sharply after meal, reached the maximum level of about 50 mM around the end of the feeding time, and thereafter decreased gradually. As expected, the glucose concentration estimated by the specific enzymatic method was much lower than the free reducing sugar concentration, about 110 mM, reported by Cole[2], who examined only during the feeding time. The difference may be due to maltose, isomaltose and other reducing substances in the intestinal fluid.

Figure 2 shows the glucose absorption rate in vivo during the feeding time at various luminal concentrations of glucose either in the presence or absence of 0.5 mM phlorizin. The glucose absorption rate in the presence of phlorizin (phlorizin-insensitive component) increased proportionaly with increase in the glucose concentration in the lumen. The difference between the rates in the absence and presence of phlorizin (phlorizin-sensitive component) was saturable, and the half-maximal concentration of glucose was about 10 mM. The rate of the phlorizin-sensitive absorption was larger than that of the phlorizin-insensitive absorption up to the glucose concentration of about 35 mM, but above this concentration, the reverse is the case. These results are in good agreement with those reported by Debnam and Levin[1], and could best be explained by supposing that the phlorizin-sensitive component and the phlorizin-insensitive one represent the absorption via the active transport system and the diffusive pathway, respectively.

It has been reported that the digestive and absorptive functions of the small intestine exhibit circadian variations, synchronizing with the feeding-fasting cycle[5-9]. In preliminary experiments, the glucose absorption rate during the nonfeeding time (24.00–3.00 h) was found to be lower than that during the feeding time shown in figure 2 either when phlorizin was present or absent, but the ratio of active/passive absorption did not change at each concentration of glucose. All these results strongly suggest that glucose is absorbed mainly via the active transport system during the nonfeeding time when the luminal concentration is low, but a larger fraction of glucose is absorbed by the diffusive pathway during the feeding time because of high luminal concentration of glucose.

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Experimental hydrocephalus following mechanical increment of intraventricular pulse pressure[1]

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Summary. Experimental hydrocephalus has been induced in lambs by artificial increase of the amplitude of intraventricular cerebrospinal fluid (CSF) oscillations related to arterial pulsations, without concomitant changes of the mean CSF-pressure. The characteristics of this hydrocephalus demonstrate that the intraventricular CSF-pulsations can play a role in the genesis of ventricular dilatation. Such a method may be used to produce an original model of hydrocephalus independent of changes of CSF-circulation or absorption.

Cerebrospinal fluid (CSF)-pulsations have been recognized for many years[3]. Their origin has been related to the arterial pulse waves[4-9] or to the venous pulse waves[10,11], or to a combination of both[12,13]. Bering[6] suggested that CSF-pulsations, as well as CSF-circulation, depend entirely on the pumping effect due to the choroid plexus systolic expansion. As the choroid plexus fills with blood, a local CSF-pressure wave is generated. This wave is normally absorbed in part by the ventricular wall, in part by pumping CSF out from the ventricular system and by compressing veins in the subarachnoid spaces.

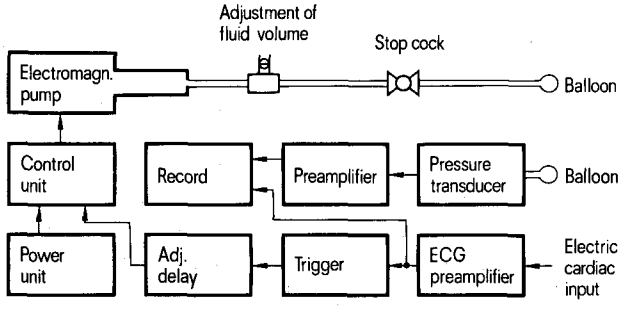

Fig. 1. Schematic drawing of the experimental electronic and hydraulic arrangement for producing and recording intraventricular CSF-pulses.

Bering[7] also stated that this local force generated by the choroid plexus accounts for the ventricular dilatation in a blocked ventricle, independently of the back pressure due to the arrest of CSF-flow. Experiments by Wilson and Bertan[14] supported Bering's thesis on the pathogenetic effect played by undamped pulse waves. In fact, the combination of intracisternal injection of lampblack and of occlusion of the anterior choroidal artery of one side in dogs, caused the enlargement of the ventricle with intact vascular supply and had no effect on the contralateral one. Milhorat[15] found that hydrocephalus invariably occurred in plexectomized monkeys in which ventricular obstructions of various types were performed, except in case of extensive plexectomy scars. On this basis, he concluded that the choroid plexus is not essential in generating a pulsatile mechanism for expanding the ventricle in the hydrocephalus. In dogs in which one foramen of Monro was plugged while the other one was pervious, Sybayan and al.[16] showed that the mean CSF-pressure was always higher in the blocked and dilated ventricle, so that the rise in the mean pressure could be considered 'a necessary factor responsible for ventricle enlargement'.

The aim of this report is to bring forward new experimental data suggesting the importance of abnormally high intraventricular CSF-pulsations in the development of hydrocephalus, even when the mean CSF-pressure

remains normal and the CSF-absorption pathways are patent. This purpose was satisfied by the use of a device[17] which allows an increase in the arterial CSF-pulse wave without modifying the mean CSF-pressure.

