Four harvesters who smoked regularly excreted levels of cotinine averaging 900 μg. per 100 mg. creatinine, a value much greater than that seen in harvesters who did not smoke. However, excretion of cotinine by the four novice smokers was considerably less and was well below the peak excretion noted in the croppers (see figure).

Discussion

Dew on green tobacco leaves dissolves nicotine, and 100 ml. of dew may contain as much as 9 mg. nicotine or the equivalent of the nicotine content of six average cigarettes. Although we have no accurate measurements of the amount of dew to which croppers are exposed, 600 ml. would be a conservative estimate of the soaking they get while harvesting. The percentage of nicotine in dew that is absorbed through the skin is not known. The extent of skin contact and the pH of the solution would be determining factors since greater absorption occurs when nicotine is in the form of the free base.[10]

Excretion of cotinine by non-smoking workers is evidence that significant nicotine absorption takes place. Absorption is greatest among croppers who have most contact with the wet leaves and less in stringers and tractor drivers who are less exposed. Decreased absorption occurs among croppers who wear protective raincoats. The amount of nicotine taken in by harvesters seems to be greater than that absorbed by novice smokers inhaling the smoke from three cigarettes. Dizziness and nausea have been noted in novice smokers who smoked 3–6 cigarettes in a 30–45 minute period.[11] This suggests that the quantity of nicotine absorbed by harvesters is sufficient to cause symptoms. However, harvesters excreted much less cotinine than regular smokers, supporting the observation that regular cigarette smoking, which is known to induce tolerance to nicotine,[4] affords protection from tobacco sickness.[2]

It is possible that nicotine is only a marker for another poison that causes the disease. However, the high pharmacological potency of nicotine compared to other constituents of tobacco, the similarity between symptoms of tobacco sickness and known nicotine intoxication, and the immunity displayed by nicotine-tolerant individuals, suggest that nicotine is the likely cause of this common occupational illness.

REFERENCES

1. Weizenecker, R., Deal, W. B. J. Fla. med. Ass. 1970, 57, 13.
2. Gehlbach, S. H., Williams, W. A., Perry, L. D., Woodall, J. S. J. Am. med. Ass. 1974, 229, 1880.
3. Gehlbach, S. H., Williams, W. A. Unpublished.
4. Johnston, L. M. Lancet, 1942, ii, 742.
5. McKennis, H., Jr. in Tobacco Alkaloids and Related Compounds (edited by U. S. von Euler); p. 53. Oxford, 1965.
6. Isaac, P. F., Rand, M. J. Nature, 1972, 236, 308.

ASSESSMENT OF OUTCOME AFTER SEVERE BRAIN DAMAGE

A Practical Scale

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Summary Persisting disability after brain damage usually comprises both mental and physical handicap. The mental component is often the more important in contributing to overall social disability. Lack of an objective scale leads to vague and over-optimistic estimates of outcome, which obscure the ultimate results of early management. A five-point scale is described—death, persistent vegetative state, severe disability, moderate disability, and good recovery. Duration as well as intensity of disability should be included in an index of ill-health; this applies particularly after head injury, because many disabled survivors are young.

Introduction

MANY patients now survive illnesses which would previously have proved fatal, especially those associated with acute failure in one bodily system or another. In most systems survival is followed by good recovery, and, even if functional reserve is subsequently diminished, the patient can usually accommodate to this. But when the brain is the organ affected, the persisting disability usually comprises both mental and physical handicaps which can seriously impair the quality of life. This makes the assessment of outcome after brain damage a matter of some complexity, calling for the exercise of considerable effort and skill. In practice the state of health of survivors is often described in vague terms which make it difficult to judge what degree of recovery has really occurred.

