MORPHOLOGICAL ALTERATIONS IN THE GASSERIAN GANGLION CELLS AND THEIR ASSOCIATION WITH SENESCENCE IN MAN *

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The experimental and morphological studies of Dogiel,[1, 2, 3] Nageotte,[4] Ranson,[5, 6] Cajal [7] and De Castro [8] have contributed much to our present knowledge of sensory ganglia, and for a complete review of the literature the reader is referred to these investigations.

The literature on the effect of age and the problem of distinguishing normal from senile and pathological alterations of cell cytology has remained incomplete. An earlier report by the author [9] demonstrated these alterations in sensory ganglia, and Kuntz [10] has recently described similar structural changes in aged autonomic ganglia. Although no mention of such a similarity was made, this corroborative evidence should be pointed out inasmuch as it indicates a widespread degenerative process involving both somatic sensory and visceral efferent ganglia of the body. The age factor is more directly correlated with a process of ganglion cell degeneration since there is ample clinical evidence in man which demonstrates a gradual decrease in sensitivity after the third decade (Pearson [11]). Corbin and Gardner [12] have shown that such a loss of sensitivity is due to a decrease in the number of myelinated dorsal root fibers after the third decade.

The present investigation was made in an attempt to determine whether the destructive process was of pathological etiology or merely a normal cytomorphological alteration in a neuron which accompanies human senescence. In addition, the incidence and variations of ganglion cell structure were studied to determine whether such atypical cells might serve as criteria for age determination and whether they represent neuronal expressions of degeneration, regeneration or senility.

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Material and Methods

Gasserian ganglia from individuals of different ages were used in this investigation. Only fresh ganglia in which the ante mortem clinical symptoms and subsequent postmortem findings were mild and localized were used for this study. No specimen is included that manifested generalized septicemia, toxemia, carcinomatosis or similar pathological conditions. Ganglia from both sexes were used. The males ranged from 27 months to 66 years of age, the females from 26 to 81 years.

Fixation was in ammoniated absolute alcohol, 10 per cent alcoholic chloral hydrate, or in 10 per cent neutral formalin. Following fixation the tissues were carried through the Ranson pyridine-silver and Cajal silver impregnation methods, respectively. Sections of silver preparations were cut in a craniocaudal plane at 12 μ. The formalin fixed specimens were cut at 8, 10 and 12 μ and alternate sections were stained with the Bodian protargol (1936) and cresyl violet technics.

Cell counts were made of five alternate (every fifth) sections through the center of each ganglion from patients of different ages. The various atypical cell forms and cells in the process of degeneration were tabulated. Possible error by repetitional counting was minimized, so far as possible, by placing a rectangular metal disc in the ocular to prevent overlapping fields of vision. Only cells demonstrating a distinct nucleolus were counted. The studies were made with a Leitz microscope equipped with an X15 ocular and a No. 6 objective. An oil immersion lens was used for minute details and for purposes of questionable identification.

Observations

A. Normal Ganglion Cells

The typical cells of the sensory ganglion of the fifth cranial nerve are of the unipolar type. The perikaryon possesses a smooth rounded contour and is invested in a delicate connective tissue capsule. Normal unipolar ganglion cells, as shown with low and high magnifications (Figs. 1 and 2), are readily recognized in most silver preparations. The single process arising from the cell body is occasionally observed dividing into its peripheral and

central branches. One is impressed by the frequency of subcapsular coiling of the so-called axon or stem prior to its terminal division.

Melanin pigment is present in many of the normal cells from patients of all ages. It occurs as angular granules dispersed throughout the cytoplasm, or clumped into deeply staining peripheral and perinuclear masses.

B. Atypical Ganglion Cells

While atypical cells occur most frequently in pathological sensory ganglia, they are also found in smaller numbers in the apparently normal gasserian ganglia from patients of all ages. The appearance of such cells varies extensively and no limitation can be placed on the number or complexity of the processes of a cell. In spite of this wide variation in appearance the atypical cells fall into general cell types manifesting specific characteristic features. After careful study of hundreds of diverse silver preparations, the following appears to be the logical classification of such types of cells:

1. Frayed Cells (of Cajal): This type is the most frequent atypical element observed in gasserian ganglia (see Table I). It occurs in abundance in toxic conditions and in advanced age, but is also observed in normal young ganglia. It shows a frayed and festooned outline due to the supernumerary processes arising from the soma and axon. Each process of the cell, as shown in Figure 3, terminates primarily below or within the capsule as a thickened small knob. In other instances the processes divide near the capsule into shorter branches which may or may not possess varicosities and terminal expansions. Only rarely do such processes extend beyond the limits of the capsule and in even rarer instances they may acquire a distinct capsule of thin connective tissue fibrils. Frequently numerous processes are observed arising around the entire circumference of the cell, and such cell formations give one the impression of a cog-wheel, as pointed out by Cajal.[7]

De Castro [8] has described two new cell entities which he believes to be entirely separate from the frayed cells of Cajal. Figure 4 shows an erethized cell which possesses the spiny, hooked and palm-leaf expansions proceeding from both soma and axon.

