosclerosis.
Chronic fibrous endocarditis.
Chronic fibrous pericarditis.
Chronic adhesive pleuritis.
Absence of diploë.
Chronic external adhesive pachymeningitis.
Chronic fibrous leptomeningitis (notably over vermis of cerebellum).
Pedunculated polyp of cervix uteri.
Hypertrophy of right lobe of thyroid gland.
Tumor (probably hypernephroma) of right kidney.
Diffuse cerebral atrophy.
Slight granular ependymitis of accessory sinuses of fourth ventricle.

Acute conditions:

Lobar pneumonia, bronchitis, and fibrinous pleuritis of right upper lobe.
No cultures taken.

CASE V.—D. I. H., 12334, Path. Lab. 1103. Woman, born 1835. *Heredity*: Negative. *Personal history*: Diphtheria and scarlet fever as child. Bright scholar. Married, 1856. Two boys (both alive 1904); one miscarriage. Married again, 1874. Three or four children. Widowed, 1894. Tailoress

till 1903. Corneal thickening of left eye began 1894. Gave up work on account of impaired vision. During 1904 absent-minded, gradually increasing amnesia, visual and auditory hallucinations.

Committed to D. I. H., 1904. Senile skin, slight anemia, teeth poorly preserved, muscular weakness, slight incoordination of finger movements, coarse tremor of tongue, vision absent in left eye and impaired in right, hearing defective. Died October 21, 1906.

The autopsy showed *chronic conditions*:

Emaciation.

Aortic sclerosis with calcification and ulceration in distal half.

Sclerosis of coronary, renal, carotid (especially distal extremities of internal carotid) arteries.

Mitral sclerosis.

Cicatrices and local ulcerations of ileum (perhaps tuberculous, but not proved).

Chronic adhesive pleuritis.

Chronic diffuse nephritis.

Old scar and local fibrosis of liver.

Cholelithiasis.

Calvarium thin.

Chronic internal hemorrhagic pachymeningitis (right).

Diffuse cerebral atrophy (masked by edema).

Acute conditions:

Lobar pneumonia.

Hematoma of right side of scalp.

Bruise of face.

Cultures from blood and cerebrospinal fluid showed streptococcus pyogenes.

CASE VI.—D. I. H., 13442, Path. Lab. 1123. Woman, born 1832. *Heredity*: Father died of tuberculosis at 35. Mother died of old age over 80. One sister became melancholy after loss of four children and died in this condition at 75. Five brothers and two sisters normal, lived to old age. *Personal history*: Normal child. Common school education. Shoe-stitcher of fair capacity. Unmarried. Ceased mill work 1885. After 1885 occasionally nursed for small fees. Gradual physical failure since 1887 (then aet. 55). In September, 1906, worried over selling of relatives' house. Later insomnia, visual and auditory hallucinations, confusion lasting a week. Similar episode in October. Again in January, hallucinations, confusion, delusions of poisoning, disorientation for time, place, and persons.

On commitment, January 4, 1907, senility, vision defective, tremor of tongue, lips, and hands, muscular weakness, slurring and stumbling speech, radial and brachial arteriosclerosis, pulse 120, weak and thready, heart enlarged, organic reflexes defective, amnesia for both recent and remote events, complete disorientation, diminished impressibility. The temperature rose from 99° on entrance to 101° evening of January 8, and to 103° evening of January 14. Death January 15, 1907.

The autopsy showed *chronic conditions*:

Emaciation.

Brown atrophy of heart.

Mitral and aortic valvular sclerosis.

Chronic fibrous endocarditis.

Aortic sclerosis.

Coronary, pulmonary, carotid, and basal cerebral arteriosclerosis.

Small saccular aneurysm of right middle cerebral artery.

Chronic diffuse nephritis.

Chronic gastritis.

Chronic adhesive pleuritis.

Uterine polypi.

Calcified lymph nodes in perirectal tissue.

Hemangioma of liver.

Chronic fibrous pachmeningitis.

Diffuse cerebral atrophy.

Acute conditions:

Bilateral bronchopneumonia with acute bronchitis and lymphnoditis.

Acute splenitis.

Acute typhlitis and colitis.

No cultures were taken.

CASE VII.—D. I. H., 13358, Path. Lab. 1134. Woman, born 1840.

Heredity: Unknown. *Personal history*: Largely unknown. Attack said to have been gradual in onset; 9 months before admission, about one year before death. Alcoholism probable. Disorientation, vagrant tendency, delusions of suspicion, wandering talk. Emaciation.

On admission feeble, senile skin, arcus senilis, left eye enucleated, cataract of right eye, enlargement of finger joints. Radial arteriosclerosis. Gait tottering. Slight tremor of hands. Brisk knee-jerks and Achilles jerks, plantar reaction slight, abdominal reflexes absent. Delirium and restlessness, with occasional attempts to walk about. Visual hallucinations probable. Was able to obey a few simple directions. Few relevant replies could be obtained. Amnesia for recent events complete; a few isolated facts from past life were recalled.

The patient remained completely disoriented for time, place, and persons; but her attention improved somewhat during the first week after admission. Motor restlessness occasionally appeared during December. Reactions occasionally suggested auditory hallucinations.

Death January 15, 1907.

The autopsy showed *chronic conditions*:

Emaciation.

Carcinoma of pylorus with metastatic nodule in stomach wall.

Brown atrophy of heart muscle.

Chronic fibrous endocarditis.

Aortic and mitral valvular endocarditis with calcification.

Aortic sclerosis with calcification.

Coronary, pulmonary, basal cerebral (including primary branches), splenic, and renal arteriosclerosis.
Slight hydropericardium.
Scars of left apex.
Bilateral chronic adhesive pleuritis.
Chronic splenitis.
Superficial fibrosis of liver, mesentery, and peritoneal wall.
Left eye absent.
Thyroid small.
Irregularity in thickness of calvarium.
Chronic fibrous pachymeningitis.
Diffuse cerebral atrophy.

Acute conditions:

Bronchopneumonia of right lower lobe with lymphnoditis.
Central necroses of liver.
Culture from cerebrospinal fluid yielded *B. coli communis*.

CASE VIII.—D. I. H., 14099, Path. Lab. 1262. Woman, born 1838. According to patient father died at 72 of asthma. Mother at 50 of pleurisy. Two brothers were still-born; one lived 3 weeks. One sister alive at 65. No insanity or alcoholism in the family. At school till 16. Orthopedic operation at Massachusetts General Hospital in 1854. Occupation, housemaid. Since 1906 at Lynn poor-farm. Noisy and troublesome, singing and screaming at night.

