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Neurological damage related to open-heart surgery

A clinical survey

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A survey has been carried out on all cases submitted to open-heart surgery at one hospital during 1970 to determine which operative features were associated with the occurrence of neurological damage.

Four hundred and seventeen subjects survived the operative period. Neurological dysfunction, defined as impairment of consciousness, voluntary movement or vision, apparent within three days of operation, was noted in 80 patients (19·2%). Twenty-one of these 80 patients died in the postoperative period, neurological damage contributing to the fatal outcome in 11 cases. The remaining 59 patients survived to leave hospital but 17 were left with some residual neurological disability.

A number of features were found to be positively correlated with the development of neurological damage when considered alone, but multiple regression analysis revealed that only three factors were significantly associated, independent of all other variables. These factors were age, duration of perfusion, and a history of previous neurological disorder.

The use of a Temptrol oxygenator was associated with a lower incidence of neurological dysfunction to a degree which was probably significant ($P<0·02$). The small number of patients perfused with the Temptrol oxygenator (30 cases) reduces the clinical importance of this finding.

Neurological damage continues to occur following open-heart surgery in spite of changes in both the nature and technique of operation and the method of perfusion.

The reported incidence varies (Gilman, 1965; Sachdev, Carter, Swank, and Blachly, 1967; Javid *et al.*, 1969) depending in part on the criteria chosen to define neurological damage, but also because multiple factors are probably responsible and their relative importance may vary in different series.

Possible aetiological factors include emboli from within the heart or perfusion apparatus (Allardyce, Yoshida, and Ashmore, 1966; Abrams, 1967; Brierley, 1967; Hill *et al.*, 1969; Bass and Longmore, 1969) and inadequate cerebral perfusion related to hypoxia, hypotension, venous obstruction or malpositioning of intravascular cannulae (Adelman and Jacobson, 1960; Paton, Pearcy, and Swan, 1960; Hasbrouck and Rigor, 1969; Magner, 1971). Profound hypothermia (Björk and Hultquist, 1960; Drew, 1961) and acute biochemical changes (Michenfelder and Theye, 1969) may contribute in some cases. Psychological manifestations may be related to organic brain damage (Blachly and Kloster, 1966) and could represent a response to the stress of facing life-threatening surgery and exposure to the abnormal environment of a postoperative intensive therapy unit (Kornfeld, Zimberg, and Malm, 1965).

At least some of these factors could be eliminated or their effects minimized but this requires a knowledge of their relative importance. In an attempt to define these priorities, a clinical survey of all cases submitted to open-heart surgery at the Brompton Hospital in 1970 was undertaken to establish which pre- and peri-operative features were most frequently associated with the appearance of neurological damage in the postoperative period.

METHODS

Data were obtained from 417 cases; patients who died in the operating theatre were excluded as were those who succumbed within the first few post-operative hours before a neurological assessment could be made. Although some studies were carried out prospectively, more than 50% of the data was collected retrospectively; in 52 instances, one or more items of information were not available.

Neurological damage was defined as impairment of consciousness, voluntary movement or vision, separ-

ately or together, apparent within three days of operation. Impaired consciousness ranged from coma to confusion of a severity sufficient to interfere with response to simple commands. Confusion alone in patients who were hypoxic postoperatively (arterial oxygen tension less than 60 mmHg) was discounted. The information recorded is listed in Table I.

Age was quoted in years. For patients less than 2 years of age an approximation was used:

less than 3 months	= 0
3 to 9 months	= 0·5
10 to 18 months	= 1
19 to 24 months	= 2.

PREOPERATIVE NEUROLOGICAL STATUS The preoperative evaluation included an account of current neurological symptoms, a history of previous neurological disorder, a note of mental status, particularly in patients with severe heart failure or those undergoing emergency surgery, and a record of abnormal neurological signs detected on examination. For statistical analysis, the preoperative neurological status was recorded as normal or abnormal. A history of syncope associated with Fallot's tetralogy or aortic valve disease was not regarded as evidence of neurological abnormality. Four patients with severe acute pulmonary embolic disease who were operated on as emergencies and who were confused preoperatively but had no abnormal neurological signs were considered to be neurologically normal, as were two patients with a history of previous trauma (one head injury and one peripheral nerve lesion). The aetiology of the preoperative neurological abnormality in the remaining 35 cases is listed in Table II. Fifteen of the 35 cases had residual neurological signs preoperatively.

