useful in determining the changes in arterial blood pressure which occur in man during exposure to centrifugal force on a human centrifuge[7,8] (Fig. 4). In this case the output current of the strain gauge was carried from the rotating centrifuge through mercury ring contacts and recorded in another room about 60 feet from the subject.

Summary. The use of a resistance wire strain gauge to convert pressure to electrical energy in making direct measurements of arterial blood pressure is described. The electrical circuits involved are simple. Recording is by means of a galvanometer without the use of electronic amplifiers. The calibration of the manometer is linear, stable and relatively insensitive to temperature changes. The natural frequencies of the manometer and galvanometer are 60 and 40 cycles per second, respectively.

Addendum. Manometers constructed with strain gauges of a more recent model (P6-15D-250, serial No. 275) have natural frequencies up to 100 cycles per second when fitted with an 18-inch (45.7 cm) lead tube and a 19-gauge needle. Their sensitivity has remained the same as that of previous strain gauge manometers.

7 Lambert, E. H., and Wood, E. H., *Fed. Proc.*, 1946, **5**, 59.

8 Wood, E. H., Lambert, E. H., Baldes, E. J., and Code, C. F., *Fed. Proc.*, 1946, **5**, 327.

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Sodium Cyanide: Time of Appearance of Signs as a Function of the Rate of Injection.*

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The effects of sudden intravenous injections of NaCN in animals have been described elsewhere.[1] On the basis of both human and animal studies,[2] certain conclusions have been drawn as to the probable detoxification rate for this compound based on the assumption that this rate is constant. Because of possible therapeutic applications, it is important to determine in what manner the body responds to slow, constant infusions of dilute solutions of the sodium salt of cyanide, and whether the detoxification rate varies as a function of the rate of injection.

Method. Experiments were carried out on cats of about 2 kg paralyzed with dihydro-beta-erythroidine hydrobromide† (10 mg *i.v.* followed by about 0.1 mg per min. continuously) and maintained on artificial respiration at 25 strokes/min. of 35 cc/stroke. The skull was laid bare and the electrical activity of the cortex obtained with skull electrodes was recorded with a 6-channel, ink writing Grass oscillograph, the EKG being recorded with the same apparatus, using the conventional leads. Changes in the oxygen tension of the cortex were concurrently recorded.[3] NaCN was injected continuously‡ by an accurately calibrated 50 cc syringe driven by a synchronous motor, delivering from 0.033 ml/min. to 0.54 ml/min. By

* The work described in this paper was carried out under a contract between the Medical Division, Chemical Corps, U. S. Army, and the University of Illinois College of Medicine.

1 McCulloch, W. S., and Wheatley, M. D., in press.

2 Loevenhart, A. S., Lorenz, W. F., Martin, H. G., and Malone, J. Y., *Arch. Int. Med.*, 1918, **21**, 109; Loevenhart, A. S., Malone, J. Y., and Martin, H. G., *J. Pharm. and Exp. Therap.*, 1922, **19**, 13.

† The author wishes to thank Merck & Co. who kindly supplied this drug.

3 Davis, E. W., McCulloch, W. S., and Roseman, E., *Am. J. Psychiat.*, 1944, **100**, 825.

‡ The author wishes to thank Dr. R. K. Richards of the Abbott Laboratories who loaned to us this apparatus.