Figure 5 demonstrates the ragged (corroded) surface of a corroded cell. Formation of separate categories for these later two cell types (erethized and corroded cells of De Castro) does not seem advisable, inasmuch as they possess a pitted or excavated soma and smaller, accessory subcapsular processes in serial section. The thicker spines and processes appear to represent merely a more marked growth and hypertrophy of neurofibrils.

2. Fenestrated Cells: This type includes cells that are perforated in the region of the axon by two, three or more window-like openings. The union of such protoplasmic cordons, which bound the fenestrations, may form the definitive axon, while in other instances they may have no discernible connections with the axon. The protoplasmic loops vary from a single delicate fibril to others with short thick cordons consisting of masses of interwoven neurofibrils.

This cell type is not of common occurrence in the gasserian ganglion and in this investigation was observed only in ganglia from patients over 50 years of age. The origin of the slings and loops lies in different optical planes, making satisfactory microphotographs impossible. Therefore, no figures of this type have been presented. Their small incidence did not seem to warrant space in the table.

3. Cells Possessing End-Bulbs: The cell outgrowths that have a terminal expansion are very often seen in ganglia from patients of all ages. The terminal club shaped enlargement is composed of masses of interwoven neurofibrils and is attached to the cell of origin by either a slender or a short thick pedicle. Figure 6 shows the less frequently observed form which possesses a short, stout protoplasmic bridge between cyton and axon. Occasionally the more slender filaments leave the cell body or axon and follow a spiral course for considerable distance within the capsule before reentering the subcapsular space and presenting its terminal bulb. Similar cells belonging to this category have been described in the gasserian ganglion of the chicken, where the intrinsic structure and neurofibrils are more conspicuous (Truex [13]).

In view of the many distinct alterations in neurofibrillar size and distribution in cells with such extraneous processes it is possible that neurofibrils play an important rôle in the formation of

these outgrowths. For this reason the cells possessing end-bulbs have likewise been included with the frayed and erethized cells in Table I.

4. Cells with Nerve Arborizations: This peculiar association of nerve fibers with certain ganglion cells was considered to be quite abundant in cranial sensory ganglia by earlier investigators. In our material they have been observed in ganglia of patients ranging from 27 months to 81 years of age, but never in very large numbers. The nerve fibers entering into the intricate arborization are seldom of homocellular origin. Usually they are heterocellular nerve fibers derived from an adjacent bundle of axons which forms a plexus about the ganglion cell. Based on the nature of the plexus and its relation to the cell, the following classification has been adopted from Cajal:

(*a*) *Pericellular Plexus:* By far the most frequently observed type of arborization was that in which many fibers of uniform diameter completely encircle a ganglion cell. The fibers interlace profusely and traverse both the capsule and the subcapsular space to form a woven basket or network about the cell, as in Figure 7. The unipolar process of the cell is distinct and plays no part in the plexus formation.

(*b*) *Periglomerular Plexus:* Figure 8 clearly demonstrates the structure of this type in which the axon becomes invested with a special plexus of finer fibers which follow a spiral course. The initial coiled portion of a unipolar process has frequently been termed the glomerulus; hence the extracapsular plexus observed in Figure 8 is designated as "periglomerular." It should be pointed out that no cells of a "sympathecoid" nature were observed in relation to any of the plexus formations observed.

C. Fatty Degeneration

The degenerative process which involves the neurons of this ganglion most constantly is similar to that described by De Castro.[8] The earliest stage of this process, not demonstrable with the usual silver technics, consists of a general clumping of the cytoplasmic Nissl bodies into the large angular masses shown in Figure 9. The destruction of the neurofibrillar reticulum is initiated as a foamy area in the periphery of the cytoplasm, usually in the region of the axon hillock. Figure 10 demonstrates this

early stage and the foamy appearance is due to the formation of minute fatty vacuoles in the cytoplasm.

Further progression of the cytoplasmic degeneration with the formation of more vacuoles leads to the second stage, as shown in Figures 11 and 12. Although this stage is frequently accompanied by an increase in cell diameter, the nucleus remains normal in structure and centrally located.

The third stage results from a progressive destruction of the cytoplasm, with a fusion of the smaller vacuoles to form larger compartments, as demonstrated in Figures 13 and 14. Additional features appearing for the first time are the gradual loss in staining capacity of the axon, a marked increase in the cell diameter and the margination of the nucleus. In the later phase of this stage (Fig. 14) the degeneration invades the axon and henceforth it is not demonstrable.