CARDIAC RHYTHM A number of arrhythmias were recorded and in some patients the rhythm was unstable. For statistical purposes the rhythm was documented as sinus rhythm (283 cases) or 'other than sinus' (130 cases).

NATURE OF OPERATION Classification of the nature of the operative procedure was undertaken as outlined in Table III. It was intended that this distinction should separate as far as possible those patients in whom embolism, particularly of air, could occur easily from those in whom it was less likely.

CALCIFICATION, CLOT, AND VEGETATIONS Calcification in one or more sites was recorded as present or absent. Thrombus and vegetations were considered together, and one patient with a left atrial myxoma was included in this group. Patients with pulmonary emboli were excluded except one case with a patent foramen ovale who had sustained a paradoxical embolus simultaneously. Calcification was present in 129 patients and either clot or vegetations in 29.

OXYGENATOR The perfusion apparatus was either a rotating plastic disc oxygenator with a filter and bubble trap in the arterial line or a disposable bubble oxygenator (Rygg or Temptrol). A filter for microemboli (Patterson and Kessler, 1969) was not used in the arterial line with any system. For most elective procedures the rotating disc was employed; a Rygg oxygenator was used for elective procedures which were expected to be of short duration (e.g., closure of atrial septal defect, relief of isolated pulmonary stenosis, or open mitral valvotomy) and the Temptrol was largely reserved for emergency surgery. Three hundred and twenty-six perfusions were carried out using the disc oxygenator, 56 with the Rygg, and 30 with the Temptrol.

Duration of cardiopulmonary bypass This was recorded in minutes. No distinction was made between partial and complete bypass, or supportive perfusion. In three instances where the technique of profound hypothermia and circulatory arrest was employed, the total time of perfusion including the arrest period was used.

TABLE I

FACTORS CONSIDERED IN RELATION TO INCIDENCE OF NEUROLOGICAL DAMAGE

Age
Duration of perfusion
Mean flow rate
Preoperative neurological status
Cardiac rhythm
Presence of calcification
Presence of clot or vegetations
Use of hypothermia
Nature of operation
Type of oxygenator
Nature of priming solution
Technique of arterial return

TABLE II

AETIOLOGY OF PREOPERATIVE NEUROLOGICAL DISORDERS

Cerebral embolism	27
Arteriosclerosis	2
Epilepsy	3
Congenital basal ganglia disease	1
Acute ischaemic spinal cord damage	1
Hemiplegia following previous bypass	1

TABLE III

OPERATIVE PROCEDURES

Mitral valve	142
Aorta and aortic valve	115
Multiple valve replacement	31
Left-to-right shunts	56
Right-to-left shunts (inc. potential shunts)	39
Relief of right heart obstruction	16[1]
Ischaemic heart disease	10[2]
Miscellaneous	8[3]

[1]Right heart obstruction included pulmonary embolectomy and relief of isolated pulmonary stenosis.
[2]Surgery for ischaemic heart disease included resection of ventricular aneurysm and excision of acute infarct.
[3]Miscellaneous conditions included: Ebstein's anomaly ×2; isolated tricuspid valve replacement ×2; excision of left atrial myxoma; coronary artery aneurysm with fistula to right ventricle; mitral valve replacement with closure of atrial septal defect.

Flow rate This was calculated as millilitres per minute per kilogramme body weight. It is customary in this unit to perfuse adult patients at a flow rate of 60 to 80 ml/min/kg, whereas higher flows are preferred in children (100 to 300 ml/min/kg for infants and up to 100 ml/min/kg for children under 12 years).

Nature of priming solution. The oxygenator and circuit were primed with fresh citrated blood (less than 72 hours old), reconstituted with heparin and calcium chloride, together with 5% dextrose solution, 1·26% sodium bicarbonate, and Ringer's solution. The choice of priming solution was determined by the patient's age, weight, and preoperative haematocrit, and the volume of fluid required for a particular circuit. Whole blood was used for infants and children under 3 years of age; for patients aged 3 to 60 years up to 30 ml/kg of electrolyte solution were used provided the haematocrit was more than 40%. Smaller volumes of electrolyte solution were used for patients over 60 years, or if there was evidence of poor renal function or considerable preoperative fluid retention. The priming fluids were classified as blood only or electrolyte solution alone or a mixture of the two. On 288 occasions both blood and electrolyte solution were used whereas blood alone was employed on 59 occasions and electrolyte solution in 39 instances.

