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CRYOGENIC SURGERY.

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During the past half century a great deal of attention has been paid to methods of preserving tissues by low temperature, tissues both alive and dead. Understandably perhaps, less attention has been paid to the destruction of tissue by this means. And yet, theoretically, this method has many advantages over the more conventional ones used, most of which generate heat or at least give up energy in the area to be destroyed. .....

Tissue can be cooled to a degree which will slow or even stop its function without running any risk of permanent damage to cells. This usually takes place at some level above o°c and well above levels of tissue freezing temperatures. Lowering the temperature of a local area below its freezing point will result in destruction of most of the cells in this area. The process is well-localised and can be precisely predicted from the known parameters of the instrument used. The process is, in the best sense, haemostatic, and the risk of bleeding from damaged vessels, always present in blind cerebral lesions, must be minimal.

The precise way in which freezing destroys cells has been investigated by many skilled workers but still remains somewhat obscure. The older theories laid great stress on crystal formation and imagined that intra-and extra-cellular water formed crystals of ice and these, either at the time of formation or in he process of breaking up when reheated, pierced the cell membranes and so destroyed the cell. Present-day workers believe that this process is relatively unimportant in producing cell damage though, occasionally, such cell damage does occur. It has been shown, for instance, that the commoner course of events is for the extra-cellular water to form crystals whilst the cell supercools and water is progressively extracted from the cell. It has been shown that extracellular water can be repeatedly frozen without damage to cell membranes. Some cells can also be subject to repeated intracellular freezing without cell damage though the proportion of undamaged cells is lower. Such intracellular crystal formation usually follows rapid freezing.

Most cell damage following freezing is probably related to this process of cellular dehydration. When the extracellular water crystallises the super-cooled water within the cell is attracted to the outside to form crystals which are added on to those already present. As a result there is

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a concentration of salts within the cell, change in pH and finally denturation and dissolution of the lipo-proteins of the cell membrane.

The degree to which this process takes place, i.e. the number of cells destroyed in an area, depends therefore, on the rate of freezing, the absolute temperature and the length of time. Information on all these points is still not sufficiently complete to define the ideal conditions. In general terms relatively slow freezing would seem desirable, a period of time not more than two to three minutes and a temperature lower than - 15 °C.

Many methods of localised cooling are available and in my Department we have investigated three of these. 'Electronic' cooling using the Peltier effect in a Piezo-electric transducer seemed an attractive method. In practice, however, this proved to be a poor method to use. As with most cooling methods, the main problem is how to get rid of the heat extracted. The commercial elements available were of such a size that negated their inseration into the brain. Elements of sufficiently small size, even if we could have persuaded the manufacturers to make them, were of quite low power and probably incapable in their present form of producing the temperatures we desired.

The second method in general terms, is to take liquid at very low temperature to the area to be cooled and allow it to extract heat from the area by becoming converted into a gaseous form at body temperature. A convenient liquid for this purpose is liquid nitrogen which can be kept liquid at normal atmospheric pressure and has a temperature of - 196°C. This can be poured down a central tube in a brain probe, allowed to expand and gasefy at the lower end, thereby extracting heat from the surrounding tissue and the resultant gas can escape through a second outer concentric tube.

We constructed one of these probes and also a similar one on a slightly different principle, namely to pour the liquid nitrogen into a reservoir at the top of a silver rod and rely on conduction cooling of the tip. Both of these had certain disadvantages.

Firstly, liquid nitrogen has to be kept heat insulated and it is not easy material to handle. Secondly, to confine cooling to the probe tip very efficient heat insulation is needed on the shaft. This implies a third concentric tube completely evacuated which not only added to the bulk of the probe but also required repeated evacuation every few weeks.

We finally investigated a third method, that of using liquid material at room temperature and kept liquid by pressure. The gas we used was the ordinary commercial refrigerant Freon 22. This gas, in liquid form under pressure, was run down the outer of two concentric tubes at room temperature. At the lower end of the probe the two tubes were in communication forming an expansion chamber and the entry of the liquid gas to the chamber controlled by a simple valve. The liquid gas entering the chamber is exposed to atmospheric pressure, expands and vaporises and extracts the heat of vaporisation from the surrounding tissues. The gas so formed escapes up the central tube to air.