The fourth or terminal stage of the fatty degenerative process is shown in Figures 15, 16 and 17. By coalescence of the individual small vacuoles larger, more discrete compartments have been formed. Subsequent fusion of the compartments leads from a multilocular to a unilocular stage, as in Figure 15. The cytoplasm and nucleus have become pushed toward the periphery and only a thin marginal layer of cytoplasm remains in contact with the indistinct plasma membrane. The remnant of the cell wall is in turn more or less blended with the surrounding capsule (Figs. 16 and 17).

Following formation of the unilocular stage, it is not uncommon to observe that the unsupported cell wall with the thin marginal layer of cytoplasm has collapsed (Fig. 16). In other instances the multilocular stage may persist until the ganglion cell has been completely destroyed. Figure 17 shows such a cell with three slender cytoplasmic girders supporting the skeleton of the cell. This degenerative process continues until the swollen ganglion cell is completely destroyed. Remaining in the region of the cytoplasm one may or may not see evidence of débris. The small pyknotic and marginated nucleus is often the last discernible cell structure.

Recent investigators attribute phagocytosis of the degenerated cell to the satellite cells. However, in view of the connective tissue reaction adjacent to the capsule I am inclined to believe

that the macrophages play a dominant rôle in the phagocytosis of such tissue wreckage. The migration of leukocytes to the area suggests also the possibility that transformed lymphocytes (histiocytes) may assist in the phagocytic process.

Many ganglion cells demonstrating fatty degeneration also bear supernumerary processes, as demonstrated in Figure 18. This consistent association indicates that neurofibrillar hypertrophy may precede or accompany fatty degeneration.

D. Proliferation of Capsular Nuclei

The connective tissue nature of the ganglion cell capsule is easily recognized by the ordinary azocarmine stain. A section of a normal capsule shows from five to eight spindle shaped nuclei which appear spherical in cross section. A wide variational increase in such capsular nuclei is observed in association with ganglion cells undergoing fatty degeneration or those demonstrating supernumerary processes. In many instances the density of the mass of nuclei is further increased by the presence of very fine nerve fibers. The fibers are of homocellular and heterocellular origin and follow complex overlapping courses among the nuclei. These features are demonstrated in Figure 19.

E. Residual Nodules

Following the destruction and phagocytosis of a ganglion cell there appears a mass of cellular and fibrous elements which literally constitutes a grave marker. The chief cellular constituents are the endocapsular nuclei interspaced with leukocytes. In addition one is able to distinguish fibroblast and satellite cells in smaller numbers with appropriate stains. Fibrous elements penetrate the cell mass of the nodule and form a maze of irregular complex skeins. These so-called "neurotizing fibers" arise as outgrowths from axons in the region of the nodule and appear to be attracted by some strong orienting agent. Such a heterogenous mass is shown in the lower field of Figure 20, although the divergent courses of the fine fibers do not allow their complete capture in this microphotograph. Also, one can see the advancing features of fatty degeneration in the cell at the top of this figure.

F. Calcification

The deposition of calcium granules occurs quite frequently in ganglia of patients over 40 years of age. It may be observed occasionally as intracellular masses, or distributed as individual granules throughout the cytoplasm. Most frequently the calcium is deposited in the capsule or intercellular spaces of the ganglion as concentric refractive corpuscles. The lamellated corpuscles or irregular bits of calcium are commonly associated with branches of the axial artery supplying the gasserian ganglion, as in Figure 21.

Additional alterations of older ganglia appear as elastic intimal thickening of the arteries and arterioles, and occasionally as complete fibrous occlusion of an arteriole. The vascular changes thus noted may play an important rôle in the degenerative processes described above.

G. Cell Counts of Ganglia of Different Ages

The results of the tabulation of cells from patients of different ages are shown in Table I. Application of statistical methods proved undesirable due to the variation of sections, inconsistency of cell distribution and the small number of specimens involved.

The percentage of cells in the fatty degenerative process, as well as the frequency of plexuses, frayed and bipolar cells in ganglia of different ages, are shown in this table. Ten individuals were examined with a total of 93,426 cells being counted and classified. Of this number, 72 per cent were considered as normal unipolar cells. They varied from 65 per cent in a female 75 years old to nearly 97 per cent in a 27 months old male child.

Cells possessing pericellular plexuses and nerve arborizations were demonstrated in each specimen but never in large numbers. They were found to be present in 1.5 per cent of the cells of a female 55 years old, whereas they were present in only 0.047 per cent of the cells of another female 56 years old. Such structures do not appear to be correlated with age or sex and comprised only 0.257 per cent of the total number of cells tabulated.