Need for a Scale

The outcome of serious illness concerns not only the patient and his family but therapeutic teams and the whole community. As medicine becomes more expensive, and major illness increasingly the corporate concern of society rather than a private contract between patient and physician, there is growing awareness of the need to assess the results of different types of management. In cases of brain damage, not only is the initial treatment dependent on the use of scarce resources, but the outcome may be permanent disablement which requires continuing social support. If measures of the efficacy of health services are to take account of humanitarian benefits, as well as economic costs and benefits, then some attempt must be made to measure the quality of life. The Institute of Social

DR GEHLBACH AND OTHERS: REFERENCES—*continued*

7. Garrod, J. W. Personal communication.
8. Langone, J., Gjika, H. B., Van Vunakis, H. Biochemistry, 1973, 12, 5025.
9. Welcher, F. (editor). Standard Methods of Chemical Analysis; vol. II, part A, p. 1091. Princeton, N.J., 1963.
10. Travell, J. Ann. N.Y. Acad. Sci. 1960, 90, 13.
11. Bisset, G. W., Lee, J. Lancet, 1958, ii, 715.

and Economic Research at the University of York has proposed that a " state of health " indicator should be devised.[1] It has been observed elsewhere [2] that indices of health which are intended to be applicable to illness in general are likely to have limited practical value, and that the only way to make progress in this complex area is to deal with one problem at a time. This paper considers the special case of brain damage in the light of the principles propounded by the York workers.

Quite apart from the needs of those who plan health services and of those who hold the purse-strings, those who treat the critically ill are anxious to know the results of their efforts, for their morale depends crucially on some assurance that their endeavours have a reasonable chance of success; and this depends on knowing what has happened to previous cases of the same kind. It is now widely recognised that success should be measured less by the fact of survival and more by the quality of survival—but quality is an ill-defined concept.

On scientific grounds we need to have a reliable assessment of the ultimate outcome after alternative methods of management. Soon after the demonstration that improved respiratory care for unconscious patients could considerably reduce the mortality-rate after severe head injury, it was stated that " the majority of patients who recovered have developed little in the way of severe mental symptoms . . . and most will be fit to return to productive work and will not remain a burden on their family or the community ".[3] That has proved to be an over-optimistic speculation.

Much of the difficulty which doctors experience in making decisions about brain-damaged patients, both in the acute stage and during recovery, results from uncertainty about the outcome. If this could be reliably predicted, then management decisions could be based on logical grounds; definition of outcome is the first step towards making possible the prediction of outcome.[4]

Existing Systems

Outcome is usually described in terms of a restricted number of exclusive categories, some of which inevitably include patients with a wide range of disabilities. Thus Vapalahti and Troupp [5] recognised only two types of survivors—vegetative existence or recovery. Carlsson [6] subdivided patients who were better than vegetative into those with " persisting dementia " and those who underwent " mental restitution ". This latter category included patients who had considerable physical disability but who were able to resume some kind of work or to participate in active rehabilitation; such a class obviously spans most degrees of persisting disability. Understandably, as many patients as possible are put in the best category of recovery; even the word " excellent " can sometimes be found to include patients with persisting hemiplegia if they can be judged to be " fully active ". Terms such as " practical ", " useful ", or " worthwhile " to define recovery are usually euphemisms which conceal major and persisting disabilities. A tendency to optimism about outcome is understandable in those who have worked hard to save the patient's life in the

CLASSIFICATION OF OUTCOME IN HEAD INJURY SURVIVORS

Classification	Outcome categories
Carlsson et al.[6] ..	Persisting coma; persisting dementia; mental restitution
Pazzaglia et al.[7] ..	Prolonged coma; partially reintegrated; recovered
Heiskanen and Sipponen[8]	Permanent invalid; recovery
Vigoroux et al.[9] ..	Serious sequelæ; nil/slight sequelæ
Overgaard et al.[10] ..	Apallic; severe deficit; good recovery
Vapalahti and Troupp [5]	Vegetative existence; recovery

acute stage; even a modest degree of recovery may seem impressive when compared with the original state of life-threatening coma. The patient, remembering only how well he was before his injury, is unlikely to share the satisfaction of his doctors when he finds himself left with serious permanent disability. But, even when late assessment is made by other doctors, disability may be underestimated, usually because routine interview fails to reveal the extent of the mental handicap. On the other hand, it is possible to be unduly pessimistic, especially if too much attention is paid to minor persisting abnormalities revealed by neurological examination: there may be some evidence of persisting brain damage, but if this is limited to, say, exaggerated reflexes or nystagmus, the phrase " permanent neurological signs " can overstate the case. The most confusing aspect about outcome is the wide range of terms used. Six recent papers on outcome after head injury have only one term which appears more than once, and that is the rather vague word " recovery " (see table).

