A progress report on the prevalence of Alzheimer's lesions in a Bombay hospital population

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Preliminary neuropathological findings are presented for a nonrandom subset of 100 older patients (ages 59–90 years) chosen from among a sample of 2000 autopsies performed at the Sir J. J. Group of Hospitals from October 1989 to April 1991. Gross examination included brain weights and estimates of cortical atrophy. Microscopic examination of sections from 13 regions of the brain included hematoxylin and eosin, Gross–Bielschowsky silver stains and Congo red stains (examined by polarized light). For the aggregate sample, increasing degrees of cortical cerebral atrophy were observed with advancing age. A regression analysis of brain weight versus age revealed age-related declines in brain weights for males, but not for a smaller sample ($n=28$) of female subjects. A few neurofibrillary tangles were found in 88% of cases and in all sites, surprisingly including frequent involvement of Purkinje cells of the cerebellum, an observation that will require confirmation with other methodologies. The most prevalent type of neuropathology involved cerebrovascular accidents, especially old infarcts. Only five cases exhibited numerous neurofibrillary tangles. Neuritic plaques were seen in six cases and amyloid was detected in seven cases. Of two cases with a clinical diagnosis of dementia, one 65-year-old male had multiple cerebral infarcts and a 60-year-old male had, in addition to multiple lacunar infarcts, moderate numbers of tangles and a few neuritic plaques (without amyloid cores) sufficient to warrant a diagnosis of 'probable Alzheimer's disease' by consortium to establish a registry of Alzheimer's disease (CERAD) criteria. The overall impression from this initial survey is that Alzheimer's disease does not appear to be particularly prevalent in our population. Given the biased nature of the sampling, however, and the limited numbers of subjects of advanced ages, no definitive conclusions as to prevalence can be made. This study, however, does indeed point out the potential for obtaining a substantial amount of relevant clinical and neuropathological data in a developing country.

THE world population has been undergoing an accelerating growth, with an expected 6.25 billion people by the year 2000 according to a report of the United Nations Fund for Population Activities (*The State of the World Population 1990*). India alone is expected to have a population of one billion by the year 2000, about 68 million of whom will be over the age of 60. Given the evidence for steady increases in life expectancy in India and in other developing countries, medical, social and economic problems related to an ageing population are likely to become increasingly urgent. Judging from epidemiological reports from the developed nations, Alzheimer's disease (AD) is likely to be among the most important of these problems. It is not clear, however, to what extent this particular type of age-related pathology affects all ethnic-population groups around the world. We therefore have initiated a survey of neuropathological specimens obtained from autopsies of a population largely derived from the Bombay region of India. In this progress report, we review our initial findings. While the initial study design was such that no conclusions can yet be made as to prevalence rates in our community for the various neuropathological lesions of AD, the general impression is that lesions sufficient to cause AD appear to be rare in this particular geriatric sample of a general hospital population. Only two subjects of the group of 100 examined had clinical evidence of dementia and of these only one had lesions sufficient to warrant a diagnosis of probable AD by the criteria of CERAD (consortium to establish a registry of Alzheimer's disease)[1].

Materials and methods

Nature of the hospital population

All autopsies were obtained from patients admitted to the Sir J. J. Hospital in Bombay. It is one of the largest in Asia, with 1339 beds. Approximately 75% of the patients come from the city of Bombay. Of the remaining 25%, most come from neighbouring regions in the state of Maharashtra, while a very few patients come from other states of India and from other Asian countries. The monthly outpatient department attendance is 55,000, with 3000 hospital admissions. As treatment is completely free of cost, some 87% of patients are members of the lower socioeconomic groups, including members of all castes and creeds. Some 85% of admissions are adults (more than 12 years old); 70% of these are males. The hospital death rate is 6.5% and the

autopsy rate is 66%. Criteria for autopsy include death within 24 hours of admission, medical-legal questions and academic interest. Of the average number of 800 autopsies per year, 75% are males and 16% are aged 55 or over.

Origin of neuropathological specimens

The 100 brains selected for this study were collected during the 2.5-year period between October 1989 and April 1991. All were from subjects autopsied between 6 and 12 hours, after death; specimens from subjects having longer intervals between death and autopsy were excluded. The selected specimens were derived from patients admitted to all major services of the hospital, including medicine (66), surgery (16), neurology (4) and neurosurgery (13). Only 1 case came from the psychiatric service (P-643, Table 1). There is no separate dementia clinic or ward in the hospital, so that demented subjects could be ascertained via a number of different services. For cultural reasons, however, it is probably the case that most older subjects with cognitive declines are not referred to our hospital.

Clinical data

Age, sex, and clinical diagnoses are listed in Table 1. Eighteen patients were in the age range from 55 to 59; 56 were 60 to 69; 18 were 70 to 79, 4 were 80 to 89 and 4 were 90 to 99 (all of whom were age 90). Seventy-two per cent were males. Only 2 subjects had a clinical diagnosis of dementia. Case P-643 was a 60-year-old male with a differential diagnosis of chronic schizophrenia and AD. Case Q-717 was a 65-year-old male with a clinical diagnosis of both AD and pulmonary tuberculosis. There was a great variety of other diagnoses – infectious, inflammatory, neoplastic, vascular, traumatic and degenerative (Table 1).