On admission emaciation, contractures of legs and right arm, radial sclerosis slight, prominent temporal arteries, pulse small, rapid, of low tension. Sensations adequate with rough tests. Left ankle-jerk and knee-jerk brisk. Plantar reflexes and right ankle-jerks not obtained. Deafness, facial muscles normal. Blind. Incontinence of urine and feces. Stereognosis for many objects good, but patient could not tell a cent from a quarter by touch. Amnesia for both recent and remote events. Memory somewhat better for remote events.

Death August 16, 1908.

The autopsy showed *chronic conditions*:

Emaciation.
Contractures of legs and right arm.
Brown atrophy of heart muscle.
Chronic valvular endocarditis.
Aortic and coronary sclerosis with calcification.
Chronic obliterative pleuritis (right) and adhesive pleuritis (left).
Healed tuberculosis of apices.
Generalized adhesions of peritoneum.
Cholelithiasis.
Chronic diffuse nephritis.
Chronic atrophic hepatitis.
Perforation of right tympanum.
Slight diploë.

Cysts and calcified nodules in both ovaries.

Diffuse cerebral atrophy.

Acute conditions:

Tuberculosis of lungs.

(Tuberculous?) ulceration of transverse colon.

Cystitis.

Sacral decubitus.

GENERAL CLINICAL ANALYSIS.

SEX.

This series of eight cases happens to be composed throughout of women. This fact is in accord with previous experience in the type of senile case termed by Kahlbaum *presbyophrenia*. Systematists like Kraepelin, for example, mention the predominance of females in presbyophrenia, but fail to note any sex differentiation in other mental disorders of the senium (senile depressions, deliria, delusional insanities).

A peculiar fact looking in the same direction was the statistical point made two years ago by Mitchell and the writer,⁴ viz., that the female brains accruing from a series of insanities developing in the sixth and seventh decades were more often atrophic (8 of 11) than the male brains (5 of 12). As we then pointed out, the average age at onset of the females (58.4 years) was not much different from the male average age (59.5 years). But the females survived after onset on the average 8.8 years, whereas the males survived on the average only 2.8 years.

Assuming (what has not yet been proved) that a large series of statistics would yield similar results, we should be confronted with the problem how to explain the remarkable viability of females presenting the clinical features of senile dementia and *pari passu* undergoing cerebral atrophy.

A large series of cases is strictly necessary for the solution of this problem. For the moment it is enough to call attention to the somewhat remarkable fact that of all the cases (42) agreed upon as senile demented at the Danvers State Hospital, 1904-8, there were eight cases which showed a relatively pure brain atrophy, and these eight were all females.

HEREDITY AND ANTECEDENT FACTORS.

The data concerning *heredity* are lacking in four cases. Two cases have no heredity of insanity, whereas two more have some

taint (872, "father and two brothers senile demented"; 1133, "one sister melancholy after loss of children"). Two cases appear to have been born to asthmatic parents (mother of 872, father of 1262).

The history with respect to *antecedent factors* is unobtainable in three almshouse transfers. Alcoholism is probable in one case (1134), the same which showed pyloric cancer at autopsy. The onset in one case is somewhat doubtfully related with a fall four years before death (849), and in one case is more definitely related with a fractured thigh (872). This case of mental disease subsequent to fractured thigh is the case in which we have the best evidence of hereditary taint, in which also we have record of a melancholy disposition throughout life and delirium during fever at the age of 51.

In two cases it appears that there were no upsetting factors (1103, 1133).

It would be of the greatest interest if we knew what relation these conditions bear to the menopause, but the data are lacking.

The important antecedent factors (except heredity) may be briefly enumerated as follows, based in part on clinical history and in part on autopsy findings:

872. Always melancholy, delirious in fever at 51 (old double pleurisy), fracture of thigh at 74, marked general and coronary arteriosclerosis, scar of right apex, chronic Bright's disease, malnutrition, double cataract, deaf.

849. Fall at 82, gall-stones and chronic fibrous peritonitis, obsolete tuberculosis of both lungs, radial, brachial, basal cerebral (no coronary) arteriosclerosis, chronic Bright's disease, obese, blind in one eye, deaf.

1050. Varicose veins; coronary, splenic, and renal arteriosclerosis; chronic Bright's disease; heart hypertrophy; impairment of vision and hearing.

1058. Heart hypertrophy, edema of legs, chronic Bright's disease; aortic, coronary, and basal cerebral arteriosclerosis; thyroid hypertrophy; malignant tumor of right kidney; vision defective.

1103. Corneal thickening at 59, left eye blind and right eye defective at 68, hearing defective, chronic Bright's disease, gall-stones, scars and ulcers of ileum, emaciation.

1133. Physical failure after 55, business worry at 74; radial, brachial, coronary, pulmonary, carotid and basal cerebral arteriosclerosis, chronic gastritis, chronic Bright's disease, organic reflexes defective, vision defective, emaciation.

1134. Alcoholism, pyloric cancer, general arteriosclerosis; left eye enucleated, cataract of right eye; emaciation.

1262. Gall-stones and generalized adhesions of peritoneum, chronic Bright's disease, healed tuberculosis of apices, aortic and coronary arteriosclerosis, blind and deaf.

SOCIAL FACTORS.

The above histories appear at first sight to have little of importance in common. There is, however, certainly little convincing evidence that social factors play much part in the antecedents of these cases (even in Case 1133 the business worry seems to be part and parcel of the disease, as it set in long after the onset of physical failure). Whatever the causes of the brain atrophy, it seems that they cannot be social.

DEFECTS OF VISION AND HEARING.

But, if social factors are wanting, it is not so certain that individual psychic factors play no part. It is remarkable that all eight subjects showed severe defects of vision, combined in five cases with considerable deafness. The hypothesis lies very near that some part of the mental picture must be related with these defects of the long-distance receptors. Opinions differ as to the capacity of such defects to produce insanity. Congenital or early defects of the sort notoriously fail to produce insanity. But may not acquired blindness and deafness become effective in producing insanity when other senile conditions coexist? The history of case 1103 might suggest this.