Technique of arterial return Three methods for providing arterial return from the oxygenator were employed. A straight metal cannula was used for the femoral artery, inserted most commonly on the left side. Alternatively, arterial return was to the aorta using either a flexible plastic end-hole Bardic cannula or a fenestrated metal cannula (Parker, 1969). The choice between these three techniques was to some extent a reflection of the policies of different surgical teams, but all three methods were well represented (181 femoral; 106 Bardic aortic; and 111 fenestrated aortic).

Hypothermia Body temperature was recorded in the nasopharynx, and small variations (35 to 38° C) were common during 'normothermic' perfusions. A decrease in body temperature below 35° C was employed electively in 220 cases, generally to a temperature between 30 and 33° C, but occasionally to much lower levels. In 13 instances, hypothermic circulatory arrest was employed at temperatures between 12 and 28° C. For the statistical analysis, hypothermia was defined as any reduction in nasopharyngeal temperature to less than 35° C.

VARIABLES NOT INCLUDED Three potentially important factors were excluded from this study—haematocrit and carbon dioxide tension during perfusion and the level of arterial blood pressure during the entire operative procedure.

Haematocrit and arterial carbon dioxide tension were recorded intermittently so that any estimate of the duration at a particular value was not possible.

Arterial blood pressure was recorded continuously throughout but is highly variable, may change rapidly or slowly, may be low in the presence of either a low or high total flow, and may be pulsatile or not depending on surgical conditions and the performance of the heart. A reliable reading, for statistical correlation, of blood pressure during the procedure was considered to be impossible.

RESULTS

Using the criteria previously defined, 80 patients out of 417 sustained neurological damage, giving an overall incidence of 19·2%. The nature of the lesions is listed in Table IV.

Twenty-one of the 80 cases with neurological damage died in the postoperative period; 11 of these deaths were wholly or partly attributable to the neurological lesion. The remaining 59 patients survived, but 17 were left with some residual neurological disability at the time of discharge from hospital. The 22 patients with confusion as the sole index of neurological damage all recovered and left hospital with no grossly detectable disability.

Statistical analysis of the significance of the factors recorded was carried out in two stages. Initially, each item was considered in isolation using simple regression, and several were found to be significantly correlated with the appearance of neurological damage whereas others were associated with a lower than average incidence. These findings are presented in Table V.

In view of the probable interrelationship of many of these factors, e.g., calcification with advancing age, the data were reconsidered by multiple regression analysis and the results are shown in Table VI.

This demonstrated that the only factors significantly related to a higher incidence of neurological damage independent of all other variables were increasing age, longer duration of bypass, and a history of previous neurological deficit. The use of the Temptrol oxygenator was significantly less likely to be associated with subsequent neurological injury ($P<0·02$) although this group was rather small (30 cases).

TABLE IV

NATURE OF NEUROLOGICAL DAMAGE DETECTED POSTOPERATIVELY

Right hemiplegia	14
Left hemiplegia	22
Coma	20[1]
Confusion	22
Midbrain damage	2
Quadriplegia	1
Epilepsy	2

[1]Three patients in coma had localizing signs of a left hemiplegia.

TABLE V

RESULTS OF SIMPLE REGRESSION ANALYSIS RELATING OPERATIVE FEATURES TO INCIDENCE OF NEUROLOGICAL DAMAGE

	Variance Ratio (F)	P
Age	21·28	< 0·001
Duration of perfusion	21·1	< 0·001
Mean flow rate	−7·25	< 0·01
Preoperative neurological abnormality	13·26	< 0·001
Cardiac rhythm	3·80	> 0·05
Presence of calcification	8·31	< 0·01
Presence of clot or vegetations	0·23	> 0·05
Hypothermia	3·75	> 0·05
Mitral valve	0·82	> 0·05
Aorta and aortic valve	0·97	> 0·05
Multiple valves	4·51	< 0·05
Left-to-right shunts	−9·42	< 0·01
Right-to-left shunts	−0·98	> 0·05
Right heart obstruction	−0·88	> 0·05
Ischaemic heart disease	0·60	> 0·05
Rygg oxygenator	−7·15	< 0·01
Temptrol oxygenator	−3·88	< 0·01
Disc oxygenator	12·47	< 0·001
Prime—electrolyte solution only	−3·80	> 0·05
Prime—electrolyte and blood	10·94	< 0·001
Prime—blood only	−6·32	< 0·05
Femoral arterial return	3·64	> 0·05
Aortic return—fenestrated	0·01	> 0·05
Aortic return—Bardic	−5·12	< 0·05