Neuropathological methods

After weighing the brain and noting the degree of cortical atrophy, each brain was suspended in 10% neutral buffered formalin immediately after slitting the corpus callosum and was fixed for about 4–6 weeks. Subjective, semi-quantitative estimates were used for the determination of the degree of brain atrophy (Table 1), principally the degree of widening and deepening of the cerebral sulci and the corresponding narrowing of the cerebral gyri. The degree of estimated atrophy was frequently but not uniformly correlated with brain weight. The well-fixed brains were cut according to the procedure of Roberts and Hanaway[2]. To maintain uniformity, all sections were taken from the left hemisphere unless there were gross lesions of that hemisphere. Microscopic sampling was as follows: 1) frontal gyrus rectus; 2) superior and middle frontal gyrus; 3) superior and middle temporal gyrus; 4) precentral gyrus; 5) calcarine cortex; 6) hippocampus and parahippocampal gyrus; 7) amygdala; 8) anterior basal ganglia; 9) substantia innominata with nucleus basalis of Meynert; 10) midbrain with substantia nigra; 11) pons with locus ceruleus; 12) medulla with inferior olivary nuclei; 13) cerebellum. This numerical code is utilized for the data of Figure 3. Gross lesions were noted during brain cutting. The tissue samples were embedded in paraffin and sectioned at thicknesses of approximately 6–8 micrometers. All sections from each brain were stained with hematoxyline and eosin, the Gross–Bielschowsky silver impregnation method[3], and Congo red. Sections stained with hematoxyline and eosin were examined for evidence of neuronal loss. This was a subjective assessment, the final grading of which was determined by the maximum loss observed in any of the sections. Semi-quantitative grading of the number of neurofibrillary tangles (NFT) was estimated with the Gross–Bielschowsky silver method, which is said to have high sensitivity for the detection of NFT[4]. A case was considered positive for NFT if only a single NFT was found in any region. Semi-quantitation of NFT was based upon the number of lesions found per high-powered microscopic field (total magnification ×480): 1–2 (mild), 3–4 (moderate), and 5 or more (severe). Similar criteria were used for the semi-quantitation of neuritic plaques (NP). For the determination of amyloid deposits in either NP, cortical blood vessels or meningeal blood vessels, Congo red stained sections were examined by polarized light for the characteristic dichroic birefringence[5].

Statistical analysis

A statistical package for a personal computer, STATGRAPHICS System 3.0 (Statistical Graphics Corp., Rockville, MD, USA) was used for regression analyses of brain weights as functions of subject ages for male and female subjects (Figure 1).

Results

Gross findings

Figure 1 gives the results of a statistical regression analysis weights versus age for male (A) and female (B) subjects. For males, there was a statistically significant negative regression of brain weights on age of subject (slope = −4.1 with standard error of 1.6 and p of 0.013); the correlation coefficient was −0.29. The regression was not significant for the female subset of only 28 subjects.

Table 1. Summaries of clinical and gross neuropathological data for series of selected autopsies on subjects 55 90 years of age carried out at the Sir J. J. Hospital from October 1989 to April 1991.