On the other hand, it might not be unreasonable to see in the blindness and deafness merely effects of the cerebral atrophy. This is possible, though it must be pointed out that the blindness in some cases was partly peripheral, originating in cataracts in some cases and in corneal thickening in Case 1103. Careful cortical study is essential in the solution of this problem. In any event, we may suspect that a vicious circle exists in these blind and

deaf dements, such that by a process of diaschisis the loss of long-distance perceptions reacts unfavorably upon a mental life already damaged in a variety of ways.

Are there any further common factors in these antecedents? As in the case of heredity and social environment, so too in the case of vicious habits, infectious diseases, and malignant disease, we find no constant or common factors in this small series.

RELATION TO MANIC-DEPRESSIVE INSANITY.

A specific question likely to be raised about any senile mental disorder is, have there been previous attacks? Should we align these cases with the manic-depressive group of Kraepelin? There is, I suppose, no *à priori* reason why a manic-depressive subject may not eventually succumb to cerebral atrophy. I am disposed to think, however, that the brains of such cases usually stand up well and that manic-depressive cases, when they reach the senium, will be found rather in the arteriosclerotic group or the "normal" senile group than in the group of atrophies now under discussion.

The present small group of cases is in some respects unsuitable for this purpose. 872 is possibly, if by no means probably, a manic-depressive case.

The problem has been approached in an interesting manner by the English Commissioners in Lunacy (1905 and 1907),⁸ who have shown that, in 20,680 admissions to English and Welsh insane hospitals (1903), the cases of first and not-first attacks were distributed as follows:

	First Attacks.	Not-First Attacks.
All cases not senile dements.....	13,970	5,546
Senile dements	1,058	106

Making all due allowance for the inadequacy of data in these aged subjects, it would appear certain that senile dementia cannot be made to include a tremendous proportion of manic-depressive cases.

We are reduced, then, in the particular small group of cerebral atrophies here considered, approximately to one of two etiologies—either to inherited tendencies or to causes operating in some concealed fashion in or prior to the senium. Obviously too, these two factors—inheritance and certain senile or presenile agents—may coöperate to produce senile mental disorder.

ARTERIOSCLEROSIS.

Since our data are thus far neither for nor against inheritance as a factor, we must consider the most prominent senile condition with which we are familiar—arteriosclerosis.

It has been the fashion to ascribe senile dementia, or a great part of its phenomena, to cerebral arteriosclerosis. Perhaps this relation was first asserted most confidently in Forel's clinic, whence Nötzli in 1895* issued a monograph on senile dementia, without, however, offering microscopic confirmation of the gross relationship asserted. This subject is considered at length in the anatomical sections.

Five of our series showed palpable sclerosis of the radial arteries (one of these, 1262, in which the radial sclerosis was slight showed prominent temporal arteries). Two cases, 872 and 849, were markedly arteriosclerotic clinically, and these proved to show the most marked general arteriosclerosis anatomically.

Three cases gave little clinical evidence of arteriosclerosis, and three more were but moderately sclerotic clinically.

In short, it would be difficult to prove any close clinical relation between arteriosclerosis and senile brain atrophy.

It must be borne in mind, however, that no one of these cases failed to show anatomically a certain amount of arteriosclerosis. In accord with general experience, this sclerosis was of focal and irregular distribution, affecting some organs and sparing others.

The clinical lesson appears to be that neither the presence nor the absence of radial arteriosclerosis offers important clues to the presence of cerebral arteriosclerosis. Not even the presence of severe changes in the radial arteries, or the concomitance of brachial arteriosclerosis, will permit us to divine the degree or even the presence of arteriosclerosis affecting the smaller or even the larger arteries of the encephalon. The same relation holds between peripherally demonstrable arteriosclerosis and, e. g., renal arteriosclerosis.

GENERAL CLINICAL FEATURES.

From the etiological or genetic points of view, we have incidentally considered several general features of these cases, such as the *blindness* constantly present in some degree, coupled frequently

with some *impairment of hearing*, the tendency to peripheral *arteriosclerosis*, etc. These findings may be unified as follows:

Our group consists of eight blind old women, who all presented characteristic signs of senility on inspection, having a senile skin, and, as a rule, also *arcus senilis*, being almost or quite toothless, and diffusely wasted or weak in the voluntary muscular system, and subject as a rule to general emaciation. In short, these subjects could scarcely be distinguished from so many old almshouse inmates, non-insane. Even the blindness would not serve as differentia, as it seems to be grounded in a variety of lesions in the different cases.

Upon further examination, we find no constant situation or degree of peripheral arteriosclerosis, and little agreement in the general characters of the pulse (tendency to increased rate in the more obviously sclerotic cases). The heart is not constantly enlarged, nor are there any constant features upon auscultation. The renal data have not been consistently worked up (partly by reason of difficult collection of urine), but the autopsies have shown always either a chronic diffuse nephritis or renal arteriosclerosis. No other metabolic phenomena have been thoroughly examined. There is certainly no obvious metabolic fault in these cases beyond that which may accompany senility.

Comparatively few signs of focal lesion were made out upon neurological examination:

872. Questionable paraphasia, organic reflexes defective, pupils non-reactive to light (double cataract).

849. Lingual and labial tremor, left knee-jerk, left elbow and forearm reflexes exaggerated, right leg held flexed and weaker than left, incoordination in foot movements, muscle sense in legs diminished.

1050. Not remarkable.

1058. Lingual tremor, tremor of hands, wrist and triceps reflexes brisk, knee-jerks and Achilles jerks diminished, gait unsteady.

1103. Lingual tremor, slight incoordination of fingers.

1133. Slurring and stumbling speech; lingual, labial, and manual tremor; organic reflexes defective.

1134. Slight tremor of hands, abdominal reflexes absent, knee-

jerk and Achilles jerks brisk, plantar reaction slight, gait tottering.

1262. Left knee-jerk and Achilles jerk brisk. Right Achilles jerk and both plantar reflexes absent. Organic reflexes defective. Stereognostic sense impaired (?).

Thus, *tremors*, *absence* of certain *superficial reflexes*, *variations* in some *deep reflexes* (tendency to loss of leg reflexes), *defective organic reflexes*, alterations of *gait*, and occasional slight *speech* disorder characterized these patients. Correlations with the details of the protocols and with the microscopic findings has so far not shown adequate reasons for the majority of these clinical findings. 1058 and 1134 seem especially consistent with present neurological knowledge. An examination of the spinal cord in 1134 showed a slight bilateral (approximately equal) pyramidal tract degeneration, as evidenced both by the Marchi preparations and by the neuroglia reaction. This degeneration appears to have been due to the atrophy of the brain which showed "convolutions, except of orbital surface, markedly atrophic, and atrophy especially marked in the Rolandic, parietal, and superior temporal gyri." The Betz cells of both precentral gyri are reduced in number, but the survivors show both axonal reactions and satellitoses. From these findings it may be concluded that such reflexes as those of 1134 do not directly depend upon focal lesions due to arteriosclerosis, but many hang upon atrophic cortical changes, in some instances at least.