A negative value indicates a lower than average incidence.

TABLE VI

FACTORS SIGNIFICANTLY RELATED TO INCIDENCE OF NEUROLOGICAL DAMAGE, INDEPENDENT OF ALL OTHER VARIABLES (MULTIPLE REGRESSION ANALYSIS)

	t Value	P
Age	3·39	< 0·001 +correlation
Duration of perfusion	3·10	< 0·01 +correlation
Preoperative neurological abnormality	2·74	< 0·01 +correlation
Temptrol oxygenator	2·52	< 0·02 −correlation

DISCUSSION

There were several reasons for selecting relatively crude criteria to define neurological damage. Uncomplicated anaesthesia and non-cardiac surgery in elderly patients may sometimes be followed by transitory and minor signs of neurological or psychological dysfunction which are of doubtful aetiology (Bedford, 1955). Psychological manifestations alone may be related to aspects of the cardiac surgical procedure other than the operative period itself (Cohen, 1967), and clinically important long-term sequelae are seen only in patients who show severe dysfunction in the immediate postoperative period. By restricting the study to gross and obvious disability, the hazard of data-loss through retrospective collection was minimized.

The importance of age has been emphasized previously by Javid *et al.* (1969) in a study restricted to patients aged between 21 and 65 years. No age group was excluded in the present series, but a significant increase in the incidence of neurological damage was shown in the older age group. When analysed on the basis of each decade of life, a marked increase in incidence was noted in patients more than 50 years old (see Table VII).

The duration of bypass was found by Javid *et al.* (1969) to be significantly associated with subsequent neurological injury, especially when perfusion lasted more than 120 minutes. A positive correlation between neurological damage and the duration of perfusion was demonstrated in the present series, and the incidence following perfusions of different durations is recorded in Table VIII.

Episodes of circulatory embarrassment are inevitable when complex cardiac surgery is undertaken in critically sick patients. Such episodes could be responsible for postoperative neurological deficits and it is quite possible that the most complex and hazardous surgery is undertaken in the older age groups and takes longer to carry out. To clarify this point the records of the 80 patients with neurological damage were inspected to ascertain how often an episode of technical difficulty or cardiorespiratory embarrassment had been recorded. Potential aetiological factors were recorded in 32 of the 80 cases and these are detailed in Table IX. The mean age and duration of bypass

TABLE VII

INCIDENCE OF POSTOPERATIVE NEUROLOGICAL DAMAGE RELATED TO AGE

Age (yr)	Total No.	No. With CNS Damage	%
< 1	9	1	11·1
1–10	58	2	3·5
11–20	43	6	14·0
21–30	42	8	19·1
31–40	58	4	6·9
41–50	78	15	19·2
51–60	89	29	32·6
61–70	39	15	38·5
> 70	1	0	0

TABLE VIII

INCIDENCE OF POSTOPERATIVE NEUROLOGICAL DAMAGE RELATED TO DURATION OF PERFUSION

Duration (min)	Total No.	No. With CNS Damage	%
< 30	54	4	7·4
31–60	62	5	8·1
61–90	81	17	21·0
91–120	86	13	15·1
121–180	96	28	29·2
> 180	34	12	35·3

Information on the duration of perfusion was lacking in four instances, including one patient with neurological damage.

TABLE IX

SUSPECTED AETIOLOGY OF NEUROLOGICAL DAMAGE IN 32 PATIENTS

Hypotension, hypoxia or cardiac arrest	24
Suspected embolism of clot or air	5
SVC obstruction	2
Drug-withdrawal epilepsy	1

	32 Cases, Aetiology Suspected	48 Cases, Aetiology Unknown
Average age (yr)	42·8	49·5
Average duration of perfusion (min)	129·5	124·2

of these 32 patients and the remaining 48 cases (in whom no untoward events had been recorded) were compared and no significant differences were found ($P<0{\cdot}05$).