We found under these conditions that a very smooth control of temperature could be achieved by controlling the rate at which gas entered the chamber. The probe tip could be taken down to any temperature in vivo from body temperature to - 22°C and held at that level quite steadily. The shaft of the probe was self-insulated by the outer tube containing liquid gas at room temperature and cooling was confined to the area of the expansion chamber.

The area of tissue cooled or destroyed depends on the physical dimensions of the expansion chamber and on the temperature achieved at the tip of the probe. This latter is dependent on the volume of liquid gas vaporised in unit time. We found that with our probe we could achieve temperatures round about-22 °C under ordinary conditions. The temperature could be lowered by applying suction to the exhaust tube and thereby increassing the pressure gradient. The outside diameter of the probe is 2.3 mm. and the length of the expansion chamber 5 mm. With this we expect to destrory an area of about 4 by 7 mm.

Various animal experiments were carried out during the course of design of these probes and we found that we could make satisfactory lesions in the cat and rabbit by this means. We also repreated the experiments of the American and French workers and found that when a probe was placed in the vicinity of the third nerve nucleus in the cat we could produce reversible pupillary dilatation by cooling the area to +5°C without any permanent damage.

So far we have used this probe on 15 patients during the course of surgical treatment of Parkinsonism. In treating this condition we have been making a series of standard lesions in the anterior an dposterior portions of ventral oral nucleus. Those in the anterior part are intended to control tone and those in the posterior part tremor. Like many other workers in this field we have found that more posterior and inferior the lesion the better control there is of tremor. At the present time our most posterior lesion would be well to the posterior limit of the oral ventral nucleus and well below the anterior-positerior commissure line, somewhere, in fact, in the pre-rubral field.

The all-important factor in making stereotactic cerebral lesions is to have some estimate of the effect of such a lesion without inflicting permanent damage. We have normally used an insulated probe and made radio-frequency lesions, preceding the lesion by a period of stimulation. We found that whilst this method gave valuable information when one was in the wrong place, for instance, the internal capsule or sensory nuclei, the effects of stimulation in the right place were variable and less exact.

Using the cold probe we first take it down to +5°C and leave it there for two minutes. If the probe is correctly placed this results in cessation of tremor or improvement in limb tone, or sometimes both. The probe is then warmed again to body temperture and in most instances the tremor reappears or tone increases. This seems to be an excellent measure of the effect of the final destructive lesion. This is then made by taking the probe tip down to-22°C and keeping it there for five minutes. If the effect has been localised only, say to the arm, then the probe is moved in the appropriate direction and further test and destructive lesion made.

In the cases so far done there have been no ill-effects from the procedure other than those resulting from a lesion of any sort in the given area.

It is difficult to judge results from so small a series of cases but my impression has been that these cold lesions have been slightly less effective when compared with some 200 radio-frequency lesions in the same situation. I think that this is probably because the lesions are slightly smaller and we shall certainly consider enlarging the lesions by lowering temperature still further and leaving it for a longer time. It may even be necessary to enlarge the expansion chamber itself slightly to get a larger lesion.

The present probe is non-insulated but we are now considering both insulating the shaft and adding two micro-electrodes to the tip. In this way we should have a universal instrument with which one could make a trial lesion by cooling, assess the effects of stimulation and determine the position by micro-electrode recording as well as make destructive lesions by r.f. current or freezing.

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HEMIBALLISMUS FOLLOWING LATERAL THALAMIC LESIONS.

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To operate on a patient for one type of involuntary movement and leave him with another is disquieting to say the least. This has occurred six times in my series of 187 patients operated on for Parkinsonism and although four of them have been quite transient and cleared completely within two weeks, the basis of this complication would seem well worthwhile investigating.

In four of these patients, tremor and rigidity were abolished on the operated side and the general results of surgery were excellent. Within twelve hours a curious involuntary movement appeared in the upper limb and affected the leg also in one. This increased for three days or so and then improved so that at the end of two weeks all involuntary movement had stopped. Follow-up of at least a year in each case has shown that there has been no return of involuntary movement. In the fifth case movements appeared at the time of operation and were accompanied by high voltage spiky discharges in the E.E.G. In this case there was no improvement and the movements have persisted for over two years.

The movements are difficult to describe and vary from time to time. Mostly choreiform but with some athetoid element they conform to the usual description of ballismus but, as Purdon Martin has pointed out, are better described as hemichorea.

