*Arq Neuro-Psiquiat (São Paulo) 46(2):166-175, 1988*

# CEREBROMENINGEAL HEMORRHAGE

## ANALYSIS OF AUTOPSIES PERFORMED OVER A 10-YEAR PERIOD

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SUMMARY — A study was conducted on the medical records of 353 patients who died of a subarachnoid hemorrhage (SAH) and who were submitted to autopsy over the last 10 years. SAH was associated with arterial hypertension in 180 (51%) cases, with ruptured aneurysms in 102 (28.9%), and with other pathologies in 71 (20.1%). The patients with hemorrhage associated with arterial hypertension were mostly males, and those with hemorrhage due to aneurysms were mostly females. Of the patients with aneurysms, 36 (35.3%) had aneurysms in the anterior communicating artery, 30 (29.4%) in the internal carotid artery, and 23 (22.6%) in the middle cerebral artery. Among the patients with aneurysms who suffered rebleeding and vasospasm, 59.1% and 61.5%, respectively, were classified as grade I and II upon admission, and all evolved toward grade IV after these complications, Vasospasm predominated from the 3rd to the 10th day after hemorrhage, and rebleeding from the 9 to 16th day and both were most frequent among patients with aneurysms of the anterior communicant artery. Sixty eight percent of the patients with aneurysms died during the first 9 days after hemorrhage. Because of our conduct was to operate systematically late, a considerable number of patients lost the oportunity to be treated surgically with possible favorable evolution due to vasospasm or rebleeding.

**Hemorragia cerebromeníngea: análise de autópsias em período de 10 anos.**

RESUMO — Foram analisados 353 pacientes que faleceram por hemorragia subaracnóidea autopsiados nos últimos 10 anos no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto. A hemorragia subaracnóidea estava associada a hipertensão arterial em 180 casos, a ruptura de aneurismas em 102 e a outras patologias em 71 casos. O sexo masculino predominou nos pacientes com hemorragia associada a hipertensão arterial e o feminino nas hemorragias por ruptura de aneurismas. As hemorragias associadas a hipertensão arterial predominaram em faixas etárias mais altas em relação às hemorragias por aneurismas. Dos pacientes com aneurismas, 36 (35,3%) apresentaram aneurismas no complexo cerebral anterior/comunicante anterior, 30 (29,4%) na carótida interna e 23 (22,5%) na cerebral média. Nos casos de aneurismas, o vasoespasmo predominou no período do 3º ao 10º dia e o ressangramento predominou no período do 9º ao 16º e respectivamente 59,1% e 61,5% desses pacientes apresentaram-se nos graus I e II na admissão e evoluiram para o grau IV após estas intercorrências. Ambas as intercorrências foram mais freqüentes entre os pacientes com aneurismas do complexo cerebral anterior/comunicante anterior. Sessenta e oito por cento dos óbitos por aneurismas ocorreram nos 9 primeiros dias após a hemorragia. Os pacientes admitidos em grau I e II e que sofreram vasoespasmo ou ressangramento e que poderiam beneficiar-se do tratamento cirúrgico precoce não tiveram esta oportunidade porque a nossa conduta naquela época era de operar sistematicamente no final da segunda ou no início da terceira semana após a hemorragia subaracnóidea.

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The natural history of subarachnoid hemorrhages started to be better understood after the publication of important papers in the fifties and sixties [1,2,10-12] and especially after the divulgation of the results obtained by the Cooperative Study of Intracranial Aneurysms and Subarachnoid Hemorrhage, which involved an extensive review of the literature [16] and an exhaustive study of large numbers of patients from all points of view, including an epidemiological one [7-9,14,15]. Further data were obtained in a second Cooperative Study of Aneurysms [5,6].

However, little has been published on this topic in Brazil, except for the characteristics of series of patients with aneurysms or arteriovenous malformations submitted to surgical treatment. The objective of the present study was to collect epidemiologic data concerning a group of patients who died of spontaneous subarachnoid hemorrhage or of complications thereof and who were submited to autopsy. Special emphasis was placed on patients who had a subarachnoid hemorrhage due to rupture of aneurysms.