The importance of a previous neurological lesion was demonstrated in the present series even when there were no residual physical signs. In an extended survey of the series presented by Javid *et al.* (1969), Tufo, Ostfeld, and Shekelle (1970) stated that a history suggestive of previous neurological deficit but without clinical signs at the time of preoperative examination was not related to the ocurrence of new cerebral damage. However, they noted that three patients who had focal neurological signs at the time of the initial evaluation developed new neurological signs following surgery. In the present series, two patients with acute preoperative neurological lesions (one cerebral embolus and one with acute ischaemic spinal cord damage) deteriorated neurologically in the postoperative period. These two cases were not included in the group of 80 patients who *developed* neurological damage as the postoperative physical signs merely demonstrated an accentuation of the lesion which had been present previously.

The only feature which appeared to be related significantly to a lower incidence of neurological damage was the use of the Temptrol oxygenator. The clinical importance of this finding is difficult to evaluate as the total number of cases perfused with the Temptrol was only 30. It is possible that the incidence of micro-bubble formation may be less, or the filtration system may be more efficient, but Ghadiali and Horton (1970) were unable to demonstrate any difference in the incidence of micro-embolism following perfusions with either a rotating disc or Rygg oxygenator, or, more recently (Ghadiali and Horton, 1972), with the Temptrol oxygenator.

Although positive correlation between two variables does not necessarily imply aetiological association, the implication of the present findings is that perfusion itself damages the brain. Whether this be embolic or ischaemic is less easy to define. The possibility of embolism occurring as an isolated event, e.g., air trapped during closure of the heart and ejected with the return of a spontaneous circulation, seems unlikely in view of the positive correlation of neurological damage with advancing age and duration of bypass, and the lack of correlation with those procedures in which air is more likely to be trapped in the left side of the heart. The higher incidence with advancing years suggests the possibility that cerebral ischaemia, accentuated by co-existent arterial disease, may be important. The influence of preoperative neurological damage, which in this series was largely embolic and therefore probably contributing to cerebrovascular pathology, could also be interpreted in the same way.

Alternatively, it may be argued that the effects of repeated micro-embolism would be more apparent in patients with previous cerebral or cerebrovascular pathology or when cerebral circulatory adjustments to changes in blood pressure occur less readily, as is known to happen with advancing age (Shenkin *et al.*, 1951). The data recorded here provided no means of distinguishing these two hypotheses.

Previous work reported by Javid *et al.* (1969) and by Tufo *et al.* (1970) emphasized the importance of arterial hypotension during perfusion. The details of the procedure employed to record blood pressure over a prolonged period of time are quoted by Tufo *et al.* (1970), who stated that the blood pressure was measured every 5 minutes, and $2\frac{1}{2}$ minutes was attributed to the pressure recorded at the start and end of each 5-minute period. Cerebral damage was progressively more common as the lowest recorded value for mean arterial blood pressure during perfusion fell from 60 to 40 mmHg or below. The incidence of cerebral damage tended to increase with increasing duration of arterial hypotension (less than 50 mmHg) but the results were statistically significant only within the age group 40 to 49 years. The difficulty of recording a meaningful blood pressure over a prolonged period of time and the lack of information about the aetiology of the hypotension interfere with the interpretation of these findings.

The normal cerebral circulation adjusts to compensate for arterial hypotension at least to a pressure of 50 mmHg (Harper, 1965). The factors controlling cerebral blood flow during cardiopulmonary bypass in man are less well documented (Halley, Reemtsma, and Creech, 1958; Wollman, Stephen, Clement, and Danielson, 1966).

and the importance of rate of change of pressure, total systemic flow rate, and the presence or absence of pulsatile perfusion have not been evaluated. Superimposed on these haemodynamic features are the possible effects of anaesthetic agents and the arterial carbon dioxide tension.

The weight of evidence in favour of cerebral ischaemia during cardiopulmonary bypass as a cause of postoperative neurological dysfunction suggests that further study of cerebral haemodynamics under these conditions would be worthwhile.

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