Upon the mental side, communication is often rendered difficult through the defective vision and hearing of the patients, and there may be a not unnatural lack of spontaneity in their total relations with the outer world. It is difficult to prove by coarse tests that there is any loss of peripheral sensory power beyond that in sight and hearing; nevertheless such loss or diminution may be suspected to exist.

There is at all events certainly a deficient impressibility or perceptual capacity in these patients, which, coupled with a characteristic incapacity to remember recent events, serves to narrow the mental life to a remarkable degree. Whether the disorientation for time, place, and persons, so frequently noted, is quite constant and inevitable, may be doubted. Perhaps the condition would be

better described as *lack* of orientation, than as positive disorientation.

The amnesia for recent events is constant. Whereas memory for remote events is also frequently deficient, the amnesia for recent events almost always surpasses that for remote events. (One exception, 1050, was an almshouse transfer who had apparently never been able to read or write.)

Both as a consequence of deficient sensory and perceptual capacity and by reason of the marked amnesia for current events, the intellectual life is much reduced in volume as well as devoid of variety.

So far the description qualitatively differs only slightly from what one might expect in the aged, and many writers give the impression that they regard senile dementia as a kind of projection of senility, in which the features of senility will be found to a more pronounced degree.

What is the ground of commitment of these subjects to insane hospitals? In the first place, aside from the question of insanity, these patients are difficult to handle by reason of their muscular weakness, blindness, and deafness, and sometimes by reason of disorder of organic reflexes. Strictly speaking, all these features of the disease could be handled outside of insane hospitals. Possibly 1050 was a case not, in the strict medical sense, insane.

Delusions were made out in four cases (fear of death, "holy water taken away," poisoning, suspicion), but occupy no prominent place among the symptoms.

Hallucinations or *illusions* were demonstrably or probably present in five cases at some stage. One case had before commitment many frightful dreams. The hallucinatory phenomena were as a rule visual or auditory or both, and it is difficult to say whether peripheral or central activity was the more responsible for these findings.

The hallucinations are in part chargeable with bringing about the nightly restlessness and noise of some of the patients, but apparently only in part, since the same restless, noisy, troublesome characters are exhibited by other non-hallucinated patients.

The most constant feature in these patients aside from the exaggerated senile features above enumerated, is *motor excitement*. This was present in all but two cases (1050 and 1103). Restlessness and screaming or howling at night are characteristic. The

patients have spells of motor restlessness, alternating with quiet periods. The violent movements and noisy shouting are apt to come on suddenly and to quiet down gradually. During the spells patients are resistive. The garrulity of old age was exhibited in 1050 only.

AGE, ONSET AND DURATION IN ATROPHIC CASES.

	Age at Onset.	Character of Onset.	Duration.	Age at Death.
872	74	gradual, after thigh fracture.	7	81
849	81	gradual, after a fall?	4	85
1050	70	unknown	2+	72+
1058	61	unknown	2+ +	63+
1103	69	gradual	2	71
1133	74	gradual	$\frac{1}{4}$	74
1134	66	gradual	1	67
1262	68	unknown	2	70

GROSS ANATOMY OF THE BRAIN.

The pia mater was normal or approximately normal in 5 of 7 cases in which its condition was noted; but in case 1058 it showed a slight diffuse fibrous thickening especially well marked over the vermis of the cerebellum, and case 1262 showed a few small opaque-white spots over the sulcal vessels. There was a well marked compensatory edema of the pia mater in six cases, but in one case, 1103, four days post-mortem, the brain substance had become soft and inelastic and had apparently imbibed most of the pial fluid. The basal cerebral vessels showed sclerosis in five cases; in one of these the sclerosis was confined to the basilar and vertebral arteries. One case showed involvement of the distal extremities of the internal carotid arteries, and in another case only one spot of arteriosclerosis was found in the entire brain, in a secondary branch of the circle of Willis. One case (849) showed a remarkable small varix in the right calcarine region noted and carefully studied by Prof. Barrett.

The brain weights are considered below in a separate table with comparative weights of other viscera. The convolutions, despite the assigned diagnosis of diffuse cerebral atrophy, do not show in all cases a perfectly even wasting. Thus case 872 showed more

marked wasting in the upper left central convolutions. The anterior parts of the brain of case 1058 as far back as the precentral gyri were firmer than the superior parts, and the superior surface was firmer than the inferior surface. This case also showed a slight granular ependymitis of the accessory sinuses of the fourth ventricle. In two (recent) cases it has been noted that the orbital gyri failed to show as much atrophy as the other convolutions. These two cases also showed more marked atrophy in the central and parietal regions than elsewhere. Adjacent to the central and parietal regions of atrophy, case 1133 showed atrophy involving also the frontal gyri, whereas case 1134 showed atrophy more marked in the superior temporal gyri.

The consistence of the brain was firm or increased except in two cases in which the substance was soft, moist, and with diminished elasticity. In one of these no cultures had been taken, but the patient died of lobar pneumonia; in the other (also a case of lobar pneumonia) both blood and cerebrospinal fluid showed streptococcus pyogenes.

EVIDENCE FOR AND AGAINST ARTERIOSCLEROSIS AS A CAUSE OF SENILE DEMENTIA.

Nötzli* distinguished the psychoses of the senium into two groups: those without either focal symptoms or focal brain lesions and those with focal brain lesions. The focal brain lesion group was subdivided by Nötzli into two divisions *a*: cases in which there were never any focal symptoms or in which focal symptoms supervened late in the dementia; and *b*: cases beginning acutely with strokes or other focal symptoms.

Nötzli dealt with 70 cases. Of these 70 there were 40 cases without either focal symptoms or focal brain lesion.