## MATERIAL AND METHODS

We analyzed retrospectively the medical records of 353 patients who died of spontaneous subarachnoid hemorrhage and who were submitted to autopsy at the University Hospital, Faculty of Medicine of Ribeirão Preto, from January 1976 to May 1985. These patients represented 6.1% of all autopsies performed during this period (5788).

Distribution by age, sex and color, the possible etiologies of the hemorrhage and the associated pathologies were investigated. The patients were classified in 3 groups with respect to the possible etiologies of subarachnoid hemorrhage: 1) hemorrhage associated with chronic arterial hypertension; 2) hemorrhage due to ruptured intracranial aneurysms; 3) hemorrhage due to other causes. In group 2 we also investigated the localization of the aneurysms, the interval between hemorrhage and hospitalization, the neurological state of the patient upon admission, the interval between hemorrhage and death, and the occurrence of further bleeding and/or vasospasm during evolution. The neurological state of the patients was classified according to Hunt and Hess (*3*).

Data were analyzed statistically by confidence intervals, and the comparisons concerning distribution by age, sex and color were made using as reference the characteristics of the population of the State of São Paulo provided by the Demographic Census of 1980 (Brazilian Institute of Geography and Statistics) (*4*).

## RESULTS

The 353 patients studied were subdivided into three groups according to the possible etiology of the subarachnoid hemorrhage. Group I consisted of the patients for whom it was possible to detect chronic arterial hypertension based on medical history, physical examination or autopsy findings (180 patients). Group 2 consisted of patients who suffered hemorrhage due to ruptured aneurysms (102 patients). Group 3 consisted of the patients who suffered subarachnoid hemorrhage due to other causes (71 patients).

The age distribution of the 353 patients by etiology and sex is shown in Table 1. No significant sex differences occurred in group 3. Among group 1 patients (subarachnoid hemorrhage associated with chronic arterial hypertension), there was a significant predominance of males (1.8:1), and among group 2 patients (hemorrhage due to ruptured aneurysms) there was a significant predominance of females (1.5:1). Overall age distribution showed a higher frequency of patients aged 40 to 50 years (46.7%). The most frequent age distribution of group 1 patients was 40 to 60 years (52.0%), and the most frequent age distribution of groups 2 and 3 was 20 to 60 years (86.3 and 66.2%), with a peak between 40 and 60 years for patients with aneurysms and with no defined peak for patients with hemorrhage due to other causes. Figure 1 shows a comparative summary of age distribution by etiology. Figure 2 shows the distribution of patients with subarachnoid hemorrhage by color, etiology and sex. Yearly patient distribution was 24, 23, 28, 32, 31, 46, 45, 52, 57, and 15 for the years from 1976 to 1985, respectively. Only the first 5 months of 1985 were analyzed.

The distribution of the pathologies associated with the subarachnoid hemorrhage, excluding those caused by ruptured aneurysms, are shown in Figure 3. The most frequent associated pathology was chronic arterial hypertension, isolated (34,3%) or in combination