The frayed, corroded and erethized cells, and those possessing end-bulbs, were likewise variable in their distribution and constituted only 2.986 per cent of the total number of cells. They varied

TABLE I

Specimen, sex and age	Total number of cells counted	Normal unipolar cells		Pericellular plexuses		Abnormal cells (degenerated or atypical)				Bipolar cells	
						Frayed, corroded and erethized cells, cells with end-bulbs		Vacuogranular degeneration			
		No.	%	*No.*	%	*No.*	%	*No.*	%	*No.*	%
SH 28 ♂ 27 mos.	8593	8310	96.706	9	0.104	33	0.384	234	2.723	7	0.081
SH 51 ♀ 26 yrs.	7700	6243	81.077	5	0.064	242	3.142	1206	15.662	4	0.051
SH 66 ♂ 36 yrs.	11708	7794	66.569	41	0.350	313	2.673	3558	30.389	2	0.017
SH 67 ♀ 48 yrs.	16564	10910	65.865	12	0.072	369	2.227	5273	31.834		
SH 5 ♀ 55 yrs.	7370	5173	70.189	115	1.560	464	6.295	1618	21.953		
SH 3 ♀ 56 yrs.	8415	5889	69.982	4	0.047	380	4.515	2142	25.454		
SH 61 ♂ 57 yrs.	6073	4367	71.908	3	0.049	197	3.243	1506	24.798		
SH 39 ♂ 66 yrs.	11827	8190	69.248	27	0.228	499	4.219	3111	26.304		
SH 7 ♀ 75 yrs.	6518	4265	65.434	6	0.092	54	0.828	2193	33.645		
SH 64 ♀ 81 yrs.	8658	6424	74.197	19	0.219	239	2.760	1976	22.822		
Total	93426	67565	72.319	241	0.257	2790	2.986	22817	24.422	13	0.013

from 6 per cent in a female 55 years old to 0.38 per cent in the 27 months old male child. In connection with these cells bearing abortive outgrowths and supernumerary processes it is necessary to reiterate there were no multipolar cells that could be considered as sympathetic neurons.

Fatty degeneration was the most frequently observed alteration in cell structure and was found in 24 per cent of the total number of cells counted. As one can see in the table, the distribution of this degenerative process is less variable than the above atypical cells. It was demonstrated in 2 per cent of the ganglion cells of a 27 months old child, reached its greatest frequency (33.6 per cent) in a female 75 years old, and ranged from 21.9 to 31.8 per cent in all remaining specimens between 36 and 81 years of age.

Although the number of bipolar cells observed represents only a small fraction of the total number of cells counted (0.013 per cent), it is interesting to note that they were found in diminishing numbers with age increase. They were observed in 0.081 per cent of the cells of the 27 months old male child, 0.051 per cent of the cells of a female 26 years old, and in 0.017 per cent of the cells of a male 36 years old.

Comment

In view of the data presented in Table I, it does not follow that nerve arborizations and the atypical cells can be considered as adequate criteria for age determination. The structure and distribution of the plexuses in ganglia from early childhood to old age suggest that they represent an interesting but atypical association between ganglion cells and nerve fibers. In view of our present knowledge such an arrangement cannot be rigidly classified as either degenerative or regenerative attempts of a neuron. The structural alterations of the ganglion cell which accompany the formation of frayed, erethized and corroded cells, as well as cells possessing end-bulbs, seem to place such atypical entities in the realm of degenerated neurons. Further evidence that such cells are degenerated forms may be found in their frequent association with fatty degeneration, proliferation of capsular nuclei and calcification. In addition it should be pointed out that such degenerated neurons might readily be confused with true multipolar neurons, in view of the supernumerary processes.

Indeed, Cajal [7] and other authors classify ganglion cells with multiple end-bulbs and abortive outgrowths as multipolar neurons. Strictly speaking, such cells are multipolar only in view of their possession of more than two processes without considering the nature of these processes. However, these investigators did not apply the term multipolar with the intention of denoting a motor or efferent physiological nature.

The observations recorded in Table I suggest that the clinical loss of somatic sensitivity after the third decade (Pearson [11]), as well as the actual decrease in the number of myelinated dorsal root fibers (Corbin and Gardner [12]), are the direct result of fatty degeneration in the sensory ganglion cells of the first order of neurons. The destruction of a large number of cells with their central and peripheral rami would be expected to cause a noticeable diminution in the capacity of a nerve to convey sensory impulses, as well as a loss of many myelinated fibers. Although the analogy between the percentage of cells manifesting fatty degeneration and the results of Corbin and Gardner [12] is enticing, no definite conclusions can be made from the present small number of specimens and the lack of similar data on corresponding spinal ganglion cells. However, a subsequent investigation on the spinal ganglia, now being undertaken, indicates that there is an ultimate loss of cells also in spinal ganglia. The fatty degenerative process in human spinal ganglia duplicates that described above in the gasserian ganglion. It must be pointed out, however, that ganglion cells in the early stages of fatty degeneration (Figs. 9 and 10) may retain the ability to return to complete restitution and normality. This belief is suggested by the regenerative findings of Ranson [5] in the large spinal ganglion cells following neurotomy. Ganglion cells in the terminal stages of degeneration (Figs. 12 to 17) are probably beyond ever regaining a normal healthy state.

