nm/PRELIMINARY NOTE

CEREBRAL DEATH: A RAPID AND RELIABLE DIAGNOSTIC ADJUNCT USING RADIOISOTOPES

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Intracranial blood flow was evaluated in ten comatose patients by monitoring cephalic passage of a radioactive bolus following intravenous injection. A deficit in cerebral circulation, which could be demonstrated at the bedside with relatively simple apparatus, together with absent cerebral electrical activity shown by electroencephalogram, may indicate cerebral death.

Advances in technology and medicine have made it possible to keep the human organism alive beyond the point when the brain, the essence of the human personality, has deceased. Prolonged efforts to maintain such "life" are a futile and wasteful drain of resources which could be used for those individuals who may still benefit from them. Furthermore the requirements of transplant surgery occasionally create a need for organ removal before the cardiac standstill.

Current criteria for the diagnosis of brain death (*1,2*) using the electroencephalogram (EEG) and clinical findings are open to criticism and require at least 24 hr observation.

It must be emphasized that patients may present all the signs of irreversible coma including isoelectric EEG and yet actually be in a reversible state.

A significant additional parameter which can greatly increase the reliability and probably decrease the time required to diagnose cerebral death is demonstration of the virtual absence of cerebral circulation. It has been shown angiographically (*3,4*) as well as by intracarotid injection of radionuclide (*5–7*) that individuals with "irreversible coma" have effectively lost cerebral circulation. This deficit is probably associated with severe degrees of cerebral edema (*3,8*); whether this edema is the cause or effect of the cerebral death is not known with certainty at this time. It is seldom practicable or justifiable to perform any but the most innocuous bedside procedures on these desperately ill patients undergoing extensive supportive therapy who may, or may not, be in irreversible coma. This report concerns the feasibility of demonstrating the lack of intracranial flow isotopically at the bedside using a portable scintillation probe and strip recorder to monitor the initial passage of an intravenously injected bolus of $^{99m}TcO_4^-$ through the head area.

MATERIALS AND METHODS

Although the appearance of time/activity curves of the initial head passage of an intravenous injected radioisotopic bolus in noncomatose patients is well established, a series of flow tracings in such patients were obtained partially in order to establish the technique. This was done by using a scintillation probe with an appropriate flat-field collimator. The output was recorded by a ratemeter and strip recorder. The lower edge of the collimator was placed half way along a canthomeatal line and angulated about 10–15 deg cephalad so that the lower edge of the field of view encompassed the cranial cavity only. The probe was placed in this way so that flow curves could be obtained simultaneously with conventional sequential gamma camera flow images in the anterior projection.

Ten patients in coma due to various causes were studied in a similar manner without foreknowledge of EEG findings. All but one patient had absence of spontaneous respiration as well as some degree of cardiovascular collapse requiring nor-epinephrine for maintenance of systemic blood pressure. All but one patient had systemic blood pressures of 100 mmHg or greater. In some of these cases it was also possible to perform the probe study with simultane-

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ous camera imaging as in the noncomatose patients. Correlation was made with etiology, clinical findings, EEG, and the ultimate fate of the patients as well as autopsy with special neuropathological examination when appropriate and possible.

RESULTS

Probe tracings on the noncomatose normal patients all showed the accepted pattern with a more or less sharp rise and fall of activity as the bulk of the bolus passed through the brain.

Five patients in coma with abnormal but active EEGs showed the usual evidence of intracranial blood circulation on camera imaging (flow and static). Their probe tracings all reflected the presence of intracranial blood flow (Fig. 1A) giving comparable tracings to the noncomatose patients. Five patients in coma with isoelectric EEGs and clear retrospective evidence of antemortem cerebral death all gave flow curves which were dramatically different (Fig. 1B) in that they showed no bolus effect. The time and rate of appearance of radioactivity was markedly impaired, the level of activity never approached that of the usual peak, and the activity showed no definite drop during the period of monitoring which was continued for 1 min following the intravenous injection of radioisotope. Gamma camera imaging also gave evidence of the absent cerebral circulation (*9*) on three of these patients examined simultaneously.