| Age | Subarachnoid hemorrhage | | | | | | | | | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | + Arterial hypertension | | | | Due to aneurysm rupture | | | | Due to other causes | | | | | | | |
| Sex → | M | F | Total | % | M | F | Total | % | M | F | Total | % | M | F | Total | % |
| 0 — 10 | — | — | — | — | — | — | — | — | 3 | 4 | 7 | 9,8 | 3 | 4 | 7 | 2,0 |
| 10 — 20 | — | — | — | — | 1 | 3 | 4 | 3,9 | 4 | 4 | 8 | 11,3 | 5 | 7 | 12 | 3,4 |
| 20 — 30 | 8 | 3 | 11 | 6,1 | 6 | 13 | 19 | 18,6 | 4 | 9 | 13 | 18,3 | 18 | 25 | 43 | 12,3 |
| 30 — 40 | 13 | 9 | 22 | 12,2 | 9 | 9 | 18 | 17,6 | 7 | 4 | 11 | 14,1 | 29 | 22 | 51 | 14,2 |
| 40 — 50 | 33 | 20 | 53 | 29,4 | 14 | 12 | 26 | 25,5 | 6 | 7 | 13 | 18,3 | 53 | 39 | 92 | 26,1 |
| 50 — 60 | 29 | 12 | 41 | 22,8 | 8 | 17 | 26 | 24,5 | 5 | 5 | 10 | 14,1 | 42 | 34 | 76 | 21,5 |
| 60 — 70 | 11 | 11 | 22 | 12,2 | 2 | 2 | 4 | 3,9 | 2 | 3 | 5 | 7,0 | 15 | 16 | 31 | 8,8 |
| 70 — 80 | 16 | 8 | 24 | 13,3 | — | 5 | 5 | 4,9 | 2 | 2 | 4 | 5,6 | 18 | 15 | 33 | 9,3 |
| 80 — 90 | 5 | 2 | 7 | 3,9 | — | 1 | 1 | 1.0 | — | — | — | — | 5 | 3 | 8 | 2,3 |
| Total | 115 | 65 | 180 | | 40 | 62 | 102 | | 33 | 38 | 71 | | 183 | 165 | 352 | |

*Table 1 — Distribution of 353 patients with subarachnoid hemorrhage by etiology, age and sex (M, male; F, female).*

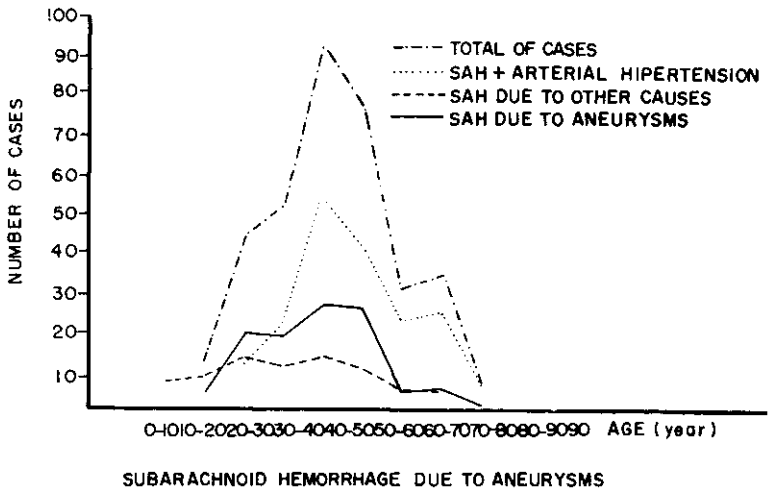


*Fig. 1 — Age distribution of 353 patients with subarachnoid hemorrhage (SAH).*

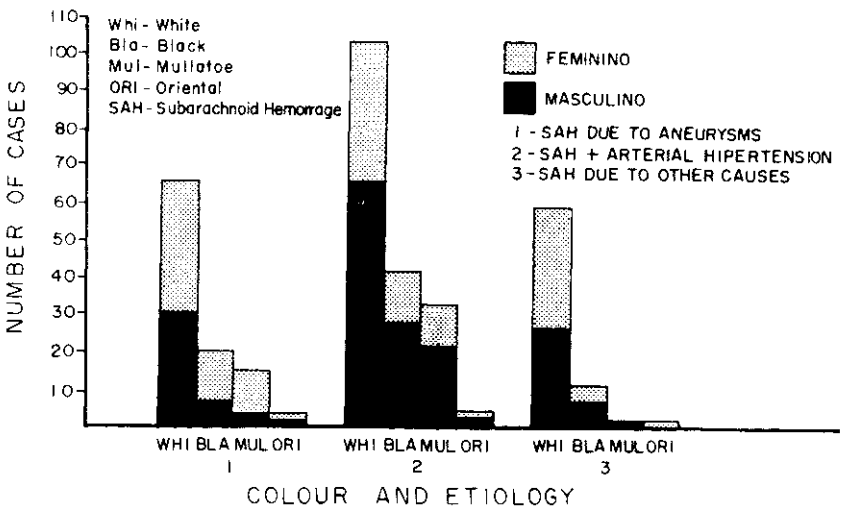


*Fig. 2 — Distribution of 353 patients with subarachnoid hemorrhage in relation to the colour and the etiology of the hemorrhage.*