Nature of Disability in Survivors of Brain Damage

Two characteristics of brain damage complicate its assessment. One is the combination of mental and physical features, and the other is the prolonged time scale during which recovery appears to continue. Both characteristics were emphasised by Miller and Stern,[11] who found that many patients considered unlikely ever to work again on the basis of examination 3 years (mean) after head injury, had in fact done so when re-examined 11 years (mean) after injury. These were not an unselected sample, having all been encountered in medicolegal practice; however, no-one would disagree that improvement, particularly in neurological signs, may continue over a long period. Neither the duration of active recovery nor its underlying mechanism has been defined; it seems likely that improvement in social reintegration many years after brain damage may be partly, if not wholly, due to adaptation to a fixed disability rather than to organic recovery. Until reliable recovery curves have been constructed it is difficult to indicate at what interval after injury ultimate outcome should be assessed.

The combination of mental and physical handicap not only complicates assessment but also tends to make the total disability greater than the sum of its parts. This seems likely to be due to interaction between the two components of the disability; either the mental or the physical symptoms alone might be well compensated for, but when occurring together the capability of coping with each is reduced. Clinicians are apt to underestimate the mental sequelæ in these

patients, for one or more reasons. Some such patients are euphoric and make little of their disability, whilst the extent of personality change, the commonest and most disabling sequel, may emerge only when relatives or close associates are questioned. Intellectual and cognitive deficits may be overlooked in a brief clinical interview, but may be revealed by formal psychometric testing. Yet it is mental sequelæ which prove more disabling than physical in most patients.[11-13] Indeed, neurological sequelæ, such as spasticity, hemiplegia, ataxia, and dysphasia, show a strong tendency to recover in time, albeit on a scale of years rather than months. Epilepsy is another important cause of disability and it may occur in patients who have otherwise made a good recovery. Although about a third of patients with severe head injury also have one or more other injuries, these rarely contribute to persisting disability.

Among a series of adult survivors of severe head injury treated in the acute stage in the department of neurosurgery in Glasgow, we found that most who were disabled had a combination of mental and physical disability; mental disability was usually dominant and was sometimes unaccompanied by neurological signs, whereas it was rare to find serious physical disability without some mental symptoms. All patients with more than 3 weeks' post-traumatic amnesia had persisting mental handicap of some degree. Using a scale of social disability, one of us (M. B.) showed that mental symptoms were more closely related to the social outcome than was physical disability.[13] And among mental symptoms it was personality change or cognitive deficits which were the main sources of difficulty, whereas symptoms of mental illness (depression or anxiety) seldom contributed significantly to a patient's difficulties.

In children it is less easy to assess outcome on the mental side because the child is growing and cannot be expected to regain his former status, especially if assessment is deferred for a year or more. During this time there may be changes in family relationships, partly resulting from the development of brain damage by the patient. A careful investigation of children who suffered focal brain damage due to a compound depressed skull fracture revealed a high incidence of psychiatric disorder persisting more than 2 years after injury [14]; few of these children had neurological signs or would be classified as being severely damaged (in terms of initial duration of altered consciousness).

Principles of Assessment

The York economists have suggested that in assessing the outcome of any major illness three separate steps should be taken. Indicators of health should first be specified, then measures devised to assess the patient's state in relation to these indicators, and lastly values should be agreed for different states of health.[1] The indicators suggested can be briefly enumerated, with comments on their applicability to brain damage.

Removal of threat to life is an obviously favourable outcome. The attraction of death or survival as indices of failure or success is that they are so easy to measure; but with the brain-damaged patient the question of whether the life saved is a life worth living makes survival an imperfect yardstick. Moreover, when evaluating the efficacy of measures for dealing with brain damage, even so obvious an outcome as death can be misleading, because it may be ascribed to other causes, such as underlying disease in another system or to other injuries.

The relief of symptoms is perhaps the most difficult aspect of assessment after brain damage because the patient often lacks insight and may even deny disability, especially in the mental sphere.

Reduction in dependency is relatively easy to measure because it is reflected in statistics about duration of stay in varying types of hospital bed. Progression through stages of lessening demand for care certainly provides a series of short-term goals, but these may obscure long-term results. Discharge alive from an intensive-care unit is a reasonable achievement for the staff of that unit; likewise discharge from acute wards, assessment units, mental hospitals, or geriatric units. But such statistics require careful scrutiny in order to discover the ultimate result.