Materials and methods. 16 lambs weighing 8–10 kg were used. Both chronic and acute experiments were carried out. All animals were anaesthetized with Nembutal (25 mg/kg i.v.). Under surgical asepsis, a latex balloon connected with a catheter was inserted in each lateral ventricle. Recording of ventricular pressure was performed by connecting the right balloon to model 268 A Sanborn pressure transducer. Delivery of artificially increased pulsations was obtained through the left balloon. For this purpose, the left balloon was connected to a device described previously[17], which could rhythmically inflate and deflate it, synchronously with the cerebral pulse. The R-wave of the ECG was used as a trigger for the electromagnet power supply of the device. By modifying delay and duration (40–100 msec) of the signal which closed the supply circuit to the electromagnet (figure 1), the summation in phase of both the spontaneous arterial CSF-pulsation and the artificial pulse occurred. Intraventricular mean pressure remained steady when the increased pulses were 2 times higher than the physiological ones (figure 2). However, a small increase in ventricular mean pressure occurred for amplitudes 3–4 times larger: by subtracting an adequate amount of fluid from the pulsating balloon before beginning trials, the mean CSF-pressure was adjusted on the previous values. Intraventricular CSF-pressure and ECG were monitored by oscilloscope and photographed by means of a Grass camera.

In the acute experiments (3 animals), artificially increased pulsations were delivered in a unique period of 3 h, the animal being kept under Nembutal anaesthesia. In the chronic experiments (6 animals), the animals underwent artificial increase of CSF-pulsations for a period of 2 h every second day, for 2–3 weeks. At the end of each experimental session, the intraventricular balloons were disconnected by the recording and inflating apparatus, the head of the animal was carefully wrapped and the animal brought to the stabularium. In the first chronic animal, all recording sessions were made under light anaesthesia; in the other 2 cases, the animals were kept awake. They did not show any sign of pain or discomfort. Control experiments were carried out in 7 animals. In 2 of them (1 chronic, 1 acute), the pulsating balloons were placed in the nervous substance, in 1 case above and in other below the floor of the lateral ventricle. In the other

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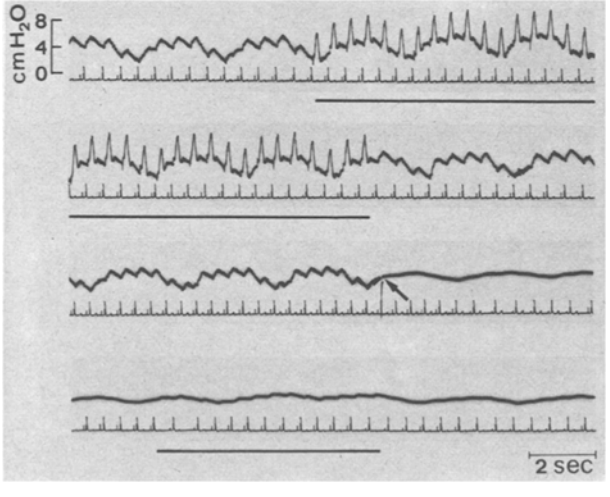

Fig. 2. Continuous recording of the intraventricular pulse and (starting from the arrow) mean CSF-pressure (upper tracing) and of the EKG (lower tracing) in a chronic lamb. The dark line indicates pump on. The artificial increase of intraventricular pulses does not influence the mean CSF-pressure.

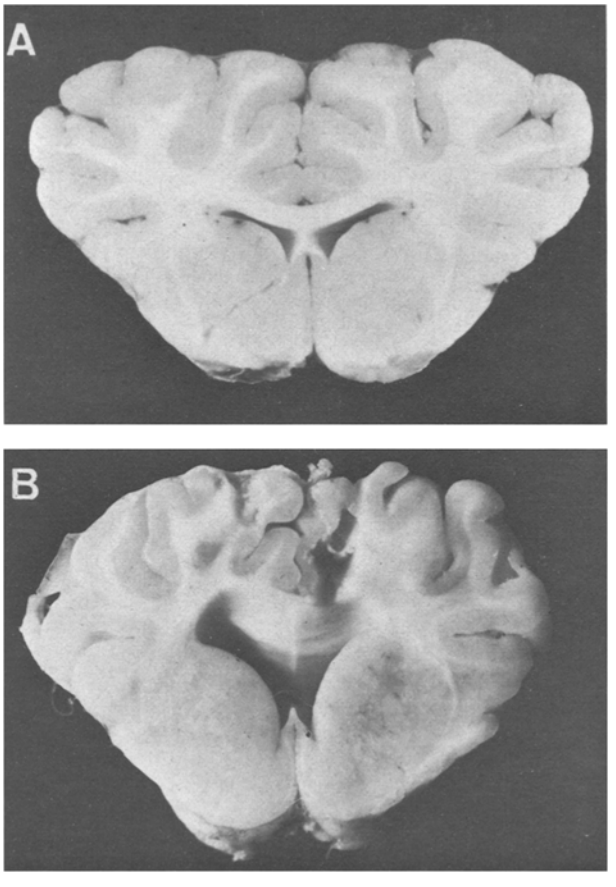

Fig. 3. Transverse brain sections at the level of the frontal horn showing normal ventricular size (A) in control animal, and ventricular dilatation (B) in chronic animals obtained through artificial increase of intraventricular pulses.