with other pathologies (16.7%). In the group of pathologies associated with arterial hypertension, 1 case each of diabetes, adrenal adenoma, toxic goiter and hepatic necrosis was observed. The pathologies most frequently associated with subarachnoid hemorrhage in the absence of arterial hypertension were blood dyscrasias (6.5%), and 1 case each of granulomatosis, septicemia, endocarditis and arteriovenous malformation was observed in the group of other associated pathologies. Twenty four of the 353 patients (6.8%) showed no pathology associated with subarachnoid hemorrhage. Figure 4 shows the distribution of secondary pathologies associated with subarachnoid hemorrhage due to ruptured aneurysms. One hundred patients had congenital aneurysms and 2 had atherosclerotic aneurysms. The most frequently associated secondary pathology was chronic arterial hypertension (48%). In 4 patients with chronic arterial hypertension associated with congenital nephropathies, the latter were polycystic kidneys.

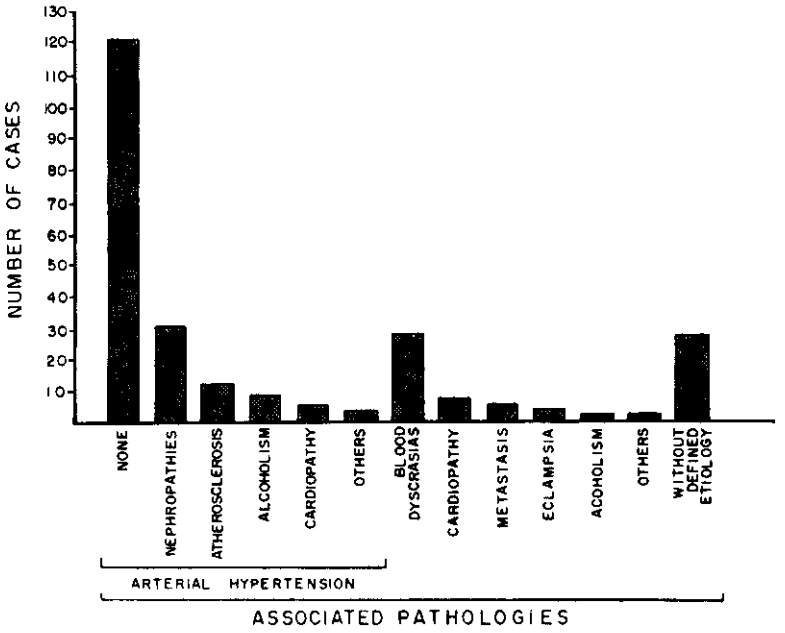


*Fig. 3 — Distribution of associated pathologies among the patients with subarachnoid hemorrhage excluding those with hemorrhage due to aneurysms.*

