Eccles et al., [5, 6, 8, 9, 10] have shown that strychnine and tetanus toxin block inhibitory synapses and eliminate all kinds of postsynaptic inhibition in motor neurones of the spinal cord. This discovery enables strychnine and tetanus toxin to be used extensively to reveal the role of inhibitory synapses in normal and pathological reflexes.

The experiments described below show the part played by inhibitory synapses in reactions caused by the very widespread pathological process - inflammation.

**EXPERIMENTAL METHOD**

A subcutaneous injection of 0.2 - 0.5 ml of turpentine into one of the hind feet of an animal was given in order to produce an inflamed area. We studied the changes in the nervous system which developed along the nervous pathway of the impulses from the inflamed area, and for this purpose we investigated spinal mono- and polysynaptic reflexes, the primary responses in the specific thalamic nucleus (VPL), the primary responses in the cortical representation in the inflamed organ - in sensory areas I and II [1, 2].

To suppress the activity of the inhibitory synapses strychnine was injected intravenously as follows: to study mono- and polysynaptic reflexes the dose was 0.05 mg/kg, and for investigation of the primary thalamic and cortical responses it was 0.5 mg/kg.

**EXPERIMENTAL RESULTS**

As we have shown previously [1] and as the present experiments have confirmed, impulses from the inflamed area cause an increase in the amplitude of the spinal mono- and polysynaptic flexor reflexes. Impulses from the inflamed area cause similar changes in the central nervous system at higher levels [2]. The primary responses in the specific thalamic nucleus (VPL) are enhanced as are also the primary responses in the cortical responses in the cortical representation of the inflamed area - in sensory areas I and II.

The occurrence of a discharge in a nerve cell depends upon the magnitude of the membrane potential. Increase in the amplitude of the spinal, thalamic, and cortical responses under the influence of impulses from the inflamed area is evidently the result of the involvement of a large number of neurones in the reflex reaction. We may therefore, suppose that the essential feature of the changes evoked by impulses from the inflamed area is that it brings about a depolarization of neurones with the result that they are more readily discharged, and a greater number of them are involved in the response to the test stimulus.

These results throw new light on one of the most characteristic features of pathologically altered organs - their increased sensitivity to ordinary stimuli. It is known that during inflammation a limb will be sharply withdrawn in response to a lighter touch than is normally required. In inflammatory processes in the lungs or heart a moderate degree of physical exercise will cause considerable dyspnea and tachycardia. In gastric ulcer there is an abnormal increase in secretion in response to an adequate food stimulus, etc. Evidently, in these cases impulses originating in pathologically altered tissues bring about a reduction in the membrane potential of neurones which regulate the
activity of the organs concerned. As a result these neurones are more readily discharged when an adequate stimulus is presented, so that their reaction is enhanced, just as we have found it to be in our experiments.

The injection of strychnine into animals having an inflamed area in one of the hindlimbs caused a marked increase in polysynaptic reflexes (most marked in the flexor reflexes both on the healthy and on the damaged side. However, in 14 out of 15 experiments the increase in the polysynaptic reflexes on the damaged side was 100–200% greater than in the healthy limb (Fig. 1). The selective increase in the polysynaptic reflexes leads us to suppose that strychnine blocks chiefly the inhibitory synapses of the interneurones.

We have already mentioned that impulses from the inflamed area by themselves (before the injection of strychnine) bring about an increase in the mono- and polysynaptic flexor reflexes. However these changes are not apparent until the 3rd–4th day after damage to the limb. In the first few hours or even days after damage to the foot the changes in the mono- and polysynaptic reflexes were varied in nature [1]. Here it is particularly interesting that the effect of the action of strychnine, even in the first few hours after damage to a limb, was entirely consistent: the polysynaptic reflexes from the damaged limb were always considerably more enhanced than they were from the healthy limb. In the period immediately following the damage the individual variations of the mono- and polysynaptic reflexes may have been related to the degree of activity of the inhibition synapses in the particular animal.

The primary responses in the VPL and in the somato-sensory cortical areas evoked by stimulation of the superficial peroneal nerve were also increased by the injection of strychnine. Here the effect was much better shown when the nerve on the damaged side was stimulated; in the contralateral hemisphere the responses were increased by twice as much as in the ipsilateral hemisphere Figs. 2 and 3). In many of the experiments secondary responses which had not been seen previously occurred in the contralateral hemisphere (see Fig. 3).

It is important to note that no facilitatory influence of strychnine of the primary cortical responses following stimulation of the VPL could be found. This result is in line with the most recent investigations of Eccles et al. [4, 7], who found that not all inhibitory cortical synapses are blocked by strychnine. Apparently, the facilitatory influence of strychnine on the thalamic and cortical responses (which are best shown in the contralateral hemisphere) are caused by a corresponding facilitation evoked by strychnine at a subthalamic level.