Experimental studies have demonstrated a remarkable protective effect of glucose and procaine against injury to the central nervous system by contrast media. This protection was obtained by injection of the selected vascular bed with large doses of one or the other of these prophylactic agents immediately prior to the administration of the radiopaque medium. The present study was designed to test the possible clinical application of these experimental findings. Since the incidence of serious toxic reactions to carotid arteriography with newer contrast media is so low and unpredictable, the demonstration of a protective action in man was not considered as an appropriate goal. Rather, this present investigation had other objectives. The first was to determine the physiologic effects in man resulting from the intracarotid administration of glucose and procaine. The second was to establish whether this procedure affected the degree of filling of the cerebral vessels with the contrast medium.

METHOD

Laboratory studies had shown that maximal protection from contrast-medium injury was obtained with both glucose and procaine when these agents were administered 15 seconds prior to the injection of the contrast agent (70 per cent sodium acetrizoate). The lowest dose with which maximal protection was still obtained was 0.5 gm. of glucose and 10 mg. of procaine per kg. body weight. The optimal protective concentration for glucose was 20 per cent and for procaine, 0.5 to 1.0 per cent. The clinical tests, particularly with glucose, followed closely the procedures and dosage schedules established by animal experiments. Because glucose is free of potential convulsive effect and its physiologic and metabolic actions are more predictable, it was considered the agent of choice in these studies. Experimentally it has been established that the volumetric ratio of glucose to contrast medium affording maximal protection was 2.5:1. In order to insure that the exposed vascular bed in the clinical studies was covered completely by glucose this

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ratio was maintained or slightly exceeded, i.e., a total of 30 cc. of 20 per cent glucose and 8 to 10 cc. of contrast agent being administered.

A total of 45 patients with the presumptive clinical diagnosis of acute subarachnoid hemorrhage or brain tumor were studied. No patient with evidence of depression of consciousness or striking neurologic deficit was included in this series. Arteriography was performed by percutaneous puncture of the common carotid artery under local anesthesia (xylocaine—1 per cent). Bilateral arteriograms were obtained in 15 of these patients. The contrast medium used in all cases was 50 per cent Hypaque (sodium diatrizoate).

Preliminary studies were carried out in 33 of the 45 patients immediately before arteriography in order to determine the physiologic effects of the intracarotid administration of glucose and procaine. These patients were divided into three groups as follows:

1) Thirteen patients in whom continuous electroencephalograms were recorded during one or more intracarotid injections of 20 per cent glucose.* In 8 of this group continuous electrocardiographic recordings were also made. The electroencephalogram and electrocardiogram (lead 2) were recorded using a Grass model 111 D electroencephalograph.

2) Twelve patients in whom continuous measurements of arterial pressure were made during one or more intracarotid injections of 20 per cent glucose. Arterial pressure was measured through an 18-gauge needle in the opposite common carotid artery, using a Sanborn electromanometer.

3) Eight patients in whom continuous electroencephalograms were recorded during one or more intracarotid injections of procaine.†

The rate of administration of glucose varied between 1 and 2 cc. per sec. Procaine was administered in doses varying from 3 to 10 cc. and in concentrations ranging from 0.2 to 2.0 per cent. A total of 1 to 5 injections of procaine were given to each patient at 1- to 5-min. intervals. The rate of injection varied between 0.1 and 0.73 cc. per sec. These procaine doses were far smaller and the injection rates much lower than in the reported experimental studies.‡ The injection rate of the contrast agent was approximately 5 cc. per sec. All intracarotid injections were made manually by one of the authors (GTT). All studies were controlled by injecting saline in equivalent volumes and rates of administration.

The effects upon the arteriogram of glucose administered at specific intervals prior to the contrast agent were studied in 71 instances in 45 patients. These intervals, which were measured from the end of the glucose injection to the beginning of the injection of Hypaque, were 15, 30, 60 and 120 sec. For each study one or more selected time intervals were used and a comparison was made of the test arteriogram and control arteriograms, which were obtained 2 min. preceding and 3 to 10 min. following the injec-

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* 20 per cent glucose in water (Abbott Laboratories).
† Solutions prepared by dissolving crystalline procaine HCl in isotonic saline.
EFFECT OF PROCAINE AND GLUCOSE IN ARTERIOGRAPHY

The effect upon cerebral arterial circulation time of glucose administered 15 sec. prior to Hypaque was studied in 3 cases, using a Sanchez-Perez automatic seriograph. In each of these studies a total of six films at 1-sec. intervals starting from the initiation of the injection was obtained. To determine whether a retrograde carotid flow of the contrast agent resulted from the administration of glucose, a 14 X 17 inch anteroposterior film encompassing the head, neck and upper thorax was made in 5 patients. In this series the interval between glucose and Hypaque was also 15 sec.

The projected studies of the effect of the intracarotid administration of procaine upon the arteriogram and arterial pressure were not carried out because of toxic manifestations encountered during preliminary phases of the investigation of this agent.

RESULTS

A. Clinical Effects of Intracarotid Administration of Glucose. Glucose produced no marked electroencephalographic or electrocardiographic changes. Minor electroencephalographic changes occurred on 5 occasions in 4 patients during or immediately following injection. These changes consisted of slowing in 2 cases, an increase in fast activity in 1, and suppression of alpha frequency on 2 occasions in another. Mild electrocardiographic alterations, consisting of sinus bradycardia, were seen on 3 occasions in 2 patients during the injection. Two of the 12 patients showed a rise in systolic and diastolic blood pressure greater than 20 mm. Hg after the administration of glucose. This alteration in blood pressure was accompanied by a bradycardia in each instance. These changes did not occur when an equivalent volume of saline was injected into the carotid artery at the same rate as glucose.