The author is well aware that neuron vacuolation may result from delayed fixation. Ewing [14] has expressed the belief that vacuolation of ganglion cells in most instances represents post-mortem changes and is devoid of pathological significance. However, vacuolation is demonstrable in fresh, formalin fixed human specimens as well as in ganglia of normal animals killed and perfused with the same fixation agent. Such observations do not appear compatible with the belief that vacuolation is primarily a

postmortem alteration of a neuron. Similarly, fatty degeneration, as observed in senile sensory ganglia, cannot be attributed solely to the ante mortem septicemia as found by De Castro [8] in vacuogranular degeneration.

Table I shows considerable variation in the number of degenerated cells after the third decade. Due to the few cases involved, the reason why fatty degeneration should occur in 30 per cent of the cells at 36, 48 and 75 years of age, and drop to consistently lower percentages (21–26 per cent) in the remaining specimens from individuals over 50 years of age, calls for no extended discussion. It may represent only individual variability which extends over a large range.

That the large number of cells demonstrating fatty degeneration may be one criterion of age, has recently received support from the tissue culture work of Weiss and Wang.[15] Transplants of thoracic spinal ganglia of 8– to 11–day chick embryos in a mixture of blood plasma and embryonic extract demonstrate somewhat correlated stages with the age of the culture transplants. The 9th day marks the end of the normal and healthy appearance of the neurons. The interesting degenerative phenomena begin in the cell with the appearance of clear vacuoles. Many of the small vacuoles become confluent and produce blisters that cause parts of the cell wall to protrude. Soon the protoplasm assumes a granular appearance and the cell walls collapse. Fixed preparations of such cells reveal the nucleus lying on the surface of the cell outside the fibrillar structure.

The above rapid life cycle of tissue culture ganglion cells suggests a recapitulation of the processes being carried on regularly in apparently normal human ganglia. The similarity of senile degenerative changes of both is found in the granular clumping, vacuole formation, margination of the nucleus, and collapsed cell walls.

While McKinniss [16] found an increase in the number of spinal ganglion cells in human fetuses between 7.5 and 13 weeks of age, no data have been presented to indicate just when such proliferation ceases. The occurrence in the semilunar ganglion of bipolar neurons in diminishing numbers until the third decade (Table I) seems to indicate that certain stages of differentiation from the bipolar to the unipolar phase may continue in man long after birth.

Summary and Conclusions

Carefully selected human gasserian ganglia obtained at autopsy from 10 individuals who were free from severe ante mortem clinical symptoms, and localized postmortem changes, were studied by means of various technics. The frequency and age distribution of normal, atypical and degenerated unipolar neurons were noted with the following conclusions:

1. Nerve arborizations and plexus formations occur in semilunar ganglia of all ages and apparently represent neither degenerative nor regenerative attempts of a neuron.

2. Atypical cells (frayed cells of Cajal, erethized and corroded cells of De Castro, and cells possessing end-bulbs) represent degenerated neurons. The dominant factor in altered cell formations appears to be neurofibrillar hypertrophy which may result in many aberrant processes on otherwise unipolar cells.

3. No multipolar cells, in the classical sense, were encountered and hence no evidence for the presence of sympathetic ganglion cells was found.

4. The atypical cells show an increase in incidence in pathological ganglia, but occur in apparently normal human ganglia of all ages as well. Such cells do not serve as a specific criterion for age.

5. Fatty degeneration of sensory ganglion cells appears to be responsible for the loss of many neurons after middle age, which may account for decreased sensitivity after the third decade in man.

6. Fatty degeneration appears to represent a senile process occurring in the normal cytomorphosis of a neuron, as well as in severe pathological conditions.

7. The observations of elastic intimal thickening in axial arteries of aged ganglia suggest that vascular disturbances may be a factor in the above degenerative processes.

8. Pigmentation in the gasserian ganglion of man is so variable that it shows very little correlation with age. Calcification is most common after 40 years of age.

9. There is evidence of postnatal differentiation of bipolar cells into unipolar cells to the third decade.

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DESCRIPTION OF PLATES

PLATE 63

FIG. 1. Normal unipolar neurons under low magnification. From a male child, 27 months old. × 450.

FIG. 2. Normal unipolar neurons with high magnification. From a female, 75 years old. × 950.

FIG. 3. A frayed cell of Cajal. Note the short subcapsular accessory processes. From a female, 53 years old. × 650.