Neuropathology no.	Age and sex	Clinical diagnoses	Brain wt. (g)	Neuropathological diagnoses	Degree of cortical atrophy
Q-248	55 F	Pulmonary tuberculosis	890	Unremarkable	(+ +)
Q-280	55 F	Craniopharyngioma	1000	Craniopharyngioma	(+)
Q-569	55 F	Chronic renal failure	1160	Unremarkable	(+)
Q-227	55 F	Lt. intracerebral bleed	1090	Lt. insular fresh and Rt. lentiform old infarct	(+)
Q-324	55 F	Ca stomach	1100	Unremarkable	(+)
Q-476	55 M	Polyradiculopathy	1110	Unremarkable	(+)
Q-210	55 M	Hypertrophic cardiomyopathy	1150	Unremarkable	(+ + +)
Q-325	55 M	Alcoholic brain damage	1160	Unremarkable	(+ +)
Q-974	55 M	Lt. intracerebral bleed	1160	Lt. basal ganglia haemorrhage	(+)
Q-466	55 M	Acute MI with ventricular fibrillation	1320	Unremarkable	(+)
Q-226	55 M	Rt. intracerebral bleed	1350	Rt. frontoparietal IC bleed	(−)
Q-142	55 M	Guillian–Barre syndrome	1470	Unremarkable	(+ +)
Q-180	56 M	Bronchogenic carcinoma	1150	Unremarkable	(+ +)
Q-307	57 F	Hypertensive IC bleed	1060	Rt. parietooccipital IC bleed	(+)
Q-323	57 M	PM diagnosis lobar pneumonia	950	Unremarkable	(+)
Q-421	57 M	Rt. TB bronchopneumonia-	1120	Unremarkable	(+)
Q-420	57 M	Cervical spondylosis PM diagnosis post-op. pneumonia	1250	Unremarkable	(+)
Q-337	58 M	Aspiration pneumonia	1160	Rt. claustral lacunar infarcts	(+)
Q-104	60 F	33% superficial burns	940	Unremarkable	(+ +)
Q-203	60 F	DIC with gastroenteritis	980	Rt. old parietooccipital infarct	(+ +)
Q-328	60 F	Amoebic dysentery	1040	Unremarkable	(+)
Q-286	60 F	Rt. lobar pneumonia	1050	Unremarkable	(+ +)
Q-415	60 F	Ca head of pancreas	1060	Unremarkable	(+)
Q-192	60 F	Post-op. peritonitis	1100	Unremarkable	(+ +)
Q-220	60 F	Pulmonary tuberculosis	1120	Lacunar infarcts	(+ +)
Q-113	60-F	COPD with corpulmonale	1200	Unremarkable	(+)
Q-580	60 F	Acute gastroenteritis	1220	Cerebral malaria	(+)
Q-245	60 M	Lt. MCA bleed	930	Lt. frontoparietal fresh infarcts	(+ + +)
Q-34	60 M	Myocardial infarction	950	Lt. parietal old infarction	(+ + +)
Q-393	60 M	Hepatic encephalopathy	950	Unremarkable	(+)
Q-335	60 M	Acute LVF	970	Unremarkable	(+)
Q-112	60 M	Alcoholic brain damage	1000	Lt. frontoparietal IC bleed	(−)
Q-388	60 M	Lt. pyopneumothorax	1000	Unremarkable	(+ +)
Q-249	60 M	CCF with pulm. embolism	1030	Unremarkable	(+)
Q-576	60 M	Generalized debility + LRTI	1030	Unremarkable	(+ +)
Q-179	60 M	Mitral stenosis + AF + CCF	1050	Unremarkable	(+)
Q-730	60 M	Polyneuropathy	1060	Rt. + Lt. basal ganglia lacunar infarcts	(−)
Q-432	60 M	Ca stomach	1070	Unremarkable	(+ +)
Q-110	60 M	Head injury	1080	Lt. subdural haematoma	(−)
Q-308	60 M	Acute myocardial infarction	1110	Unremarkable	(+ +)
P-643	60 M	? Chronic schizophrenia ? AD PM diagnosis-bronchopneumonia	1130	Multiple lacunar infarcts, Lt. frontal	(+ +)
Q-376	60 M	Rt. subdural haematoma	1150	Rt. subdural + intracerebral bleed	(+)
Q-448	60 M	Oesophageal varices + hematemesis	1155	Unremarkable	(+)
Q-402	60 M	Pulmonary tuberculosis	1170	Unremarkable	(+ +)
Q-199	60 M	PM diagnosis lt. lobar pneumonia	1180	Unremarkable	(+)
Q-369	60 M	Meningitis	1180	Rt. post parietal abscess	(+ +)
Q-374	60 M	Head injury	1250	Lt. temporal IC bleed	(+)
Q-213	60 M	Pulmonary tuberculosis	1260	Lt. parietal old infarct	(+ +)
Q-356	60 M	Rt. frontoparietal SOL	1340	Rt. frontoparietal astrocytoma	(+)
Q-202	60 M	Cirrhosis + hematemesis	1360	Unremarkable	(+ +)
Q-316	60 M	Lt. temperoparietal SOL	1400	Lt. temperoparietal glioma	(−)
Q-387	60 M	Ischaemic heart disease Death during angiography	1400	Unremarkable	(+ +)
Q-107	60 M	? SAH, ? ICH	1420	Pyogenic meningitis	(+)
Q-129	62 F	Pott's spine (D8-D9)	1050	Unremarkable	(+ +)
Q-309	62 M	Parkinsonism ?MID	1040	Multiple old cortical infarcts	(+)
Q-200	64 F	Lt. intracerebral bleed	1180	Lt. basal gangha bleed	(+)
Q-345	64 M	Lt. MCA-hypertensive bleed	980	Lt. internal capsule + frontal infarcts	(+)
Q-106	64 M	Cirrhosis + hematemesis	1110	Small meningioma at lat. ventricle	(+)
Q-414	65 F	Ventricular aneurysm + LVF	820	Unremarkable	(+ +)
Q-178	65 F	Paralytic ileus	950	Old Rt. parietooccipital infarct	(+ + +)
Q-317	65 F	Head injury	1150	Rt. subdural haemorrhage	(+ +)
Q-103	65 M	Status asthmaticus	980	Unremarkable	(+ +)
Q-453	65 M	Ca bronchus	1020	Unremarkable	(+ +)

Contd

Table 1. *contd* ..