The subjective response of the patient during the intracarotid administration of glucose consisted of an unpleasant burning sensation in the face on the side of the injection, accompanied by flushing of the skin and hyperemia of the conjunctiva. These changes developed within 10 to 20 sec. after beginning the glucose injection and persisted for 30 to 60 sec. after completion of the injection.

B. Effect of Intracarotid Administration of Glucose on the Arteriogram. Glucose injected at 15- and 30-sec. intervals prior to Hypaque affected adversely the degree of radiographic contrast of the internal carotid system in 38 out of 44 tests (Fig. 1). In 6 of the 38 instances, no radiopaque material could be seen in the internal carotid system intracranially (Fig. 2). The effect of glucose was considerably diminished when the interval was lengthened to 60 sec. and absent at the end of 120 sec.

The serial radiological studies demonstrated no significant alteration of cerebral arterial circulation time by glucose. Nor was there evidence of a
retrograde carotid flow of contrast agent following glucose in the patients studied with large roentgenograms.

C. Clinical Effects of Intracarotid Administration of Procaine. Procaine caused seizures in 3 of 8 patients studied. A severe generalized convolution was produced in 1 patient by the injection of 10 cc. of 1 per cent procaine at the rate of 0.4 cc. per sec. and a focal motor seizure occurred in another following the injection of 10 cc. of 0.2 per cent at the rate of 0.25 cc. per sec. In the third patient a mild focal motor seizure following the injection of procaine was not accompanied by significant electroencephalographic changes. There were no striking clinical or electroencephalographic changes in the remaining 5 cases.

![Image of arteriograms](image-url)
DISCUSSION

The intracarotid administration of 20 per cent glucose in the volume and rates of injection used in this study is nontoxic as shown by the absence of significant electroencephalographic and electrocardiographic changes accompanying the injections. Although a significant alteration in arterial pressure occurred in 2 of the 12 patients, the change was transient and not associated with any untoward symptoms. A total of 132 intracarotid injections of glucose were made in 45 patients without the occurrence of a single neurologic complication. These observations are consistent with those of Broman and Olsson who found that the intracarotid administration of 25 per cent glucose in rabbits caused no impairment in the blood-brain barrier.

However, it was also shown in the present study that the intracarotid injection of 20 per cent glucose had an adverse effect on the quality of the arteriogram. The degree of contrast of the cerebral vessels was consistently diminished when the injection of Hypaque was made within a brief time interval following the administration of glucose. This effect was maximal at 15 sec. and persisted as long as 60 sec. The majority of these arteriograms were not considered to be of diagnostic quality. In a few cases there was a complete lack of filling with contrast medium of the internal carotid system. The reason for this effect of glucose on the arteriogram is not clear. It is possible that it is caused by a decrease in vascular resistance of the ipsilateral external carotid system following the injection of glucose. As shown in this study, there is a marked vasodilatation of the face on the side of injection, which has its onset 10 to 20 sec. after starting and which lasts for 30 to 60 sec. after completing the injection of glucose. Theoretically, this would provide a larger vascular bed for the contrast agent to flow into which would reduce the quantity (and the degree of contrast) reaching the intracranial arteries. This possibility is strengthened by the observation that the period during which poor contrast of the internal carotid artery and its branches is obtained coincides with the time during which the cutaneous vasodilatation occurs. Whether the intracarotid injection of glucose causes a concomitant vasodilatation of the internal carotid system also is not known.

Our results in a limited number of patients, all of whom were conscious, imply that because of its convulsive action, the intracarotid administration of procaine has no place as a prophylactic agent in cerebral arteriography. Brehm et al. concluded from the results obtained in 100 patients under general anesthesia that the intracarotid administration of 20 cc. of 1 per cent procaine in a 20-sec. period was relatively safe. However, it is difficult to accept this conclusion since 22 of their patients became apneic for 1 to 3 min., 10 showed evidence of cortical irritation, and 6 had a fall in blood pressure following the injection of procaine.

The present clinical study suggests that the protective action of glucose against experimental contrast-medium injury to the spinal cord may reside largely in a shunting of radiopaque media away from the vascular bed of the nervous system. If this is subsequently shown to be the mechanism of pro-
tection, then the administration of glucose prior to angiographic procedures other than cerebral arteriography is desirable. The well known instances of severe injury to the spinal cord in clinical\textsuperscript{3} and experimental\textsuperscript{5,7} aortography illustrate the potential value of this protective action.

SUMMARY

Because of the experimentally demonstrated protective action of glucose and procaine against contrast-medium injury to the central nervous system, clinical tests of these agents in cerebral arteriography have been made. Particular study has been made of electroencephalographic, electrocardiographic, blood pressure and radiographic changes resulting from the use of these agents. The intracarotid injection of glucose produced no overt toxic or significant electroencephalographic or electrocardiographic changes. In 2 out of 12 cases, a significant rise in arterial pressure occurred during the injection.

However, arteriograms made at brief intervals following the intracarotid administration of glucose consistently showed diminished contrast of the internal carotid system. Because of this effect upon the diagnostic quality of the arteriogram, glucose cannot be used as an adjunct to carotid arteriography.

The intracarotid administration of 20 to 100 mg. procaine produced seizures in 3 of 8 patients. This agent was considered too toxic for further studies.

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