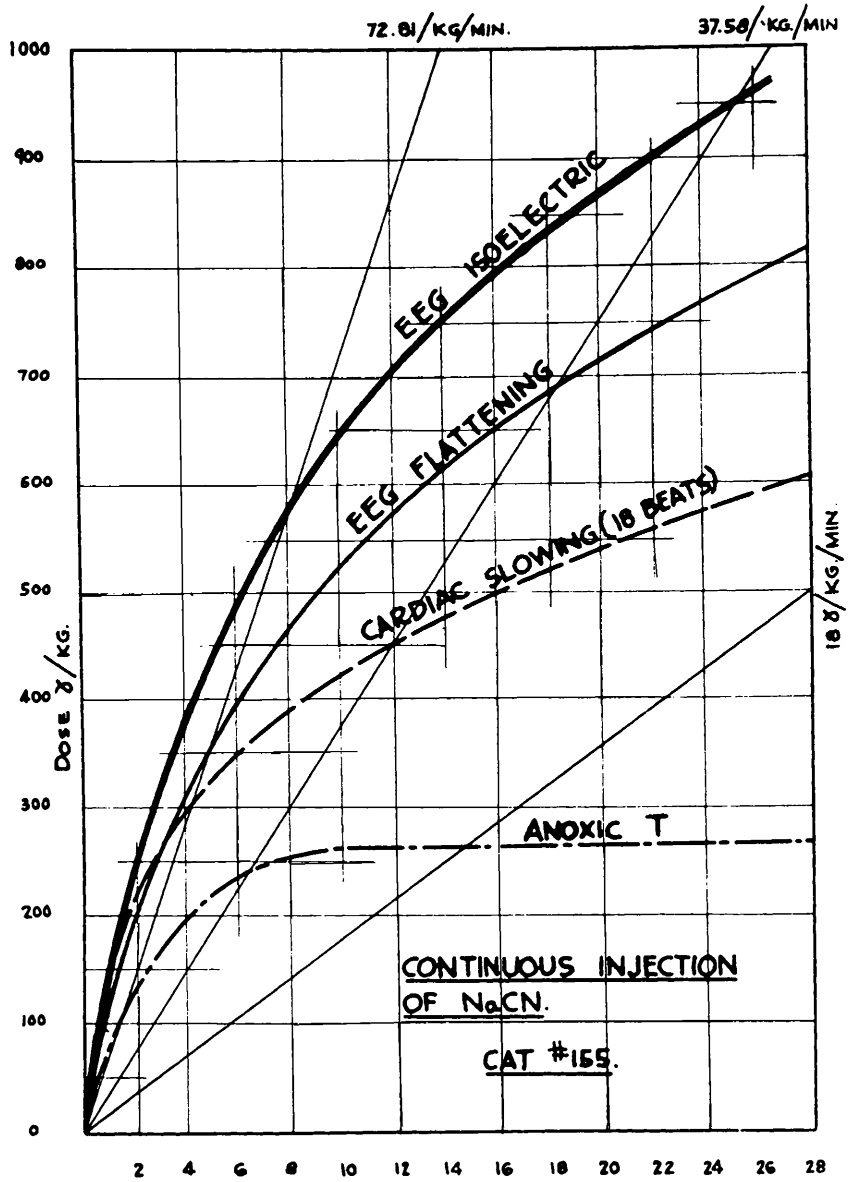

FIG. 1.

Continuous injection of NaCN at the rate of 18, 37, and 72 μg/kg/min. (diagonal straight lines). The time of appearance of the various phenomena is plotted against time at these various rates of injection (curved lines).

varying the concentration of NaCN in the solution, rates of injection from 7 μg/kg/min. to 100 μg/kg/min. could be achieved with accuracy over the entire range.

Results. The effects of slow, constant infusion of NaCN are similar to those which follow sudden injection,[1] the time of onset varying with the rate of injection. One of the first effects is a slight increase in both the frequency and amplitude of the electrical brain waves which is soon followed by the appearance of large, slow waves, with occasional superimposed bursts of fast, small waves. This is in turn followed by a gradual reduction in both the amplitude and frequency, ending, if the dose is great enough