Q-236	65 M	Rt. Hemiplegia	1100	Rt. temporal + Lt. frontal old infarcts. Lacunar infarcts, both basal ganglias	(+ +)
Q-167	65 M	Chronic renal failure	1110	Unremarkable	(+ +)
Q-634	65 M	Myocardial infarction	1120	Unremarkable	(+ +)
Q-717	65 M	Alzheimer's dementia with pulmonary TB	1120	Lt. temporal + Rt. parietal old infarcts	(+ +)
Q-419	65 M	Acute myocardial infarction	1160	Unremarkable	(+)
Q-577	65 M	Caoesophagus	1220	Unremarkable	(+ +)
Q-975	65 M	FUO	1300	Lacunar infarcts	(+ +)
Q-105	68 M	Hepatocellular carcinoma	1140	Unremarkable	(+ +)
Q-194	68 M	Pulmonary TB	1150	Unremarkable	(+ +)
Q-403	68 M	Acute myocardial infarction	1180	Unremarkable	(+)
Q-267	69 M	Lumbar and cervical myelopathy PM diagnosis-bronchopneumonia	1100	Unremarkable	(+ +)
Q-689	70 F	Nontoxic multinodular goitre PM diagnosis-intra op. death	980	Lacunar infarcts	(+)
Q-114	70 F	Cerebrovascular accident	1050	Multiple lacunar infarcts	(+ +)
Q-710	70 F	Polycystic kidney + CRF	1050	Unremarkable	(+)
Q-60	70 F	? TBM ? pyogenic meningitis	1140	Pyogenic meningitis	(+)
Q-744	70 M	Lt. focal epilepsy	880	Rt. old occipital infarct + lacunar infarcts	(+)
Q-263	70 M	Lt. hydronephrosis + CRF	910	Binswanger's disease + multiple old infarcts	(+ +)
Q-451	70 M	COPD with cor-pulmonale	950	Unremarkable	(+ +)
Q-185	70 M	Rt. pneumonia	1000	Unremarkable	(+ +)
Q-465	70 M	Ca common bile duct	1200	Unremarkable	(+)
Q-201	74 M	Gangrene of small intestine	1050	Unremarkable	(+ +)
Q-610	75 F	Lt. foot gangrene	1040	Unremarkable	(−)
Q-416	75 M	Pulm. TB + pyemic liver abscess	950	Lt. old int. capsule infarct	(+ +)
Q-273	75 M	Pulm. TB	1100	Unremarkable	(+)
Q-659	75 M	Ulcerative colitis	1130	Rt. lentiform lacunar infarcts	(+ +)
Q-446	76 F	Paralytic ileus	840	Rt. basal ganglia lacunar infarcts	(+ +)
Q-111	77 M	Lt. intracerebral bleed	1020	Lt. parietal IC bleed	(+ + +)
R-72	78 M	Head injury	1150	Lt. frontal haematoma + SAH	(+ +)
Q-108	79 F	Lt. ventricular failure	1440	Rt. fresh thalamic infarct	(+ + +)
Q-168	80 F	Lt. hemiplegia	1130	Rt. tonsilar pyogenic abscess	(+ +)
Q-109	80 M	IHD with LVF	1145	Unremarkable	(+ + +)
Q-608	82 M	Acute amoebic colitis	1240	Unremarkable	(+)
Q-348	89 M	Myocardial infarction	1130	Multiple lacunar infarcts	(+ + +)
Q-734	90 M	Head injury	920	Rt. frontoparietal IC bleed	(+ +)
Q-748	90 M	Ca stomach	1020	Unremarkable	(+)
Q-697	90 M	30% burns	1055	Rt. + Lt. lentiform nuclei lacunar infarcts	(+ + +)
Q-988	90 M	Metabolic encephalopathy	1070	Lt. basal ganglia lacunar infarcts	(+ +)

AD: Alzheimer's disease; AF: auricular fibrillation; CA: carcinoma; CCF: chronic congestive heart failure; CRF: chronic renal failure; DIC: disseminated intravascular coagulation; IC: intracranial; ICH: intracranial haemorrhage; IHD. ischaemic heart diease; LRTI: lower respiratory tract infection; LVF: left ventricular failure; MI: myocardial infarctions; MID. multiple infarct dementia, PM. post-mortem; post-op: post-operative; FUO. fever of unknown origin; SAH: sub-arachnoid haemorrhage; SOL: space-occupying lesion; TB: tuberculosis; TBM: tuberculous meningitis.
(−) No atrophy, (+) mild atrophy, (+ +) moderate atrophy, (+ + +) severe atrophy.

of brains which exhibited moderate or severe cerebral cortical atrophy (Figure 2). Forty-seven of the 100 brains exhibited gross pathology in addition to cerebral cortical atrophy, mainly the results of cerebrovascular accidents, including old and fresh ischaemic infarcts, lacunar infarcts, and hypertensive bleeds (32 cases). Sequelae of head injuries were observed in six cases, including intracerebral, subdural and subarachnoid haemorrhages. There were five cases of CNS infections and four neoplasms. A diagnosis of 'multiinfarct state' was utilized when there was no clinical evidence of dementia.

Microscopic findings

Some degree of neuronal loss was observed in most of the cases (Figure 2). In decreasing order of severity, it was detected in the precentral gyrus, the superior and middle temporal gyrus, the superior and middle frontal gyrus, the frontal gyrus rectus, the cerebellum (Purkinje cells), the inferior olivary nuclei, the hippocampus and parahippocampal gyrus and the nucleus basalis of Meynert (Figure 3).

NFT (Figures 2, 3 and 4 *a*) were found in all regions examined, including the hippocampus, and in all cases above the age of 80 years. One case in that age group had 5 or more NFT per high powered microscopic field (HPF). NFT were seen in 88% of the remaining cases and were found in all areas, but with varying frequencies. Four cases which had 5 NFT per HPF did not have clinically detectable dementia. While sparse NFT (1–2/HPF) were seen at virtually all areas of the