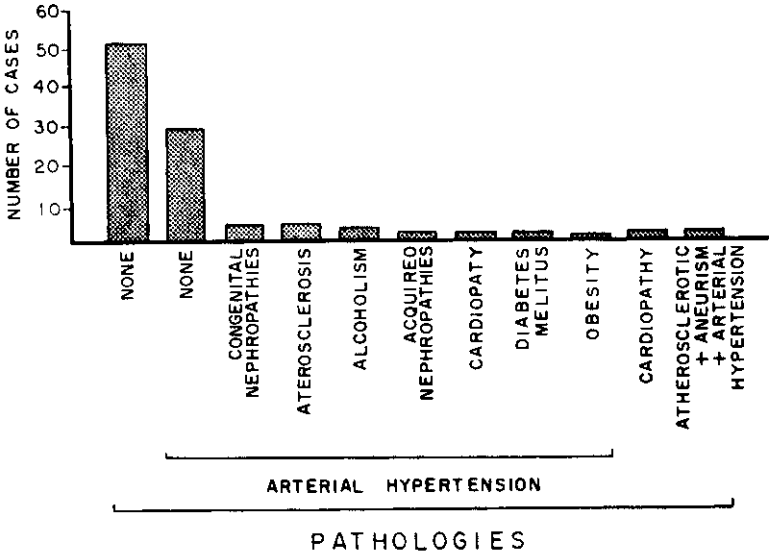


*Fig. 4 — Distribution of associated pathologies in 102 cases of subarachnoid hemorrhage due to aneurysms.*

The ruptured aneurysms were located as follows: 36 (35.3%) in the communicant/anterior cerebral artery complex, 30 (29.4%) in the internal carotid artery, 23 (22.6%) in the middle cerebral artery, 5 (4.9%) in the basilar artery, 1 in the distal anterior cerebral artery, and 1 in the posterior cerebral artery. In 6 cases (5.8%) the location of the ruptured aneurysm was not specified. In 93 cases (91.2%) there was a single aneurysm, and in 9 (8.8%) there were 2 or more aneurysms. Five of the patients with multiple aneurysms had an aneurysm of the anterior cerebral/anterior communicant artery complex, and in 4 of them this was the aneurysm that ruptured.

Figure 5 shows the distribution of patients with subarachnoid hemorrhage according to clinical condition upon admission: 27.4% were in grades I and II, 25.5% in grade III, and 47.1% in grades IV and V. Table 2 shows the distribution of patients with subarachnoid hemorrhage due to ruptured aneurysms who suffered further bleeding or vasospasm during evolution. The second bleeding episode was more frequent 9 to 16 days after hemorrhage (53.8%) and the vasospasm 3 to 10 days after hemorrhage (54.2%). The distribution of patients with subarachnoid hemorrhage due to ruptured aneurysms who suffered further bleeding or a vasal spasm in relation to the clinical condition preceding and following these events is shown in Figure 6. Before the second bleeding episode, 61.5% of the patients had been classified as grades I and II, and 59.1% of those who suffered a vasospasm had been classified as grade I and II. After the second bleeding episode or

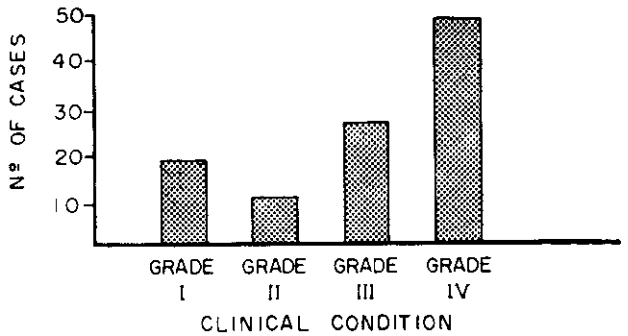


*Fig. 5 — Clinical state of the patients with subarachnoid hemorrhage at admission (Hunt & Hess, 1968).*

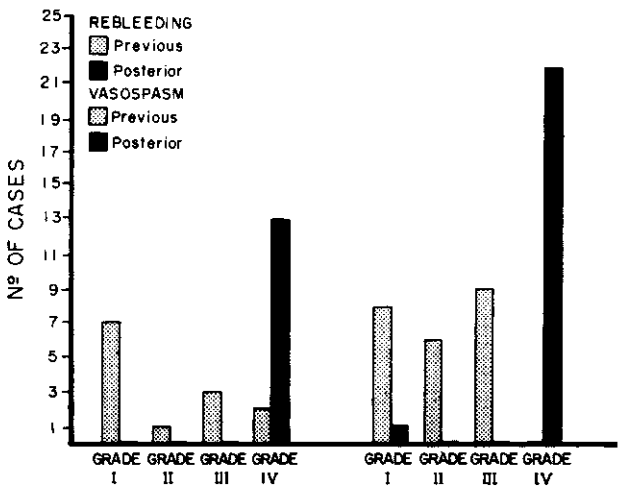


*Fig. 6 — Distribution of patients with subarachnoid hemorrhage due to aneurysms with re-bleeding or vasospasm, according the clinical state (Hunt & Hess, 1968).*