It seems well-established both from experimental work and clinical evidence in the spontaneous cases, that damage to the subthalamic nucleus is the basis for such an involuntary movement. Critical examination of this group, however, seemed to throw some doubt on this hypothesis.

The position of all lesions was carefully charted and the details of instrument settings and x-ray measurements were all double checked at the time of operation and subsequently. There seemed no basis for the belief that this was due to an error of technique and as you will see from the charts none of the lesions appeared to involve the subthalamic nucleus, most were a considerable distance away and the only one in which the lesion comes close to this nucleus, Case 6, did not develop hemichorea in direct relation to the operation.

Survey of brain sections of a large number of brains does not suggest that individual variation in position of nuclei could have lead to involvement of the subthalamic nucleus in more than one of these cases.

The only common factor in this group was that all were cases of

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long duration and slow evolution, two were post-encephalitic. The average age 44.6 years and length of history 17.6 years were significantly different from the group as a whole.

We developed the idea that at least two factors were operative here, the surgical lesion and other lesions produced by the disease. It is suggested that to produce hemichorea in these patients at least two lesions are necessary, the one accomplished by the disease, the other by the surgeon. Apparent confirmation of this hypothesis was strikingly provided at a later date by the sixth patient. An intelligent woman of 38 years of age and 11 years'history, her Parkinsonism was largely confined to one side and thalamic lesions resulted in an excellent result with return to near-normality. About nine months later, following a fall, chorea appeared in the hand and fingers and over the subsequent eighteen months has got gradually worse and now affects the leg. Further lesions in the lateral thalamic and capsular area have failed to improve or arrest the progress of her condition.

One might put this hypothesis in terms of logic and suggest that there is an inherent driving force which produces such involuntary movement. This is normally inhibited by other inputs, the whole forming an INHIBIT/AND switch. There are least two and probably many more, inputs to the inhibit line and these may form a simple OR switch. No output is possible from the 'ballismus' switch if any of the OR inputs are working.

It is interesting to speculate on the possibilities of treatment inherent in such a system. If the OR system only is present in the subthalamic nucleus then damage to this nucleus will result in hemichorea and the more severe the damage the more severe the chorea. If the INHIBIT/ AND system only is in the nucleus then partial destruction might produce hemichorea whilst total destruction would stop it. The same is true if both OR and INHIBIT/AND switches are within the nucleus.

I would suggest that the evidence I have presented to you suggests that part, at least, of the OR system is outside the subthalamic nucleus and probably in the lateral thalamic area. It would seem possible, as has been suggested elsewhere, therefore, that total destruction of the subthalamic nucleus is the rational treatment for such cases. I am not suggesting that this hypothesis represents an exhaustive analysis of the logic of such a system, the variations are numerous and it is undoubtedly a great deal more complex than I have suggested. I would hope, however, that the clinical evidence I have presented adds a little more weight to the suggestion that total destruction of the subthalamic nucleus would be worthwhile in such cases.

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TREATMENT OF INTENTIONAL TREMOR

BY

STEREOTAXIC SURGERY

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Attempts to produce tremor as a consequence of surgical lesions of the basal ganglia, the subthalamic nucleus, or the substancia nigra, have been unsuccessful. Reports concerning the production of pure parkinsonian tremor in animals are not reliable. Lesions involving the cerebellum or its efferent pathways produce an intentional tremor which persist as long as 230 days (Carpenter- Mettler). It is associated with ataxia and other asynergic disturbances. It is actually an established fact, that any lesion along the dentato-rubro-thalamic tract is followed by a contralateral or homolateral ataxia, which can be abolished or at least diminished by lesion within the pallidum.

(Fig. 1). Schematic drawing demonstrating the dentato-rubro-thalamic pathways. A lesion within this tract produce a contralateral intentional tremor.

(Fig. II). Stereotaxic lesion in the brachia conjuntiva of monkey produced an intentional ataxic tremor.

(Fig. III). In the same monkey a subsequent lesion within the pallidum releived the animal from his tremor.

Considering these phisiological facts it should be possible to abolish the intentional tremor by putting a lesion into the pallidum. A number of patients suffering from disseminated sclrosis have such a severe intentional tremor, that they are fully handicapped even in their usual living activities, such as dressing, eating and toileting. There are only five cases discribed in the literature, four cases are operated by Krayenbuhl and one by Cooper, unfourtunately there is no time to give further detail about there cases. But in whole the result are encouraging.

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