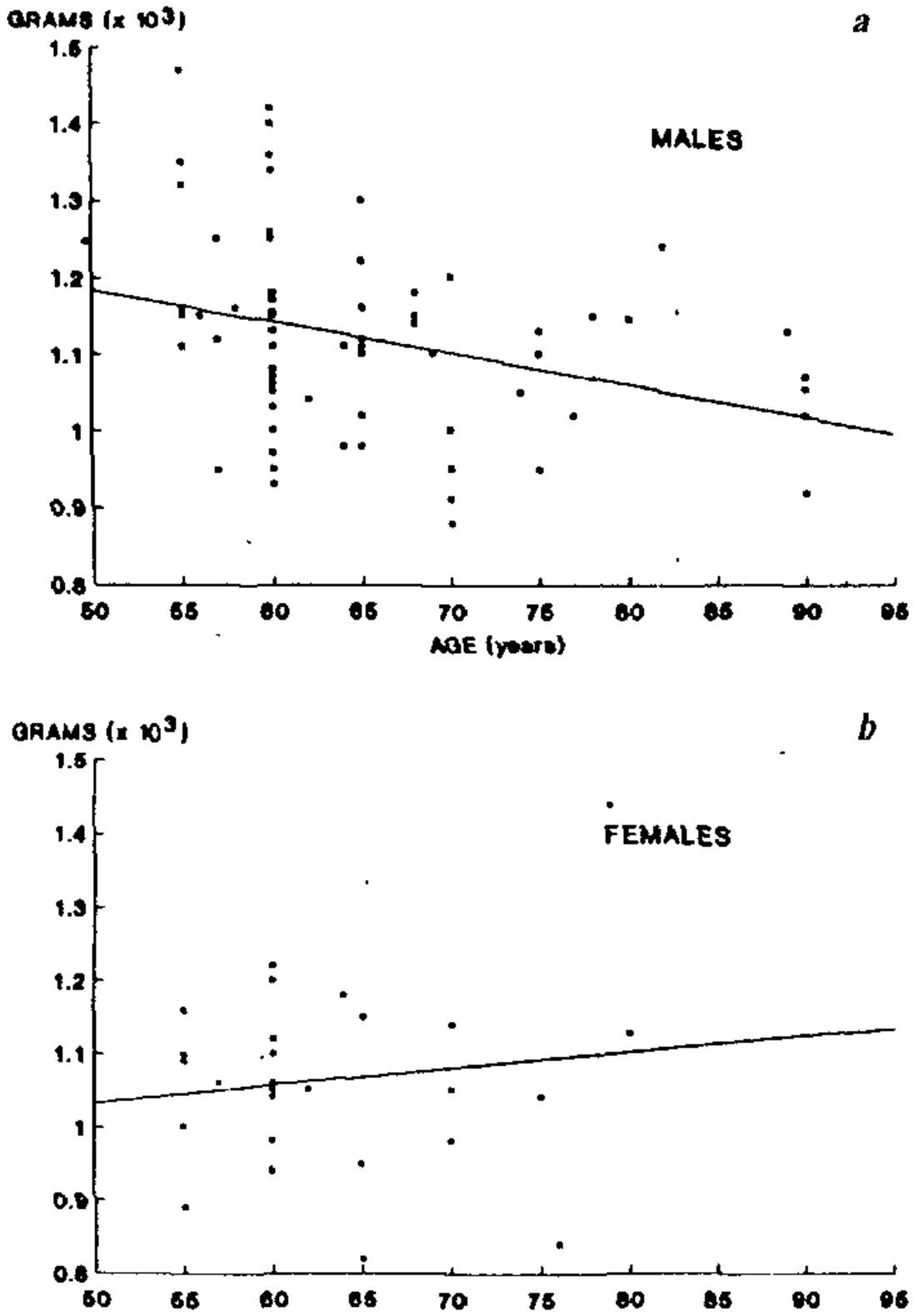

Figure 1. The distribution of post-mortem brain weights as functions of age of subjects. *a*, male subjects ($n=72$); *b*, female subjects ($n=28$). See text for statistical parameters.

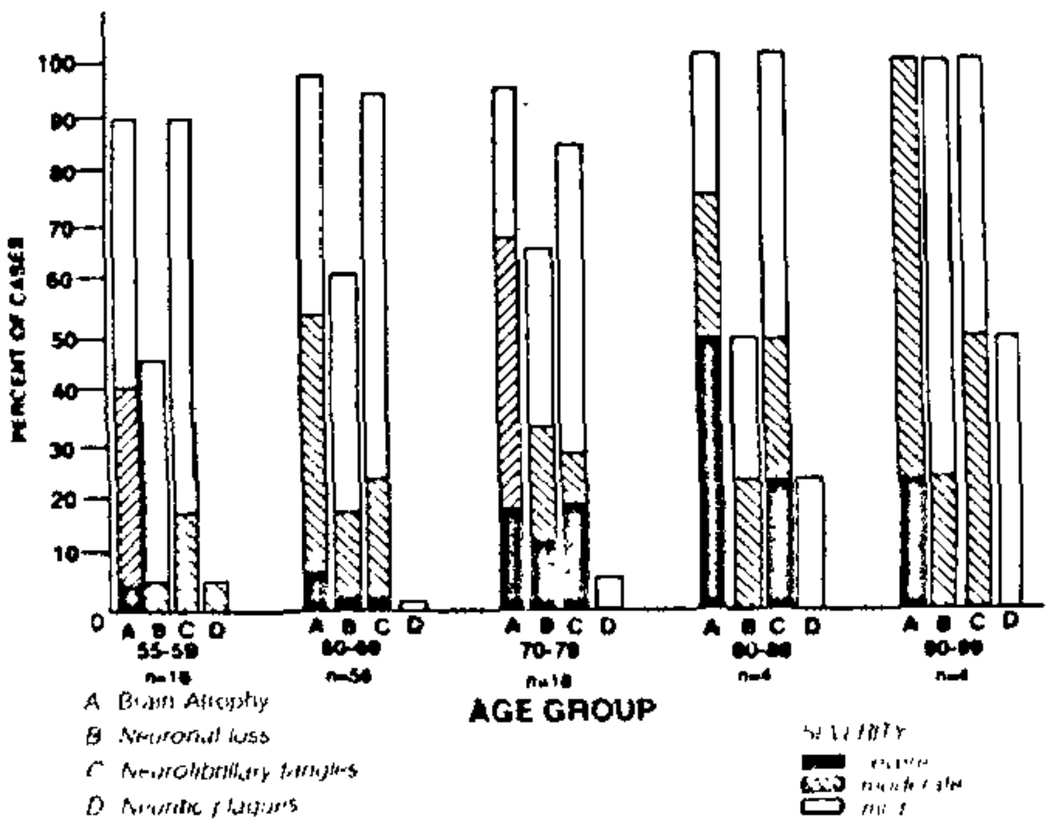

Figure 2. Histograms illustrating the frequencies and severities of various neuropathological changes in post-mortem brains grouped according to age of subjects. The degrees of brain atrophy (*a*) and of neuronal loss (*b*) were determined subjectively (see text). The extent of NFT (*c*) and of NP (*d*) was based upon counts of lesions per high power microscopic fields (magnification × 480) (see text).