The following table has been constructed from Nötzli's data to show the distribution of symptom groups in his 70 cases:

	Without focal symptoms.	With latent focal lesions.	With focal symptoms.
Senile Mania	6	..	1
Senile Melancholia	10	3	..
Senile Delusional Insanity.....	4	2	2
Senile Hypochondria	1	..	..
Dementia Alcoholica senilis	6	1	2
Typical Senile Dementia.....	13	9	10

Nötzli believes that in the group of senile mental disorders that we can distinguish two clinically different kinds. On the one hand a quiet senile dementia found most frequently in almshouses and nursing asylums, in which the dementia progresses slowly and quietly without periods of excitement. On the other hand diseases which resemble the diseases of adult life having frequently an acute onset and rapid course. Nötzli believes with Forel that the cases of the second kind (found in insane hospitals rather than in almshouses) are very probably of hereditary origin. He believes that cases of quiet senile dementia much more rarely show an inherited disposition to mental disease. In addition to the hereditary mental factor in the acute excited cases, Nötzli hypothecates a hereditary disposition to arteriosclerosis and particularly to cerebral arteriosclerosis.

The fundamental cause of senile dementia is in Nötzli's view cerebral arteriosclerosis and the often considerable atrophy of the brain conditioned thereupon, both in those cases in which atrophy is simple and in cases complicated by focal hemorrhages of softening. The brain weight was found to be diminished on the average 200 grams and in such wise that the female brain preserved its normal proportion to the male brain in weight. The cerebral cortex was determined by separate weighings to diminish more than the other parts of the brain.

The evidence which Nötzli actually brings as to the relation of cerebral arteriosclerosis and cerebral atrophy is logical rather than histological. He regards all his cases as showing a combination of both processes and answers the question which is primary, as follows: It is well understood that the brain is also affected in the general physiological involution of the organism in old age. The brain is atrophied physiologically, to what degree cannot be expressed in figures, but simple cerebral atrophy can scarcely reach so great a degree, that is to say, yield on the average so low figures for brain weights as Nötzli's series of 70 cases showed. The cause of this atrophy of high grade must rather be sought in cerebral arteriosclerosis which places the brain under such unfavorable nutritive conditions as to cause it to atrophy in greater degree and more quickly.

The cerebral disease process is regarded as a purely degenerative one and as comparable to arteriosclerotic contracted kidney.

It is unwise to conclude that the changes of Nötzli's first group are all based upon nutritive brain disorder due to cerebral arteriosclerosis. Three protocols are presented. Case 34 was a physician 67 years old. It showed thickening and opacity of pia mater, superficial convolitional atrophy, atheroma of basal arteries, extreme dilatation of posterior cornua of ventricles, moist and anemic brain substance and extreme degeneration of the fine cerebral arteries with a brain weight of 1468 grams, the largest in the whole series of 70 brains.

Case 39 was a butcher of 64 years. It showed thickening, opacity, and edema of pia mater, moderate atheroma of basal arteries, extreme atrophy of brain, dilatation of ventricles, the left hemisphere was smaller than the right and the left corona radiata harder than the right. The left corpus striatum, thalamus, and corpus candicans much smaller than right. Cortex $1\frac{1}{2}$ mm. deep on the right; on the left still narrower in many places. The total brain weight was 1044 grams.

Case 40 was a maid-servant 59 years old. Pia mater thickened and opaque. Basal arteries atheromatous. Brain atrophied; convolutions narrowed; convolitional surfaces irregular with groups of small degenerated arteries in some places. Focal atrophy of the left temporal lobe; left insula and left Broca's area thinner than right. Hydrocephalus. No cysts of softening. Brain weight 1106 grams.

Microscopic examination was not carried out in these cases.

Meyer¹ published in 1896 the data of 24 autopsies in senile dements from the Illinois Eastern Hospital for the Insane at Kankakee. Meyer reports that "in most instances there was undoubtedly atrophy of the convolutions present." The weights ranged from 942 to 1562 grams (weight taken "dissected," that is, minus membranes and ventricular fluid) and from 1025 to 1667 grams undissected. The majority of Meyer's cases have no assigned weights, and he shows in an instructive brief table of eight brain weights determinations how important a factor the dissection of the brain is in altering data. In the analysis of Meyer's data we must, therefore, rely rather on qualitative findings, and the grouping of cases is, so far as can be determined by analyzing his data, as follows:

MEYER'S KANKAKEE CASES.

Senile dementis	24
Sclerosis of cerebral end-arteries.....	11
Brains atrophic, not arteriosclerotic.....	6
Brains not atrophic, not arteriosclerotic.....	7

No endeavor is made by Meyer to consider clinical data with the autopsy notes. In 23 cases with trunk dissection, Meyer noted "as an almost uniform feature on affection of the heart and the circulatory apparatus at large." For example "atheroma of the large blood vessels with hypertrophy of the left ventricle occurred fifteen times." "In only one case the organs of circulation were relatively normal."

The proportion of cerebral arteriosclerosis is treated as follows: "The blood vessels of the brain did not show any macroscopic lesion in the two youngest cases and none are noted in "(another case, a woman of 72)." A fourth case showed slight changes. "In all of these cases there were, however, found beginning atheroma of the aorta, slightly cystic kidneys, and in the two latter ones slight atrophy of the brain; 18 cases had marked atheroma (of the aorta); six of them very advanced calcifications. There has not been a single case observed in which alterations of the blood vessels could be excluded. Most of the other findings can be indeed traced to trophic changes."

Although Nötzli's conclusions with respect to the relation between cerebral arteriosclerosis and senile dementia are quoted, Meyer himself draws no conclusions in his report.

Appeldorn^{*} from Schuchardt's Clinic in Rostock published in an inaugural dissertation in 1908 an analysis of 126 cases of insanity arising after the sixtieth year (817 per cent of the admissions to the Mecklenburg Asylum at Gehlsheim, 1897-1906) and among these considers especially 69 cases of what he terms typical senile dementia (not including senile melancholia, senile confusion, and other special forms).

Thirty-two of Appeldorn's cases came to autopsy, and, although the protocols are presented in too condensed a form, it appears that only 13 received or should legitimately receive the diagnosis of

cerebral atrophy. Cysts of softening or very extensive arteriosclerosis are noted in but five cases, although the diagnosis of arteriosclerosis is set down without further specification in numerous other cases.

Appeldorn's data are far too sketchily treated to admit generalizations, and he contents himself with repeating the commonplaces of recent years on this topic. Whereas *Altersschwachsinn* depends on "simple physiological involution of the brain," *Altersblödsinn* or senile dementia depends on a pathological degeneration, eventuating in brain atrophy of much greater degree than that of physiological involution. Appeldorn cites Nötzli's hypothesis of the arteriosclerotic origin of senile dementia, but quotes with favor the hypothesis of Alzheimer concerning ganglion-cell changes of non-vascular origin. Finally Appeldorn agrees with Kraepelin that vascular disease is not extremely prominent in senile dementia and that extremely prominent vascular disease may not lead to insanity at all.