vasospasm all patients were classified as grade IV. The distribution of patients with subarachnoid hemorrhage due to ruptured aneurysms according the interval between hemorrhage and death is shown in Table 3. Mortality was 35% during the first 3 days and 54% during the first 6 days. Considering the aneurysms located in the middle cerebral artery, 52.2% of all deaths occurred during the first 3 days, whereas for the aneurysms located in the anterior cerebral/anterior communicant artery complex, 42.9% of all deaths occurred 3 to 8 days after hemorrhage.

| | Site of aneurysm | Interval (Days) 0—3 | 3—6 | 6—9 | 9—12 | 12—15 | 15—18 | 18—21 | 21 | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| Rebleeding | ACoA/ACA | — | 1 | — | 4 | 2 | — | 1 | — | 8 |
| | MCA | 1 | 1 | — | — | — | — | — | — | 2 |
| | ICA | — | — | 1 | — | — | — | — | 1 | 2 |
| | BA | — | — | — | — | — | — | 1 | — | 1 |
| | Total | 1 | 2 | 1 | 4 | 2 | — | 2 | 1 | 13 |
| Vasospasm | ACoA/ACA | 1 | 4 | 5 | 1 | 2 | — | 1 | — | 14 |
| | MCA | 1 | — | — | — | 1 | — | — | — | 2 |
| | ICA | 1 | 3 | 1 | 2 | — | — | — | — | 7 |
| | NI | — | — | — | — | 1 | — | — | — | 1 |
| | Total | 3 | 7 | 6 | 3 | 4 | — | 1 | — | 24 |

*Table 2 — Distribution of 100 patients with subarachnoid hemorrhage due to aneurysm rupture that rebleeded or had vasospasm according the site of the aneurysm and the interval from the first hemorrhage to these events. ACoA, anterior communicating artery; ACA, anterior cerebral artery; MCA, middle cerebral artery; BA, basilar artery; NI, not identified.*

| Site of Aneurysm | Interval (Days) 0—3 | 3—6 | 6—9 | 9—12 | 12—15 | 15—18 | 18—21 | 21 | Total |
|---|---|---|---|---|---|---|---|---|---|
| PCoA | 4 | 3 | 1 | 1 | 1 | 1 | 1 | 1 | 13 |
| CAB | — | 2 | — | — | — | — | — | — | 2 |
| ICA | 5 | — | 3 | 2 | 1 | — | — | 3 | 14 |
| ACoA/ACA | 5 | 9 | 4 | 2 | 3 | 3 | 3 | 6 | 35 |
| MCA | 12 | 4 | 3 | — | 1 | 1 | 1 | 1 | 23 |
| PcA | 1 | — | — | — | — | — | — | — | 1 |
| BA | 3 | — | 1 | — | — | — | 1 | — | 5 |
| PCA | 1 | — | — | — | — | — | — | — | 1 |
| NI | 4 | 1 | — | — | — | 1 | — | — | 6 |
| Total | 35 | 19 | 12 | 5 | 6 | 6 | 6 | 11 | 100 |

*Table 3 — Distribution of 100 cases with subarachnoid hemorrhage due to aneurysm rupture according to the site of the aneurysm and the interval from hemorrhage to death. PCoA, posterior communicating artery; CAB, carotid artery bifurcation; ICA, internal carotid artery; ACoA, anterior communicating artery; ACA, anterior cerebral artery; MCA, middle cerebral artery; PcA, pericallosal artery; BA, basilar artery; PCA, posterior cerebral artery; NI, not identified.*