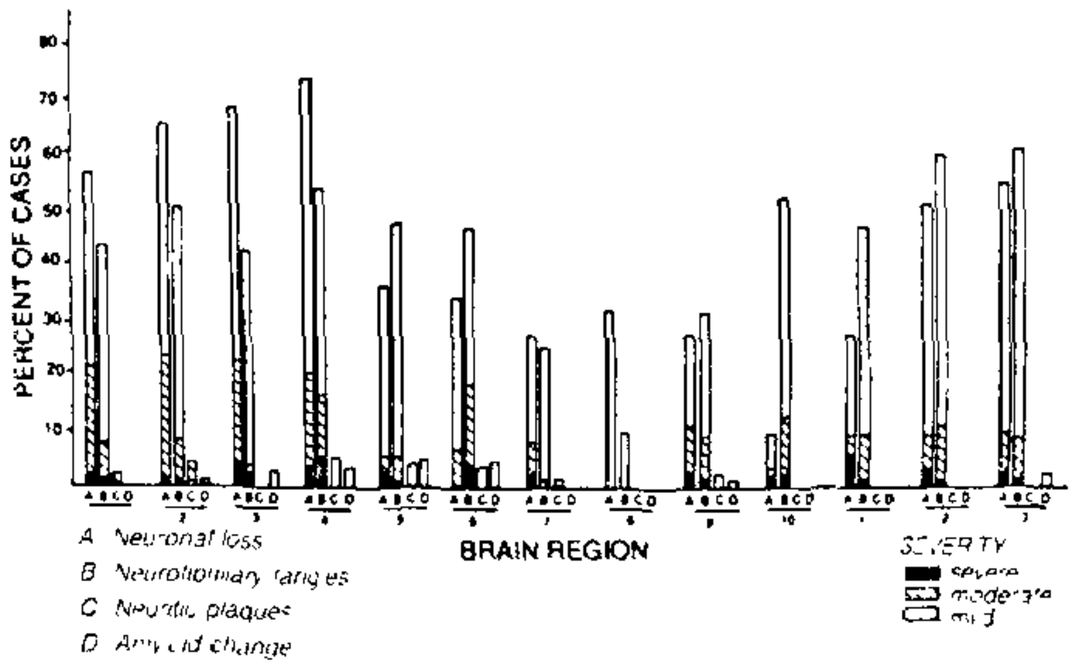

Figure 3. Histograms illustrating the regional distributions of various neuropathological changes in post-mortem brains grouped according to anatomic regions of the brain. **1**, frontal gyrus rectus; **2**, superior and middle frontal gyrus; **3**, superior and middle temporal gyrus; **4**, precentral gyrus; **5**, calcarine cortex. **6**, hippocampus and parahippocampal gyrus; **7**, amygdala; **8**, anterior basal ganglia; **9**, substantia innominata with nucleus basalis of Meynert; **10**, midbrain with substantia nigra, **11**, pons with locus ceruleus and other pontine nuclei; **12**, medulla with inferior olivary and other medullary nuclei, **13**, cerebellum. The degrees of neuronal loss (A) and of amyloid deposition (primarily in blood vessels) (D) were determined subjectively; the levels of NFT (B) and of NP (C) were determined by counting the numbers of lesions per microscopic high powered field (magnification × 480) (see text).

brain, moderate numbers (3–4, HPF) and frequent numbers (5 or more, HPF) were seen in the amygdala, precentral gyrus, superior and middle frontal gyri, calcarine gyrus and in the superior and middle temporal gyri (in descending order of prevalence). Surprisingly, cerebellar Purkinje cells showed sparse numbers in 61% of cases.

NP (Figures 2, 3, 4 *b* were observed in six of the 100 brains examined. The prevalence appears to increase with age (Figure 2). Only a few such lesions could be found, however, being present in only one or two of the many regions sampled. They were observed in precentral, superior and middle frontal cortex, occipital cortex, hippocampus, nucleus basalis of Meynert, frontal gyrus rectus and amygdala. None of the lesions had an obvious amyloid core, although one case exhibited granular deposits of amyloid when Congo red stained sections were viewed under polarized light.

Congophilic angiopathy was seen 6 100 cases. The Congo red stain identified NFT in one case (Figure 5).

Discussion

There are a number of reasons why the present sample of patients cannot be utilized to make conclusions concerning the prevalence of Alzheimer's disease in our region of India. First of all, although there is evidence from Table I that stated ages are likely to be unreliable (note the disproportionate numbers of subjects who are said to be 60 years of age), the age distribution is