5 lambs (2 acute, 3 chronic) the balloons were kept inflated, within the lateral ventricles, for a corresponding period of time without any modification of the pulse wave. At the end of the experiments, the animals were sacrificed under deep anesthesia, and then the brains were carefully examined and fixed with 10% formaldehyde solution and sectioned for checking hydrocephalus. Histological studies were also performed in order to analyze the ependyma, the periventricular parenchyma and the CSF-pathways.

Results. Acute experiments. In 2 lambs which received pulses 3 times higher than the normal ones for 3 h, an ipsilateral ventricular dilatation of light degree occurred. The septum pellucidum was always deviated contralaterally. Histologically, the ependyma appeared to be interrupted mostly at the level of the frontal horn. In the only lamb which underwent trial with pulses 5 times higher than the normal, in addition to the anatomical changes described above, necrotic lesions of the periventricular parenchyma were found. In each animal, the subarachnoid spaces were patent.

Chronic experiments. A bilateral ventricular dilatation occurred in all animals (pulses 2–3–4 times higher than the normal). The ventricle containing the pulsatile balloon was larger than the contralateral one; the septum pellucidum was deviated contralaterally or frayed (2 cases). The frontal (figure 3B) and, to a less degree, the occipital horns were mostly dilated. The ependyma was interrupted, especially at the level of maximal ventricular enlargement. In 2 animals there was a dilatation of the IIIrd and IVth ventricles and of the aqueduct. In all cases CSF-pathways were patent at the histological control.

Control experiments. Acute and chronic animals in which the balloons were kept inflated did not show significant ventricular dilatation (figure 3A). At the same time, the ependyma was found normal at the histological examination. When the pulsatile balloon was extraventricular, a necrotic cavity was the only histological finding related to the mass lesion of the balloon; no ventricular dilatation occurred and the ependyma layer was intact.

Discussion. Attention has recently been paid to the intraventricular pulse pressure in the genesis of hydrocephalus on the grounds of findings obtained by prolonged intraventricular CSF-pressure recordings in hydrocephalic patients[18,19]. Abnormal high pulse pressure, either in basal conditions or – more evidently – during physiological sleep, was well correlated with the positive results of the CSF-diversion procedures in patients affected by normotensive hydrocephalus[20,21].

High intraventricular CSF-pulsation without any significant change in the mean intraventricular pressure have been produced in the course of the present investigation. The results of our experiments stress the role of the intraventricular pulsations in the genesis of intraventricular dilatation. This view is supported by the following data:

1. Consistent recurrence of ventricular dilatation in animals which underwent artificial increase of CSF-pulse pressure.
2. Lack of ventricular dilatation in animals with extraventricular pulsating balloons or with intraventricular nonpulsating balloons acting only as a mass.
3. Obvious relationship of the degree of ventricular dilatation to the duration of application of artificial pulse.
4. Asymmetrical dilatation of the lateral ventricle submitted to artificial pulsations.
5. Larger dilatation of the ventricular regions which received the maximum impact of the pulse wave (frontal and, for a less extent, occipital horns).
6. Dilatation of the distal portion of the ventricular system in chronic experiments.
7. Absence of obstructive lesions in the CSF-pathways.

Furthermore, we stress the importance of the above-mentioned method in obtaining an original model of communicating hydrocephalus without producing impairment in the CSF-absorption and/or circulation in the peripheral subarachnoid spaces.

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False interpretation of membrane transport data due to osmotic volume changes of cells

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Summary. It is shown theoretically that in a nonsaturable transport system across a cell membrane, the kinetical analysis yields (erroneously) apparent saturation kinetics if osmotic volume changes of the cell occur and are not taken into account. Experimentally this is illustrated for the case of exit of glycerol from beef erythrocytes.

One of the criteria in current use for the recognition of carrier mediation in membrane transport is saturability, as indicated for instance by a negative abscissa intercept in the double reciprocal plot of rate versus concentration (Lineweaver-Burk plot).

This plot is reliable and valuable if certain requirements are met. They include the condition that what is used for the abscissa of the plot are reciprocal values of actual concentrations and not, as happens occasionally, of amounts of penetrating substance per cell which are taken to represent intracellular concentrations, implying that the cell volume is constant. If concentrations are involved that are sufficiently high to elicit osmotic water shifts and, thereby, changes of the cell volume, then the use of quantities, rather than true concentrations, gives rise to systematical errors. For example, a nonsaturable transport system falsely appears to be saturable or, in the case of a saturable system, the Michaelis constant evaluated from the plot can be substantially in error (too low). It is the purpose of this communication to deal with this type of error, both by quantitative discussion of the underlying kinetical equations and by experimental demonstration.