sodium luminal plus hyoscine plus hyperpyrexia and chills induced by intravenous typhoid vaccine. One might reasonably ask which of these elements in treatment has been the most important. Having regard, however, to the findings of various investigators in this field it is reasonable to assume that the important thing is the prolonged narcosis, however induced. I agree that a chemical interpretation should be possible, but I leave that to the bio-chemist who is to contribute to this discussion. At the moment I am interested only in the psychological interpretation. If it is true that the degree of forced dependence upon the environment is directly related to prognosis and that the amount of activity of the physicians and nursing staff are important factors in the recovery, does that not really mean that the important thing is to break down inhibitions and resistances in the nervous pathways and to encourage the patients by all possible means to make use of those nervous circuits which are more likely to lead to healthier thought and conduct? Why transcend the limits of ordinary physiological phraseology?

The authors go on to state:

"One of the greatest obstacles to the use of psychotherapy in schizophrenics is the defence which in the phase of narcosis is more or less completely broken through. A transference relationship is forced and serves as an avenue for the psychotherapeutic approach.

"Verbatim records of the productions of patients who have been subjected to this form of treatment have been of great value in understanding the dynamics of their psychoses. The apparent relaxation of the censorship produced by the drug allowed a free flow of significant material which later could be utilized for efforts at re-integration in the convalescent phase. We have been able to obtain from otherwise mute catatonics a history of significant precipitating factors which could be understood and correctly evaluated. Jelliffe applied the term 'drug analytic method' to this most helpful portion of the therapeutic scheme. He regards the technique as a valuable extension of our capacities for getting at and understanding repressed unconscious material.

"The stupor can be looked upon as an enforced or induced regression to the stuporous (or ante-natal) level. This deep regression furnishes the patient with the goal of his regressive yearnings. Once the avenue is opened, re-living in a friendly and protective environment can be promoted through successive phases of development and objects more in keeping with the demands of reality can be substituted."

Surely all that involved language simply means that prolonged narcosis may serve as a means of breaking down inhibitions and overcoming habits of thought and conduct which have been harmful; and that everything possible should be done to encourage readaptation to the environment with more successful modes of behaviour. It is clear, from all that has been written on the subject, that treatment by prolonged narcosis is not without its dangers; but it seems to me that it is in the possibility of readaptation to the environment which it affords that this method is worthy of consideration. It may succeed where attempts to attain the same end by other methods have failed. After all, is it not the case that recreations, games, outdoor employments, frequent and prolonged interviews and all methods of occupational therapy, to which we have long attached much importance, have the same end in view—viz., healthier adaptation to the real circumstances of life?

Biochemistry.

By J. H. QUASTEL, Ph.D.,

Biochemist, Cardiff Mental Hospital.

I WANT to speak of the work we have been doing in Cardiff on the metabolism of the nervous system. The work was carried out there because of the importance of the narcosis treatment. It seemed to us there a pity that a treatment such as

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that should be given up because of the considerable toxicity possible in relation to it. The research was undertaken to see if we could diminish the toxicity, at the same time seeking an idea as to how narcotics work. I ask that you will realize that the main substance burned by the brain is glucose. The dominant form of metabolism in the nervous system is connected with the breakdown of glucose and lactic acid, and this can be proved by experiment in the living animal and with brain-tissue *in vitro*. In doing experiments we are not able to carry out work with human brain, because we cannot get human tissue fresh enough, so we have to carry out experiments with animals. They are carried out in this way. We cut slices of the cortex of the brain as soon as the animal is dead, that is to say, within ten minutes of death the brain is out and slices have been cut. They are placed in a physiological medium in the presence of glucose, and we follow the metabolism of that tissue, which allows us to estimate the amount of oxygen being taken up by the brain. If luminal, chloretone, hyoscine or somnifaine be placed with the brain-tissue, then the respiration, instead of being at the usual level, starts lower down, and maintains a straight line. We wanted to see whether this action is reversible or irreversible. If the latter, then on removing the brain-slices from the narcotic it should no longer behave like a normal piece of tissue. Actually, when the brain-slice is removed and placed in Ringer solution, with no narcotic, the respiration goes up and becomes equal to that shown by the slice which had no narcotic. That is to say, the process is reversible.

It is important to start with the understanding that we are dealing with a biological phenomenon which is real and which is probably taking place *in vivo* in the intact animal, that it is not merely an artefact belonging to *in vitro* experiments. ·04% chloretone will bring about a diminution of this respiration from 15·6, which is a normal sort of figure, to 5·1; with 0·1% luminal it goes from 15·8 to 9. Mescaline, too, acts like a narcotic and the effect is quite reversible.