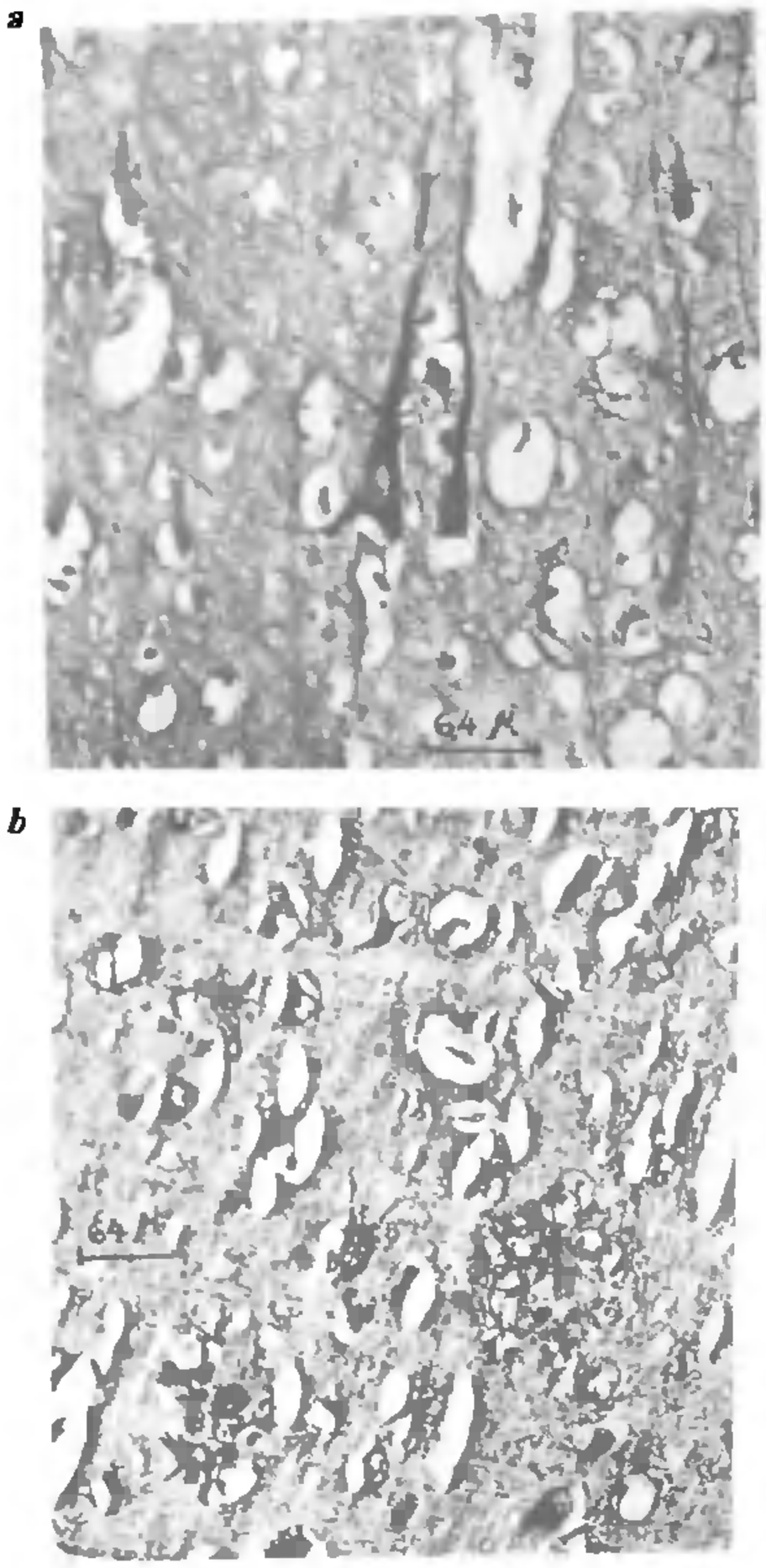

Figure 4. *a*. Two pyramidal neurons with presumptive NFT Gross Bielschowsky stain, magnification × 480, bar representing 64 microns *b*. Section from the amygdala showing two NP and a few NFT Both NP are immature, without central amyloid cores, Gross–Bielschowsky stain, magnification × 480, bar representing 64 microns.