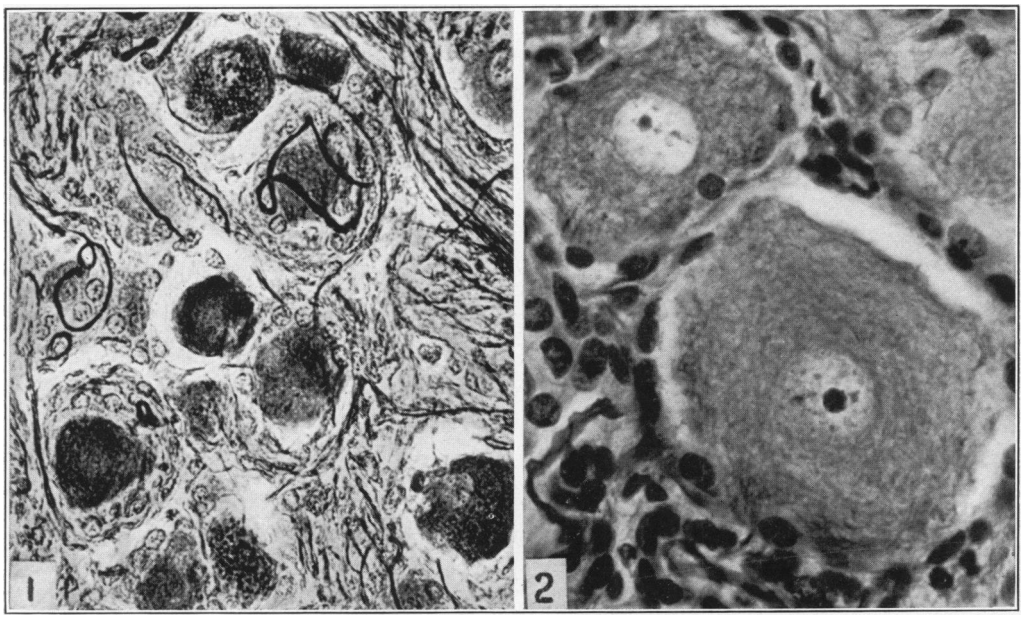
FIG. 4. An erethized or irritated cell of De Castro. Note the thick, palm-leaf expansions from both the soma and the axon. From a female, 65 years old. × 650.

FIG. 5. A corroded cell of De Castro. Note the ragged (corroded) surface of the soma and the short supernumerary processes. From a male, 70 years old. × 950.

FIG. 6. A cell possessing end-bulb formation. From a male, 47 years old. × 650.

FIG. 7. Pericellular plexus about a ganglion cell. From a male, 27 months old. × 950.

FIG. 8. Periglomerular plexus on an extracapsular portion of an axon. From a male, 49 years old. × 650.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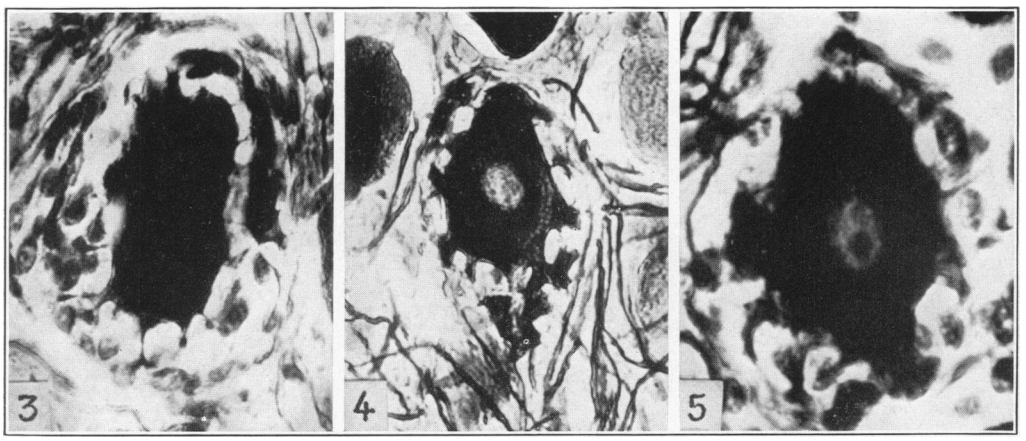
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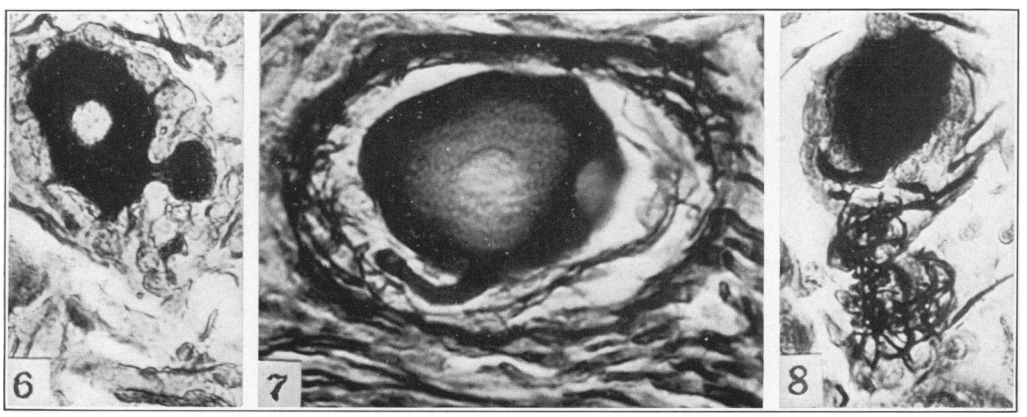
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PLATE 64

FIG. 9. The earliest appearance of fatty degeneration in neurons. Note the granular clumping of Nissl bodies. From a male. 60 years old. × 760.