Social reintegration, usually indicated by return to work, is frequently used as a measure of recovery. The variety of possible occupations (including " housewife ") makes this a crude measure because both return to work and failure to do so may depend on circumstances other than the state of health. Work also reflects a narrow concept of social reintegration, which should include the effect of persisting disability on other activity.

Glasgow Outcome Scale

For practical purposes it is essential to have a limited number of exclusive outcome categories, accepting that some will include patients with a range of different degrees of disability. The following five categories have proved practicable.

(1) *Death.*—This might seem to require no further definition, but agreement must be reached on what conditions should be met before ascribing death to brain damage. This can be difficult after head injury, when other major injuries and extracranial complications are common, and when coma complicates major systemic disease which may itself cause death, perhaps after initial recovery from cerebral symptoms. This problem can be met by accepting only deaths within a limited time interval as indicating a fatal outcome from a particular incident. Most deaths ascribable to primary brain damage, especially after head injury, happen within 48 hours.[15] But with intensive therapy patients may survive in a vegetative or severely disabled state and die after weeks or months; although such deaths may technically be ascribed to pneumonia, it would be deception to deny that they are due to the original brain damage. One device is to subcategorise deaths which have occurred after the patient has regained consciousness, regarding this as evidence of initial recovery from the incident of brain damage.

(2) *Persistent vegetative state.*—This is the least ambiguous term to describe patients who remain unresponsive and speechless for weeks or months until death after acute brain damage.[16] After 2–3 weeks they open their eyes and have cycles of sleeping and waking, which makes it inappropriate to describe this state as prolonged coma; nor is akinetic mutism an accurate label, because that term is used also for patients who respond at a much higher level, and who have potential for recovery. Although vegetative patients show an absence of function in the cerebral cortex, as judged behaviourally, the cortex may be

structurally intact. In such cases the lesion is in subcortical structures of the cerebral hemisphere or in the brainstem, or more often in both. It was for this reason that Jennett and Plum[16] considered the term " apallic syndrome " an inaccurate one to describe this state.

(3) *Severe disability* (*conscious but disabled*).—This is used to describe patients who are dependent for daily support by reason of mental or physical disability, usually a combination of both. Many will be in institutions, but this should not be a criterion, because exceptional family efforts may enable such patients to be looked after at home. It is important to recognise that severe mental disability may occasionally justify this classification in a patient with little or no physical disability.

(4) *Moderate disability* (*disabled but independent*).—Such patients can travel by public transport and can work in a sheltered environment, and are therefore independent in so far as daily life is concerned. The disabilities found include varying degrees of dysphasia, hemiparesis, or ataxia, as well as intellectual and memory deficits and personality change. These may produce considerable family disruption. Notice that independence is of a greater degree than that commonly described by geriatric physicians and others under the title " activities of daily living ", which usually refer only to ability to maintain self-care within the patient's room or house; those able to do only that would be judged as severely disabled on the present scale.

(5) *Good recovery*.—This implies resumption of normal life even though there may be minor neurological and psychological deficits. Return to work is regarded as an unrealistic index of recovery, because it may lead to false impressions in either direction. Local socioeconomic circumstances may make it difficult for anyone who has been seriously ill to return to work, even though fully recovered. On the other hand, some patients with considerable disability may be fully employed, either because their work is compatible with their particular disability, or because their employers are showing generosity by providing what really represents sheltered employment. Other aspects of social outcome should be included in the assessment, such as leisure activities and family relationships.