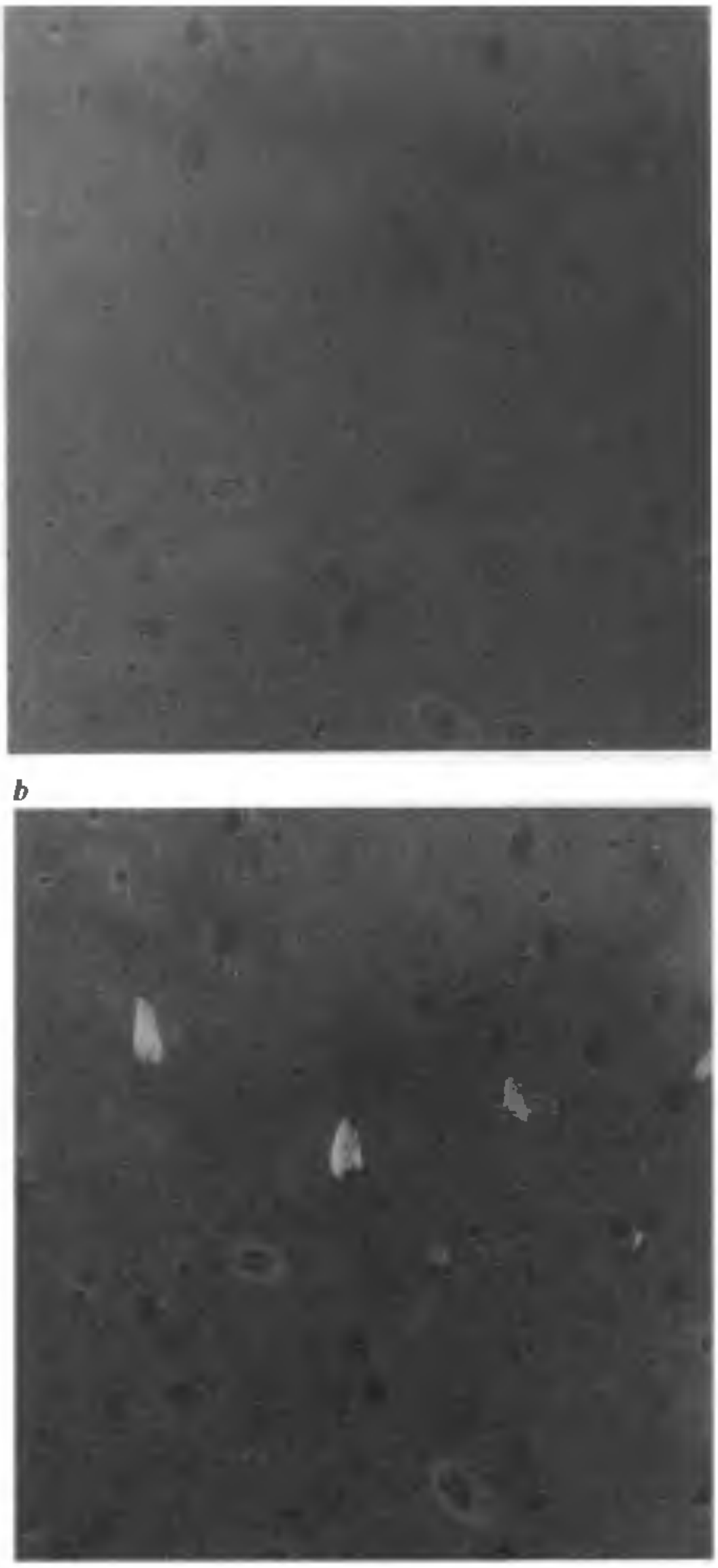

Figure 5. Identical sections of cerebral cortex stained with Congo red and visualized with either conventional optics (*a*) or with polarized light (*b*) The bright birefringence (*b*) is presumed to identify NFT (× 120)

heavily biased towards a relatively young subset of older patients. Only 8 subjects were over the age of 80, when dramatic increases in prevalence have been observed because of the exponential increments that begin at around age 65 (ref. 6). Secondly, older subjects with cognitive deficits do not appear to be referred for hospitalization or, if referred, do not die in hospital. This may be especially true for females, who are greatly underrepresented in the hospital census, apparently for cultural reasons (males are breadwinners and therefore more likely to seek medical care). Thirdly, the great majority of the patients are likely to have been derived from lower socioeconomic groups.

Nevertheless, the study does provide interesting preliminary results in an area of research that is comparatively neglected in the developing countries. In India, for example, the first autopsy documented diagnosis of Alzheimer's disease was published in 1988[7].

Perhaps the most interesting finding of this study is the extremely high prevalence of cerebrovascular

disease; some 39% had grossly detectable lesions of infarctions or haemorrhage, mostly old infarctions. By contrast, only one subject had neuropathological evidence sufficient to warrant a diagnosis of probable Alzheimer's disease, using the relatively arbitrary criteria ('CERAD') developed by an American group of pathologists[1]. Moreover, although NFT are relatively frequent, we find sparse evidence of NP and of amyloid depositions, either within plaque cores or within blood vessels. A surprising finding was that the majority of cases had at least a few cerebellar Purkinje cells with what appeared to be NFT. This has not been reported in publications from Western countries. The finding will have to be confirmed, however, using electron microscopy and immunological stains for tau epitopes[8].

Another interesting observation is the apparently infrequent deposition of amyloid in cores of neuritic plaques and in meningeal or parenchymal blood vessels (beta amyloid, known to be derived from the beta amyloid precursor protein and possibly synthesized locally). Could this be related to our observations that secondary amyloidosis (type AA, derived from a precursor serum lipoprotein) is also rare in our experience in this population? While we have a high prevalence of chronic infectious diseases (e.g. tuberculosis) and of other chronic inflammatory conditions known to be associated with type AA secondary amyloidosis, only 7 to 10 cases of systemic amyloidosis are seen in a typical year in which some 8000 surgical biopsies and 800 autopsies are evaluated. Assuming that there may in fact be some common pathogenetic factors in the genesis of these different types of amyloid (which are derived from different precursor proteins), it is conceivable that some special environmental features of life in India may be responsible. One such possibility is diet. Our patients have very simple diets comprised mainly of whole wheat, chapati and small quantities of available vegetables. It is conceivable that psychosocial factors may also be of significance. Our elderly patients are typically nurtured within a richly supportive social environment, being looked after by an extended family.

Brain weights do not always correlate with estimates of cerebral cortical atrophy (Table 1) for a number of reasons, including the need to normalize brain weight for body length (a parameter not available for this study) and the superimposition of cerebral oedema. Nevertheless, we have found evidence of a progressive cortical cerebral atrophy and associated neuronal loss within our overall sample of specimens, and strong statistical evidence for a loss of brain weight with age for the subset of specimens from males (Figure 1 *a*), which represented the substantial majority of patients ($n=72$). The extent to which such changes might be related to common disease processes, as opposed to intrinsic biological ageing, remains to be determined.

While our general impression from this study is that Alzheimer's disease may not be particularly prevalent in our community, more epidemiologically controlled investigations will obviously have to be initiated to test that hypothesis. In any case, we have shown that it is quite feasible to obtain a large amount of neuropathological data from a geriatric population within a developing country.

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