FIG. 10. The first appearance of minute fat vacuoles in the region of an axon hillock. From a female. 75 years old. × 1000.

FIGS. 11, 12 and 13. Gradual increase in fatty vacuoles at the expense of the cytoplasm. From a female. 75 years old. × 1000.

FIG. 14. The advanced multilocular stage of fatty degeneration with margination of nucleus and loss of staining capacity of the axon. Note the increase in the cell diameter. From a female. 75 years old. × 1000.

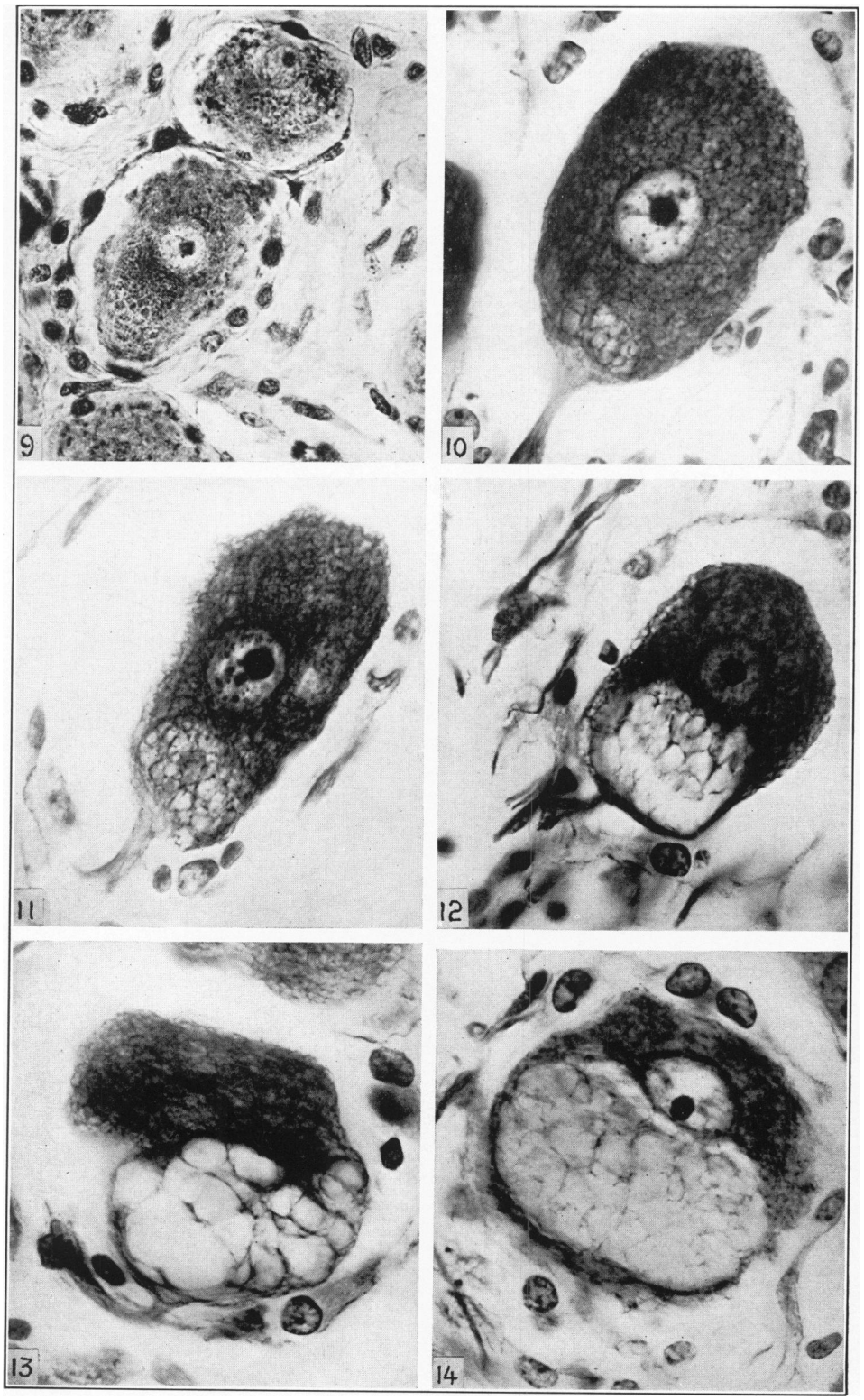
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PLATE 65

FIG. 15. The unilocular stage of fatty degeneration. This results from coalescence of smaller vacuoles. From a female, 75 years old. × 1000.