Time of Assessment

When outcome is assessed the time after presentation should always be stated. During the first year or so an increasing number of those left vegetative or severely disabled will die; on the other hand, some severely or moderately disabled will reach a better state of recovery in time. Serial studies should enable recovery curves to be constructed by which to define the interval after which it is unlikely that the outcome category will change, even though there may be substantial improvement within it. This interval may be different for the two ends of the scale. We found that more than a third of those who were severely disabled 3 months after head injury had improved to moderate disability by one year, but not one had made a good recovery. A third of those still

moderately disabled at 3 months were good by 12 months. Over 80% of those who had improved on their 3-month outcome category by 1 year had already achieved the higher grade within 6 months of injury. The time scale of recovery may also be different for the various components of the disability. Neurophysical features, such as spasticity and dysphasia, may go on improving for years, but serial psychological testing indicates that most recovery in cognitive function happens within 12 months.[17]

Practical Applications of the Scale

This scale has been used for some years and we have found a good measure of agreement between different assessors. It has been adopted by a number of centres which are collaborating in a study of the outcome of coma due to various types of brain damage; a close correspondence has been found between the proportions of patients in each outcome category in each centre, given groups of patients with similar initial severity of damage. A measure of flexibility is possible within this framework of outcomes, either by collapsing the scale, or by making subdivisions within the main categories. In those with severe or moderate disability it may be useful to indicate whether the mental or physical aspect predominates, and what the components of each disability are. This would enable recovery within a major outcome category to be recorded and the influence of rehabilitation to be studied. Whether death and the vegetative state should be regarded as a single category raises philosophical issues; there is a case for regarding the vegetative state as death anticipated, because few vegetative patients survive more than a year or so; for the purpose of predicting outcome 3 months after brain damage it is practical to consider them together. It would, however, be wrong to consider the vegetative state and the severely disabled together because a proportion of those severely disabled in the early stages may improve to a better category of outcome.

Discussion

With the range of disabilities which is possible after brain damage it is difficult to compromise between descriptive terms which are practical and those which are accurate. But unless a practical scale is adopted, there is a danger that the real size of the problem of persisting disability may remain concealed beneath a blanket of euphemisms. Not only do these hide a problem which calls for solution in terms of providing adequate rehabilitation and continuing care, but they make it difficult to evaluate the influence on outcome of newly developed methods of management in the acute stage. Some of these could consume valuable resources of staff and equipment, and this makes it important to assess the relative efficacy of such measures in comparison with less costly alternatives. This can be done only if there is an agreed scale by which to assess initial severity and ultimate outcome. One useful guide to initial severity is the depth and duration of coma, and it was to record this that the Glasgow coma scale was evolved.[18] The outcome

scale described here is designed to complement the coma scale, in order to provide the basis for a predictive system.[4,19,20]

In assessing the severity of disability it is important to take account of duration as well as intensity.[1] The influence of duration assumes particular significance after brain damage because many survivors are young, having sustained head injury in road accidents. Those left severely or moderately disabled therefore face many years of handicap and perhaps dependence. Brain damage at 25 is not only more devastating than at age 65 in its emotional impact on those who witness it; it is also more significant in measurable economic terms. On the scale of intensity of ill-health proposed by the York economists, death occupies the bottom place, with unconsciousness just above it. For the present argument the vegetative state is equivalent to unconsciousness; for the person affected this is presumably no different from death. But for the family and those tending the patient, vegetative survival may be judged " worse than death ", in humanitarian terms, because of the continuing distress which this state causes to those who witness it. In economic terms it is certainly more costly than death, because complete dependence can last many months and sometimes years.

The importance of ascribing a utility (value) to states of ill-health of varying severity has been stressed by Card and Good.[21,22] This can be done by ranking different aspects of illness (or disability), using a group of doctors with experience of the condition under study to pass judgment. Card has shown the practicality of this approach as a means of discovering what elements of an acute attack of ulcerative colitis are considered to contribute to total severity.[23] There was good consistency between different doctors' judgments, and from their recorded rankings their implicit utilities for various features could be deduced. A similar exercise could provide a guide to the relative weights which are ascribed to different aspects of neurological disability, such as hemiplegia, dysphasia, impaired memory, and personality change. There is no new principle involved in ranking disabilities nor in ascribing a monetary value to them, because this is the basis of compensation for industrial and military injuries, where the loss of an eye, a thumb, or a leg each has a specific value ascribed to it. Once values are ascribed to different outcomes it becomes possible to consider the cost-benefit approach to the management of brain-damaged patients; as Williams[24] stresses, this should take account of humanitarian as well as material costs and benefits.

It is hoped that the scale proposed will enable outcome after brain damage to be more readily assessed, and that it will stimulate study of major persisting disabilities, and of means whereby they might be reduced. It will at least provide a measure by which such means could be tested as they become available.