Is this specific for an animal? These results were obtained with guinea-pig brain; the respiration was 90% with guinea-pig, 91% with cats, 87% with rabbits, 86% with the mouse, 90% with sheep, and with human material which was four or five hours old, it was about 90%. That shows it is not specific to one animal species, but is, rather, a general phenomenon.

What do the narcotics do? Do they prevent oxygen getting to the brain? Do they prevent substances which go to the brain from being oxidized? We can show that these narcotics have one property in common, and they include ether and nitrous oxide; they all inhibit the oxidation by the brain of glucose and lactic acid, and it is those substances which are necessary for the functioning of the nervous system. It is those substances whose metabolism is inhibited by the narcotics; whereas other substances also burned by the brain but not so effectively and not supplied in the blood to the same extent as sugar and so not so biologically important, are not affected by narcotics. If the narcotics were simply preventing oxygen from reaching the brain or interfering with the oxygen being made available to the brain, all substances oxidized by the brain would be similarly affected. But it is just the carbohydrates which are affected, not the others. So there is this specificity, because glucose and lactic acid are so important in the metabolism of the nervous system.

When we add a narcotic to the brain the oxidation falls because the substances oxidized by the brain are being used up. With somnifaine or the barbituric derivatives you get a fall, and at a certain period the curves cross, so in three or four hours the respiration is greater, and that is because at this period the lactic acid, etc., in the brain were not being used up quickly, some was left over still to be burned. If, when they cross, we add sugar, the respiration goes up to the normal level. But here is a very slight increase, showing the large effect of a narcotic on the sugar oxidation. Ether does the same thing. Ether of the concentration which will bring about that narcosis inhibits the oxidation by the brain of sugar. The effect of ether is cumulative, so differing from the narcotics, and it is not easily reversible, and that is one reason why we cannot use ether for the purpose

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of causing prolonged narcosis; we should kill the patient. More damage is done by ether; it is a different type of narcotic. This effect is not just specific to brain; it works with other organs, especially the liver. And here, again, the main effect is in respect of the carbohydrate. At narcotic concentrations these substances affect the metabolism of sugar. It was the appreciation of this fact, in the early days, which led us to seek for, and to find in our cases of prolonged narcosis evidences of ketosis. It was found that in most cases of prolonged narcosis symptoms develop which might be due to ketosis.

It was those facts which led us to consider modifying the treatment by glucose and insulin, and we published a paper showing that glucose and insulin administration had a favourable effect. Glucose and insulin are favourable because they combat the toxic effects of narcotics in organs in which the carbohydrate metabolism greatly depends on the glycogen-glucose metabolism. In the brain there is no glycogen metabolism; the brain works, because it must work, on glucose supplied by the blood. Insulin cannot effect narcosis in the brain, because insulin has its effects chiefly on the glycogen breakdown; it is more or less independent of the nervous system, so insulin cannot affect the narcosis treatment. But it can combat the effects of the narcotics on other organs than the brain.

Pathology.

The Phylactic Theory in the Treatment of Neurotropic Diseases.

By W. M. Ford Robertson, M.D.

Director, West-of-Scotland Neuro-psychiatric Research Institute.

The conception underlying the phenomenon of "phylaxis", or protection of the nervous system, in neurotropic diseases was first enunciated by Billard (1931), late Professor of Physiology at Clermont-Ferrand. It was he who gave an explanation of the value of chloroform anæsthesia in tetanus. In regard to this matter, Billard wrote as follows:

> "Profoundly convinced of the essential importance of lipoids in the production of phylactic phenomenon, I wondered whether anæsthetics generally, which had already been shown by Nicloux to have an affinity for the central nervous system, and in particular, whether chloroform, which had enabled Overton to establish the existence of lipoids, did not have the power of so modifying lipoid equilibrium *in vivo* as to render animals either more sensitive or more refractory to neurotoxins."

Whether or not the role of the lipoids will ultimately be found to be as vitally important as stated remains to be seen. The essential point, however, is that experimental evidence strongly suggests that protection is afforded by chloroform against a lethal dose of tetanus toxin.

Billard was able to demonstrate the following results on guinea-pigs:

> 1. The injection into a guinea-pig of a lethal dose of toxin produced no reaction if the animal had been anæsthetized for about 3 minutes, 12–15 minutes before the injection, the animal, according to Billard, having been rendered refractory to tetanus toxin.
>
> 2. If the lethal dose of toxin is given some 10–15 minutes before the chloroform anæsthesia, the animal dies more rapidly than by injection alone. The virulence of the toxin is apparently increased. (The reason possibly being that the toxin, free and freed, becomes widely distributed

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