## COMMENTS

The distribution of the 353 patients studied was similar for both sexes and did not differ from the control population in terms of sex. In terms of etiology, in the group of patients with hemorrhage associated with chronic arterial hypertension there was a 1.8:1 male predominance. This predominance persisted throughout the various decades of life, except for the seventh, in which the distribution was similar for both sexes. An appropriate interpretation of these data is made difficult by the lack of data showing the real distribution of chronic arterial hypertension in our population. In the group of patients with hemorrhage due to ruptured aneurysms there was female predominance (1.5:1) over the various decades of life (Table 1), except for the 4th and 7th, for which the distribution was similar, and for the 5th, in which there was a slight male predominance. Even though overall distribution of the present cases was similar to that reported by the Cooperative Study [7], distribution by decade of life was different since the Cooperative Study reported male predominance during the first four decades. In the group of patients with hemorrhage due to other causes there was no significant difference in distribuition by sex, except for female predominance during the third decade (2.2:1) and for male predominance during the fourth decade (1.7:1). Overall distribution was similar to that reported by the Cooperative Study [7] but there was a difference in distribution by decade of life (male predominance below 20 years and female predominance above 70 years).

The age distribution of the patients studied showed predominance of subarachnoid hemorrhage in the 40 to 50 year group (47.6%), a predominance that is especially outstanding when we compare this series with the age distribution of the population in the State of São Paulo, in which 77.1% of all individuals are less than 40 years old. The distribution shown by the patients studied in the 40 to 60 year range is similar to that reported by the Comparative Study (50.3%)[7], but if we consider the distribution below 40 years and above 60 years there was a significant difference (32% for the present patients and 19.2% in the Comparative Study for the less than 40 age group, and 20.4% for the present patients and 30.4% in the Comparative Study for the over 60 age group). This difference may be explained by the shorter mean life expectancy for our population in relation to the North American one. Considering the etiology, the patients with hemorrhage associeted with chronic arterial hypertension and the patients with hemorrhage due to aneurysms also showed predominance in the 40 to 60 age range, but the remainder of the distribution predominated in the over 60 age range for the former and in the less than 40 age range for the latter (Fig. 1). The patients with hemorrhage due to other causes showed no predominant age distribution.

When the distribution of the 353 patients was studied in relation to color and compared to that of the control population [4] (74.7% whites, 18.4% blacks, 4.6% mulattoes, 1.9% orientals and 0.35% unknown), a predominance of subarachnoid hemorrhage was detected in blacks, followed by mulattoes and by whites (Fig. 2). This distribution was also observed in the different etiologic groups, except for the patients with hemorrhage due to causes other than chronic arterial hypertension.

With respect to the sex/color relationship, the frequency of subarachnoid hemorrhage was higher in black and white males, and similar for males and females among mulattoes and orientals. In the group of patients with hemorrhage associated with chronic arterial hypertension, males predominated in all color categories, and in the group of patients with hemorrhage due to ruptured aneurysms, mulatto and black females predominated.

It was not always possible to determine the etiology of subarachnoid hemorrhage even after autopsy. Ruptured aneurysms were responsible for hemorrhage in 28.9% of cases, and other causes could be detected in 13.3% of cases. Chronic arterial hypertension was an associated pathology that may have been responsible for the hemorrhage in 51% of cases, and in 6.8% of cases no pathologies were detected that might justify a hemorrhage (Tables 1 and 3). The frequency of ruptured aneurysms as a cause of subarachnoid hemorrhage was lower in the present series than in the population surveyed by the Cooperative Study (51%)[7], and among the other causes we observed only one case of hemorrhage due to rupture of an arteriovenous malformation, in contrast to the 6% frequency reported by the Cooperative Study [7]. This difference may be explained by the fact that the present population consisted only of patients who died due to hemorrhage. Among the patients with subarachnoid