FIG. 16. The terminal stage of fatty degeneration. The cell wall of the neuron has collapsed, although partially blended with the adjacent capsule. From a female, 75 years old. × 1000.

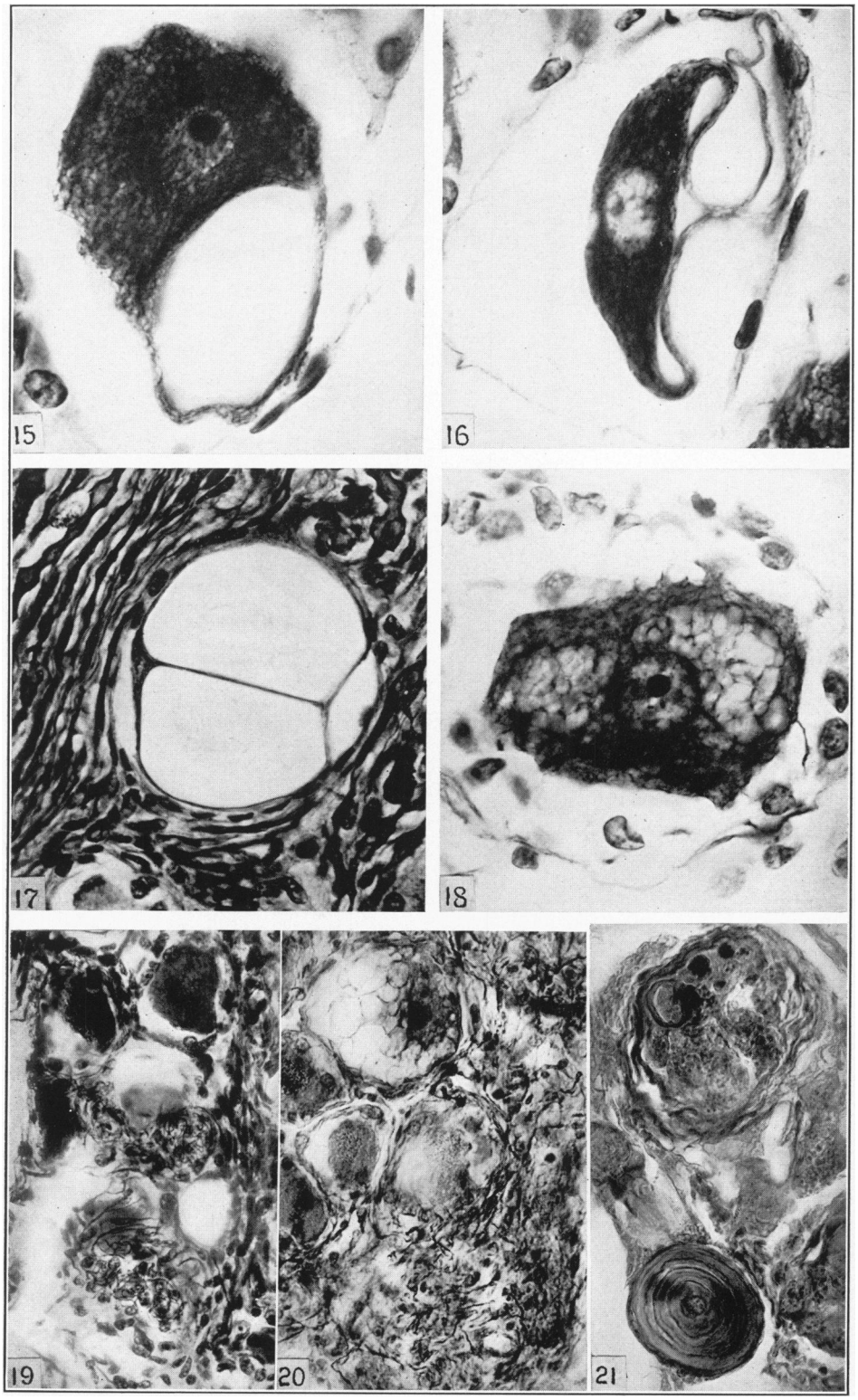
FIG. 17. The terminal stage of fatty degeneration. Multilocular conditions are retained with slender cytoplasmic girders supporting the skeleton of the cell. From a female, 75 years old. × 760.

FIG. 18. A neuron demonstrating both fatty degeneration and supernumerary processes. From a female, 75 years old. × 1000.

FIG. 19. Proliferation of the capsular nuclei. From a female, 55 years old. × 360.

FIG. 20. A residual nodule at the lower center. A neuron in the process of fatty degeneration at the top. From a female, 65 years old. × 520.

FIG. 21. A lamellated calcium corpuscle at the lower center. Note the elastic intimal thickening of the axial arterioles above. From a female, 67 years old. × 360.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