GALLBLADDER DISEASE IN HYPERLIPOPROTEINÆMIA

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Summary The occurrence of gallbladder disease (G.B.D.) (cholelithiasis, cholecystitis, cholecystectomy) was examined in patients consecutively admitted because of hyperlipoproteinæmia types IIa and IV. Altogether 37 of the 52 patients with the type IIa pattern were women, whereas 56 of the 75 subjects with hyperlipoproteinæmia type IV were men. The overall incidence of G.B.D. in the group with the type IIa was 13% in the males and 22% in the females; the corresponding figures in type IV were 41% and 68%, respectively. The findings in the major age-group (40–59 years) were compared with those from three necropsy series covering subjects of the same age. The incidence of G.B.D. was then found to be normal in type IIa but abnormally high in type IV. Patients with and without G.B.D. did not differ with regard to body-weight or glucose tolerance.

Introduction

CHOLESTEROL gallstone in man is associated with abnormalities in the relative concentrations of the major biliary lipids. In general, the bile is saturated or supersaturated with cholesterol, possibly owing to a dual defect of increased secretion of biliary cholesterol[1,2] and a reduced size of the bile-acid pool.[3–5] The administration of chenodeoxycholic acid, which results in enlargement of the chenodeoxycholic-acid pool size, has proved to be a useful way of dissolving

PROFESSOR JENNETT, PROFESSOR BOND: REFERENCES

1. Culyer, A. F., Lavers, R. J., Williams, A. *in* Social Indicators and Social Policy (edited by A. Shonfield and S. Shaw); p. 94. London, 1972.
2. *Lancet*, 1973, i, 1293.
3. Maciver, I. N., Frew, I. J. C., Matheson, J. G. *ibid.* 1958, ii, 554.
4. Jennett, B. *Clin. Neurosurg.* 1972, 19, 200.
5. Vapalahti, M., Troupp, H. *Br. med. J.* 1971, iii, 404.
6. Carlsson, C.-A., von Essen, C., Löfgren, J. *J. Neurosurg.* 1968, 29, 242.
7. Pazzaglia, P., Frank, G., Frank, F., Gaist, G. *J. Neurol. Neurosurg. Psychiat.* 1975, 38 (in the press).
8. Heiskanen, O., Sipponen, P. *Acta neurol. scand.* 1970, 46, 343.
9. Vigoroux, R. P., Baurand, C., Naquet, R., Chament, J. H., Choux, M., Benayoun, R., Bureau, M., Charpy, J. P., Clamens-Guey, J. *in* Head Injuries; p. 335. Edinburgh, 1971.
10. Overgaard, J., Christensen, S., Hvid-Hansen, O., Haase, J., Land, A.-M., Hein, O., Pedersen, K. K., Tweed, W. A. *Lancet*, 1973, ii, 631.
11. Miller, H., Stern, G. *ibid.* 1965, i, 225.
12. Fahy, T. J., Irving, M. H., Millac, P. *ibid.* 1967, ii, 475.
13. Bond, M. R. *in* Outcome of Severe C.N.S. Damage (*Ciba Fndn Symp.* no. 34). Amsterdam (in the press).
14. Shaffer, D. *ibid.*
15. Sevitt, S. *Injury*, 1973, 4, 281.
16. Jennett, B., Plum, F. *Lancet*, 1972, i, 734.
17. Mandleberg, I. A., Brooks, D. N. *J. Neurol. Neurosurg. Psychiat.* 1975, 38 (in the press).
18. Teasdale, G., Jennett, B. *Lancet*, 1974, ii, 81.
19. Jennett, B., Teasdale, G., Knill-Jones, R. *in* Outcome of Severe C.N.S. Damage (*Ciba Fndn Symp.* no. 34). Amsterdam (in the press).
20. *Lancet*, 1973, i, 523.
21. Card, W. I., Good, I. J. *Math. Biosci.* 1970, 6, 45.
22. Card, W. I., Good, I. J. *Br. med. J.* 1971, i, 718.
23. Card, W. I. *Jl R. Coll. Surg. Edinb.* 1971, 16, 388.
24. Williams, A. *Br. med. Bull.* 1974, 30, 252.