hemorrhage associated with chronic arterial hypertension, associated secondary pathologies were detected in 32.8% of cases, the most frequent being nephropathies (50.8%) and atherosclerosis (20.3%). In the absence of arterial hypertension and aneurysms, the most frequent pathologies associated with subarachnoid hemorrhage were blood dyscrasias (6.5%), heart disease (2.3%) and metastatic tumors (1.7%). In the group of patients with subarachnoid hemorrhage due to ruptured aneurysms, 100 had congenital aneurysms and 2 atherosclerotic aneurysms. Chronic arterial hypertension (Table 4) was associated in 48% of cases, 40.8% of whom showed other associated secondary pathologies, mainly nephropathies (30%) and atherosclerosis (20%). By summing all the cases with associated atherosclerosis we obtained 5% of the total number of cases studied, which is a significantly lower value than reported in the literature[7]. This fact may be explained by a lower incidence of atherosclerosis in our population, though we have no concrete data to support this statement.

The most frequent localizations of the ruptured intracranial aneurysms in the 102 cases studied were in the internal carotid artery (29.4%), in the anterior cerebral/anterior communicant artery complex (35.3%) and in the middle cerebral artery (22.6%). This distribution fits in the ranges reported in the literature[7-9,13,17,18], which may be explained by the differences in the characteristics of the series studied which may or may not include unruptured aneurysms and multiple aneurysms, and by the possible use of different diagnostic methods (angiography, surgery, and autopsy) separately or in combination. Among the present patients, 9 (8.8%) had multiple aneurysms. Five of them had one aneurysm in the anterior cerebral/anterior communicant artery complex and this was the aneurysm that ruptured in 4 of them, in contrast to the data reported by the Cooperative Studies[7,9] which showed that the aneurysms of the anterior communicant artery are less likely to be associated with a second aneurysm.

Of the patients with aneurysms, 27.4% were hospitalized in grades I and II (Fig. 5) and of the patients who suffered a vasospasm or a second bleeding episode, 59.1% and 61.5% were in grades I and II before these events, respectively, and all evolved toward grades IV or V after the complication. The period of highest incidence of further bleeding was during the second week after the hemorrhage and the incidence was highest in the aneurysms of the anterior cerebral/anterior communicant artery complex. This period was a little delayed in relation to that reported by other investigators[8] although this discrepance may be only apparent. In fact, when analyzing the number of observed deaths in relation to the interval between hemorrhage and death, we observed that 35% of the patients died during the first 3 days and 54% during the first 6 days and this high mortality during the first days was probably partially due to episodes of undiagnosed precocious rebleeding[5,6]. Among the patients with aneurysms of the middle cerebral artery, the death rate was highest during the first 3 days (50.2%), and among those with aneurysms of the anterior cerebral/anterior communicant artery complex, the death rate was highest between the 4th and 9th day after hemorrhage, a period coinciding with the highest incidence of vasospasm. These data agree with those reported by the Cooperative Study[8] which showed predominance of aneurysms of the middle cerebral artery and of the anterior cerebral/anterior communicant artery complex among the patients who died during the first 3 days after hemorrhage. Among the patients with aneurysms of the internal carotid artery, there was no preferential period with respect to the occurrence of hemorrhage. The frequency of vasospasm was highest between the 3rd and 10th day after hemorrhage, with predominance of aneurysms of the anterior cerebral/anterior communicant artery complex, in agreement with the literature.

Early surgical treatment of intracranial aneurysms is becoming progressively more accepted on the basis of the firm argument that when surgical treatment is systematically performed after the period of occurrence of vasospasm and further bleeding a considerable number of patients worsen or die due to these complications and lose their chance of being operated upon. The patients who can benefit from early surgical treatment are those in grades I and II. Analysis of the present series, performed when our conduct was to operate systematically after the period of highest incidence of vasospasm and further bleeding, shows that indeed a considerable number of patients lost the opportunity of being surgically treated with a chance of favorable evolution.

*Acknowledgement* — We are grateful to Professor Humberto de Queiroz Menezes of the Department of Pathology, Ribeirão Preto Medical School of University of São Paulo, for the permission to use the autopsy data.

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