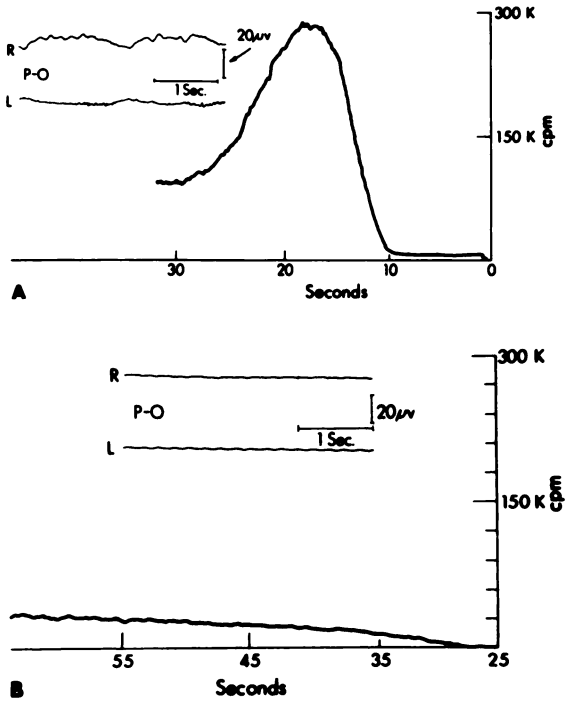

FIG. 1. (A) Patient was in deep coma because of episode of cerebral anoxia. Clinically, patient was never considered cerebrally dead according to Harvard criteria (*1*). Although abnormal, EEG shows activity. EEG (right and left parietal occipital leads, R,L,P-O) is shown in inset. Probe tracing on patient clearly indicates bolus effect of intracranial flow. Tracing is essentially indistinguishable from tracings obtained on normal noncomatose patients. Patient expired 2 days after study. Autopsy showed bronchopneumonia and purulent peritonitis; in brain, there was evidence of localized brain infarction only. (B) Patient was in coma secondary to transient cardiac arrest. EEG leads shown in inset are similar to those in A. EEG was "isoelectric", and patient was considered to have been cerebrally dead according to Harvard criteria. Probe tracing on same patient reveals no bolus effect. Gradual rise of radioactivity starting 25 sec after injection regarded as being due to extracerebral circulation. Note dramatic difference when compared to A. Patient expired with spontaneous and permanent cardiac arrest day after above study. Autopsy showed evidence of prior general brain death.

DISCUSSION

In view of the fact that the extracerebral blood probably accounts for a significant portion of the blood pool in the field of the detector (*10*), it may seem somewhat surprising that this does not appear to cause more confusion in the flow curves. However, head flow tracings represent the passage of a radioisotopic bolus through two different kinds of circulation; the large volume of flow through the relatively small cerebral blood reservoir causes a distinct registering of the passage (arrival and departure) of the radioactive bolus; this clear bolus phenomenon is absent in the relatively slower and dispersed extracerebral peripheral type of circulation.

The ability to demonstrate the lack of cerebral blood flow by means of an intravenous radioisotopic bolus, simply and safely at the patient's bedside would add a much needed parameter to the diagnosis of cerebral death (*11*). Although sufficient evidence is lacking at this time, it might seem logical that under the appropriate clinical circumstances the demonstration of absent cerebral blood flow and absent cerebral electrical activity over a defined period of time would together be diagnostic of cerebral death.

This pilot study is encouraging in that it suggests that the deficit in cerebral circulation associated with cerebral death could be simply and safely demonstrated at the bedside using a radionuclide procedure.

Since a mistaken diagnosis of "brain death" is absolutely unacceptable, mandatory rigid definable techniques and criteria must await more extensive study. A major modification concerns the simultaneous monitoring of the radioactive bolus in a part of the body other than the head; if this does not clearly indicate an adequate bolus injection, then the absence of a bolus effect in the head cannot be taken as meaningful. We are now in the process of a more extensive study using this and other modifications of the above technique and equipment.

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