RATIOS OF ACTUAL TO CALCULATED WEIGHTS OF BRAIN, AND
HEART, LIVER, AND KIDNEYS.

Autopsy number.	Sex.	Age.	Actual brain weight.	Ratio.	Actual weights heart, liver, kidneys.	Ratio.
			Calculated.*		Calculated.*	
872	F	81	1180	1.05	1280	0.85
			1121		1499	
1058	F	63†	1070	0.88	2840	1.5
			1212		1818	
1133	F	74	990	0.88	1735	1.11
			1121		1562	
1134	F	67	980	0.82	1465	0.94
			1194		1740	
1262	F	70	950	0.79	925	0.55
			1190		1670	

* From data in Vierordt's *Daten und Tabellen*, Dritte Auflage, 1906, S. 40 usw.

† Very probably too low. In case the patient was 70, the figures run

1070	0.89	2840	1.70
1190		1670	

The above table represents a fragment of some work undertaken by Mr. N. S. Burns * and myself to learn whether brain weights vary in the same or opposite directions with certain visceral weights. The general results of this work will be presented elsewhere. It will be seen that in this series the loss in brain weight varied from 21 per cent to 12 per cent, except in one instance where a gain over the calculated weight was registered. This gain was, however, only five per cent, which is almost within the limit of technical error as calculated by Mr. Burns and myself (data not yet published) ; so that at best this brain could be placed in the group of brains "normal" as to weight. As a matter of fact the surprising weight, in the presence of undoubted macroscopic and microscopic signs of atrophy, is perhaps best explained as a result of terminal infection (aureus sinus disease).

Leaving out the excess weight case, the brain weights are observed to vary with the visceral weights in two cases, against those in two others. The two cases in which the trivisceral ratio (as we have termed the ratio involving heart, liver, and kidney weights) is in excess are marked cardiorenal cases.

I present these results not as settling the problem, but as demonstrating that the hypothesis held by many that brain atrophy is due to arteriosclerosis is a quite unsafe hypothesis.

As mentioned above (under the clinical analysis of the arteriosclerosis found), Nötzli's results have had much to do with this hypothesis, but I do not find, upon analysis of his monograph, that much in the way of proof is advanced.

Alzheimer, 1898,⁹ leaves in doubt whether senile brain degeneration is due to arteriosclerosis alone, and raises the question whether primary atrophic processes in the nerve cells may not be the true factor.

ARTERIOSCLEROSIS.

No case of our series escaped arteriosclerosis completely. Nor would it be wise to exclude this factor from the chain of events culminating in brain atrophy. It seems to me doubtful, however,

* Working in the fourth-year elective in neuropathology, Harvard Medical School, 1908-9, holding an appointment as special laboratory interne, Danvers State Hospital.

whether the coexistence of these two conditions is a very strong argument for their causal relation. One prefers the non-committal position that both visceral atrophy and arteriosclerosis are conditioned upon some more remote cause, as yet unknown. It is certainly impossible to compare the degree of atrophy with the degree of arteriosclerosis, whether general or local. The distribution is as follows:

Arteriosclerosis generalized and marked.....	5
Aortic sclerosis	7
With calcification or ulceration	5
Coronary	7
Extensive or with calcification.....	2
Splenic, especially noted	2
Renal, especially noted	4
Basal cerebral	5
Internal carotid (not basal cerebral)	1
(Small aneurysm, right Sylvian artery.....)	1)

The apparent sparing of the aorta in one case is probably due to an error in the protocol. On the other hand the immunity of the coronary artery in one case was expressly noted.

A tendency to cardiac or cardiorenal disease was observable in many of the cases. The occurrence of chronic renal changes is so constant that it would appear to me far more reasonable to look in the renal direction for factors in the production of brain atrophy than to look in the direction of arteriosclerosis.

HEART DISEASE.

Cardiac hypertrophy	2
Valvular disease.....	7
Aortic valvular	4
Mitral valvular	6
Chronic passive congestion of organs.....	4

KIDNEY DISEASE.

Chronic	8
Diffuse	7
Arteriosclerotic	1
Acute	1
(Cystitis	1)

OTHER CHRONIC CONDITIONS.

Findings suggestive of tuberculosis, as a rule obsolescent, occurred in six cases, and can scarcely be excluded with safety from any case. This fact may easily be a coincidence, but the proportion is far higher than in most similar large *routine* series of examinations.

Other chronic conditions occurred in considerable variety and need not be summarized here.

THE CAUSE OF DEATH.

Lung disease was prominent in lethal factors (six cases, perhaps seven). The immediate cause of death cannot be exactly stated for all cases, but the positive indications of all properly examined cases are that bacterial infections are found in various loci (not always septicemic) with practical constancy. Thus it will be exceedingly difficult, for histological purposes, to procure an atrophic brain which can be trusted not to show acute effects. And, in a larger hygienic way, it is obvious that the better the nursing conditions, the longer these patients may be preserved.

DISCUSSION AND MICROSCOPIC ANALYSIS.

I believe that the time is not ripe for a proper analysis of the cytology of senile dementia. In point of fact, no one can yet state precisely in what old age consists, so that our normal control pictures are lacking.

One of the most striking features of old age is the progressive loss of watery constituents which several of the tissues exhibit. Nowhere is this more striking than in the blood, which according to some writers undergoes a genuine atrophy in old age. If this should turn out to be true, it might be difficult to explain the mechanism of senility on a simple cellular basis like that of Metchnikoff.

In fact it may remain impossible to explain senility either on the basis of Metchnikoff's ingenious hypothesis concerning phagocytes or on the earlier conception of a progressive failure in cell-multiplication.

When the body in senility undergoes a loss of weight affecting virtually all organs in the same proportion, it will naturally be difficult to assign the cause of such loss to any given cell-mechanism.

It is far more likely that some general tendency, e. g., a tendency to partial dehydration, underlies the process.

I believe that some light will be thrown upon this subject by statistical studies in organ weights. Mr. N. S. Burns, who has been working with me in this direction, has prepared a number of comparative tables which show that some cases exhibit differential loss in brain weight, as compared with weights of other organs, whereas in other cases all the weights fall off together.

The whole problem is, therefore, definably complex, and I feel that the communication of cases showing various degrees of neuronophagia without complete life-histories and without knowledge of special bacterial, toxic, or chemical agencies at work upon an organ like the brain will scarcely tend to clear the issue.

Granting that physiological brain atrophy occurs, how can we distinguish pathological brain atrophy therefrom? First, the loss, in weight is more marked in the latter. Secondly, the onset of the process may be premature. Thirdly, the progress of the atrophy, as distinguished by clinical observation, may be much more rapid. Fourthly, a group of cases will show differential loss in brain weight, whereas the other organs will maintain weight better.

Waiving minutiae aside for the moment, it appears that so-called senile dementia will break into several entities, into, first, a group of cases in which there is not at all a true organic dementia, but in which old subjects with normal brains become insane just as younger subjects do (*senile acute psychoses*); secondly, a group in which there is local cortical arterial disease (*arteriosclerotic dementia*); and thirdly, a group in which the brain has undergone pathological atrophy (*senile dementia proper, or atrophic dementia*). Personally, I feel that future work may show that the latter atrophic group will split up into two subordinate groups, (a) a group in which through some metabolic flaw or for some other reason, the brain suffers *pari passu* with the other major viscera, and (b) a group with differential atrophy of the brain, possibly due to a special toxin or inherited tendency. Naturally, I should not wish to exclude combinations of these conditions in given cases, but I hold that detailed analysis should be made, so far as possible, of cases showing these conditions pure.

For reasons stated in the discussion I have not attempted elaborate microscopic analysis of these cases, but will present a number

of examples of photographs illustrating the atrophy in different areas in several cases. (For descriptions, see plates.)

The matter of *neuronophagia* " has been of special interest, and my analysis of these and analogous cases has proceeded far enough to show that there is abundant microscopic evidence of the occurrence of pigmented or fat-laden neuroglia cells ("satellite cells") about the nerve cells of many layers in the senile cortex. Metchnikoff's interpretation of these findings may be upheld as against Marinesco's, as least so far as Marinesco holds the view that nerve cells undergo a kind of pressure-atrophy due to the accumulation of satellite cells. The latter interpretation is certainly not supported by preparations which I have seen.

If any hypothesis as to satellite cell action upon nerve cells need be risked, it is rather that the satellite cells exert some kind of chemical action upon the nerve cells, analogous to that exerted by osteoclasts in dissolving bone. Metchnikoff himself places this process of osteoclasts in a class logically separate from the process of phagocytosis in other organs. In fact, the process of osteoclasts, like Metchnikoff's so-called "phagocytic" action of sarcoplasm upon myoplasm in atrophy of muscle fibers, is regarded by some as not a good case of phagocytosis (in the earlier and stricter sense of a process of ingestion and digestion of particles by cells).

On the basis of observations alone, certainly such tissues as those of this series of brains go far to lend weight to Metchnikoff's assertions. But, whether or not certain trophic changes in the nerve cells antedate the appearance of satellite cells, one is scarcely able to decide. I am inclined to the conception that such changes do antedate the appearance of the satellite cells. If this be the case, Bevan Lewis' interpretation of these cells as scavenger-cells would be preferable.²¹

I have noted with interest that in three of my cases the satellite cells preferred a location alongside the apical processes of the pyramidal cells rather than the more frequent position at the bases of the cells. The frequency of this picture leads to the conception that in these cases the apical processes are the first to undergo atrophy, and possibly at a time when the axone is maintained. Two of these three cases were the oldest in my series (872 age 81, duration of mental disease seven years; 849, age 86, duration of mental disease four years). The third case, however, was but 67

years old with an assigned duration of mental disease of but one year (1134). The other cases of my series showed no preferred location for these cells, except the ordinary basal position with accumulation along the sides next the base. I have, for the present, no explanation for this finding.

The microscopic examination shows that minor vascular changes are observable even in this material, chosen especially to exclude vascular changes. Nor is it impossible that research may demonstrate a connection between these changes and the nerve cell and fiber atrophy. I am not convinced, however, that any strict proof has ever been brought of a causal relation between the changes mentioned. Notably they do not run *pari passu*. Wide stretches of tissue exhibit atrophic changes without attendant vascular changes of any consequence.

My contention is not that general nutritive conditions, in part arteriosclerotic in origin, may not have a hand in brain atrophy. Such conditions may lead to brain atrophy, as perhaps to arcus senilis, loss of teeth, or the senile skin. My argument is rather that no evidence has as yet been brought that *local* vascular changes produce brain atrophy. I feel, too, that in the long run we must also look back of the vascular system for an explanation of senile atrophic changes in general, and that we deal here perhaps with conditions similar to those unknown conditions which underlie thymus atrophy or menopause changes.

SUMMARY AND CONCLUSIONS.

1. Forty-two cases unanimously diagnosed "senile dementia" at the Danvers Hospital clinics have been reviewed clinically and anatomically, with a surprisingly low general percentage of accuracy (66 per cent) where *either* cerebral atrophy *or* cortical arteriosclerosis or both were regarded as confirmatory, and with still lower percentages: (48 per cent) where cortical arteriosclerosis was considered essential and (38 per cent) where cerebral atrophy was considered essential for a correct diagnosis.

2. The 14 cases which showed neither cerebral atrophy nor cortical arteriosclerosis (with obvious damage to the cortical tissues) are cases which probably should not have been termed senile dementia, and perhaps more properly belong in a group of acute

psychoses or other mental diseases occurring in old age but not dependent on recognizable senile changes.

3. Of the residuum, it is clear that cases in which cerebral atrophy and cortical arteriosclerosis are combined are not suitable for exact study, and attention has been concentrated upon eight cases of relatively pure brain atrophy, regarded as representing more nearly genuine senile dementia than the arteriosclerotic cases, which should be classed under the head of organic dementia.

4. True senile or senile atrophic dementia includes 1) cases in which the loss in brain weight proceeds *pari passu* with a general loss of weight in the other viscera and 2) cases in which the loss in weight of the nerve tissues is differential.

5. The mental diseases of old age, therefore, include

- (a) mental diseases occurring in, but not characteristic of, old age;
- (b) organic dementias due to cortical arteriosclerosis;
- (c) senile atrophic dementias, attended with
  - (1) general visceral atrophy,
  - (2) differential atrophy of the nerve tissues.

6. Obvious suggestions for research in the two groups of senile atrophic dementias as above stated are that the phenomena of general visceral atrophy may depend upon general decadent agencies (dehydration?) and that the more differential atrophy indicates special metabolic flaws or toxic agencies.

7. Since such a grouping has not been hitherto rigorously borne in mind, it is not possible to state the clinical features of these cases in detail.

8. Taking the group senile atrophic dementia as a whole, we find all the eight cases female, without special indications of inheritance, with very various antecedent factors (social factors not prominent), all markedly defective in vision (though for a considerable variety of reasons), often defective in hearing, all subject to various degrees of arteriosclerosis (in some instances not clinically made out), all showing the characteristic external signs of senility, and all showing either chronic diffuse nephritis (interstitial type predominant) or renal arteriosclerosis.

9. Neurologically, the eight cases showed characteristically *tremors*, absence of certain *superficial reflexes*, variations in some

deep reflexes (tendency to loss of leg reflexes), *defective organic reflexes*, alterations of *gait*, and occasional slight *speech* disorder.

10. Psychiatrically, communication with the patients is difficult and impressibility or general perceptual capacity is deficient. The amnesia for recent events is characteristic and constant. The patients are perhaps *unoriented* rather than disoriented. Amnesia for remote events is also frequently present. Delusions are not prominent. Visual or auditory hallucinations (or illusions) characterized some cases. Motor excitement and nightly restlessness and noise are characteristic, though not quite constant, and are not in all cases certainly due to hallucinations. Garrulity was surprisingly uncommon in this group.

11. Anatomically the pia mater was in general remarkably free from chronic changes, and, as the condition of the vessels was the basis of selection of the cases, the vessels naturally showed nothing grossly beyond involvement of the larger or pipe arteries (basal cerebral arteriosclerosis). The cerebral wasting was not in all cases quite uniform. One case even showed a slight granular ependymitis. The consistence of the brain tissue was in general increased.

12. A high percentage of obsolete tuberculosis characterized the autopsies.

13. Aortic sclerosis is probably constant in these cases. Sclerosis of other vessels is frequent but variable. The constancy of renal changes is interesting.

14. The cause of death is pulmonary in many cases, and is perhaps in some way bacterial in all.

15. No intensive microscopic examination has been undertaken, as the object has been rather to define the group of senile atrophic dementias. The satellite cell findings are consistent with Metchnikoff's hypothesis concerning phagocytic processes in old age. It is believed, however, that cell and fiber changes are very probably primary and "neuronophagia" secondary, or at any rate that these processes run *pari passu*.

16. A few cases showed satellite cells preferring the apical cell processes rather than the basal regions of the pyramidal cells.

17. It is alleged that no convincing evidence has been brought of a causal relation between *local* vascular changes and diffuse senile nerve cell atrophy.

REFERENCES.

1. Southard. A Study of Errors in the Diagnosis of General Paresis. J. N. M. D., 37, 1, January, 1910.
2. Vierordt. Daten und Tabellen. 3 Aufl., 1906.
3. Weygandt. Psychiatrie, 1902.
4. Southard and Mitchell. Clinical and Anatomical Analysis of Twenty-three Cases of Insanity Arising in the Sixth and Seventh Decades, with especial Relation to the Incidence of Arteriosclerosis and Senile Atrophy and the Distribution of Cortical Pigments. A. J. I., LXV, 2, October, 1908.
5. Sixty-first Report of the English Commissioners in Lunacy, 1907.
6. Nötzli. Ueber Dementia Senilis, 1895.
7. Meyer, Adolf. Report of the Illinois Eastern Hospital for the Insane, Kankakee, 1896.
8. Appeldorn. Beitrag zur Kasuistik der Geistesstörungen im Greisenalter. Inaugural-Dissertation, Rostock, 1908.
9. Alzheimer. Referat: Neuere Arbeiten über die Dementia Senilis und die auf atheromatöser Gefässerkrankung basierenden Gehirnkrankheiten. Monatsschr. f. Psychiat. u. Neurol., 3, 1898.
10. Sand. La Neuronophagie, 1906.
11. Bevan Lewis, Text-book of Mental Diseases, 1889 and 1899.

DESCRIPTION OF PLATES.

The photographs are in each instance from material fixed in alcohol and stained in unimbedded sections according to the original Nissl methylene-blue method.

The magnification is approximately 50. The sections were approximately 20 μ thick.

FIG. 1.—Left superior frontal gyrus (about midway) in Case I, female, age 81. The dementia developed gradually after a fracture of thigh, age 74. The photograph demonstrates generalized atrophy possibly more marked in the supratentorial layers and most marked in the layer of medium-sized pyramidal cells. The absence of vascular alterations is striking.

FIG. 2.—Left paracentral lobule in Case II, female, age 86. The dementia in this case developed gradually after a fall, age 82. The photograph demonstrates generalized atrophy. Some irregularity in the process is indicated by differences in the reaction of the neuroglia in the subpial layer; the neuroglia reaction is shown to be of more recent and cellular type on the left side of the photograph.

FIG. 3.—Right superior temporal gyrus of Case V, female, age 71. The dementia in this case developed gradually, age 69. The photograph demonstrates generalized atrophy. Considerable neuroglia reaction is evident in the subpial layer. Some irregularity in the process is demonstrated

prominently in the external layer of large pyramids, most of which have, however, undergone atrophy or total loss.

FIG. 4.—Left calcarine region of Case V. The photograph demonstrates generalized atrophy with considerable neuroglia reaction throughout. A solitary cell of Meynert is demonstrable below. Numerous neuroglia cells are seen in many places between the nerve cells. These are perhaps most marked in the outer pyramidal layers.

FIG. 5.—The left hippocampal gyrus of Case VII, female, age 67. The dementia in this case developed gradually about a year before death. Nerve cell losses and some neuroglia replacement are obvious in most layers.

FIG. 6.—Lamina from the right cerebellar hemisphere of Case VI, female, age 74. The dementia in this case developed gradually a few months before death. The photograph demonstrates a narrowing of the molecular layer upon the laminar surface which is striking as compared with the maintenance of depth in the molecular layer of the sunken portions of the lamina. Corresponding with the marginal diminution of the molecular layer there is a conspicuous absence of Purkinje cells as well as a development of neuroglia cells in the Purkinje cell belt. The neuroglia cells of the molecular layer are in general probably somewhat increased in number. Nor is there a proper quota of Purkinje cells in the lamina as a whole. Despite this atrophic process the vessels of the cerebellum show remarkably little alteration.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.