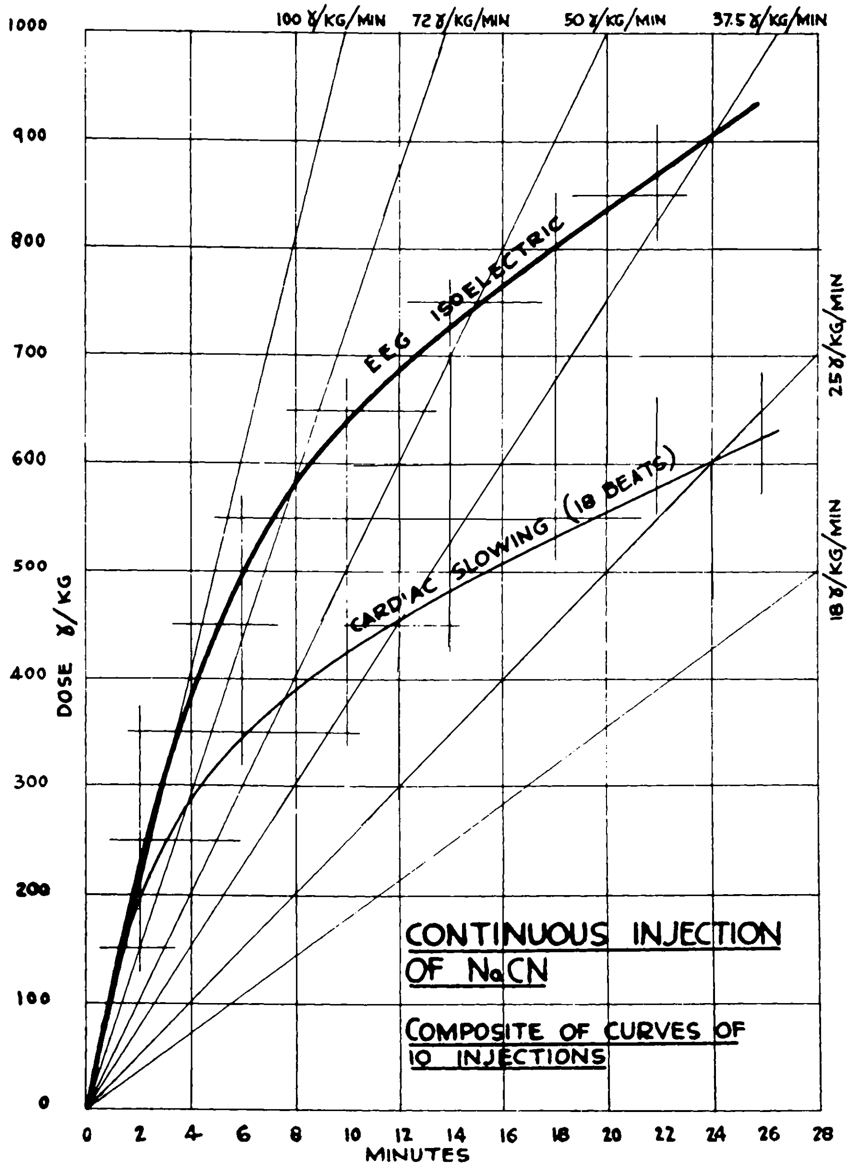

FIG. 2.
Composite curves of 10 experiments. The points of intersection of the curved and diagonal lines indicate particular phenomena occurred at that rate of injection. Dose is expressed in μg/kg.

in an absence of activity. The first cardiac change is an anoxic T-wave which becomes progressively larger and may invert. Slowing of the heart occurs slightly later and increases as the injection continues until the plateau for that dose is reached.

During the recovery from the effects of continuous injection, the electrical activity of the cortex often shows a period of hyperactivity with episodes of both tonic and clonic types of discharges. This has also been observed following sudden injections.

In contrast to the findings following sudden injection, the oxygen tension fails to show a consistent elevation, even when the EEG changes are most marked.

As an index of the action of NaCN, various clear and consistent phenomena have been chosen as end-points, namely: onset of anoxic T-wave; cardiac slowing of 18 beats/min.; increase in frequency and also flattening of the electrical activity of the cortex; and onset of isoelectricity of the EEG. The onset of these, abstracted from the continuous records, are plotted on the straight lines representing the rates of injection. The points for each variety of end-point lie on curved lines. The complete curves for one representative experiment (Cat No. 155) are presented (Fig. 1) as well as one composite curve containing the average values for 10 animals (Fig. 2). It will be noted that while the various effects of NaCN occur serially close in time at high rates of injection, at slower rates of injection they are disproportionally spread out in time.

Discussion. It is not surprising that the oxygen tension is inconsistent when both the consumption and the supply are variably decreased.

If detoxification of NaCN in the body proceeded at a constant rate, the plots of the end-points of any variety would fall on a straight line. The observed ascending curves being convex upward, indicate that the rate of detoxification increases with the concentration—as it would if it followed the law of a mass action. The clinical correlate of this concept is that a greater margin of safety obtains at slower rates of injection and for higher end-points. Thus in Fig. 1 there is an interval of 3 minutes between EEG isoelectricity and EEG flattening when NaCN is injected at 73 μg/kg/min. and an interval of 7 min. at 38 μg/kg/min. At slower rates the interval increases greatly and at 25 μg/kg/min. isoelectricity never occurs.

As the rate of injection is increased so as to approach the injection of the whole dose in 7 seconds, new factors begin to determine the time of appearance of the end-points. These include not only circulation time and time for diffusion into the tissues, but the time for the alteration of the tissue and the time for the development of the particular phenomenon as well as other things at present unknown. Any attempt to extrapolate from the curves for slow injection to the time of appearance of any sign after sudden injection is clearly unwarranted. It is important to note that these other factors determine delays too short to account for the observed curvature.

Summary. NaCN in dilute solution has been injected slowly at constant rates ranging from 7 to 100 μg/kg/min. The time and dose, at which several phenomena are first encountered, plot in ascending curves which are convex upward. This curvature probably indicates that detoxification of NaCN proceeds rapidly at higher concentrations.

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Effects of Use and Disuse on Nerve Endings, Neurosomes, and Fiber Types in Skeletal Muscle.*

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Pathologic neurosomes were first identified in the muscles of man[1] and monkey[2] during the early acute changes produced by poliomyelitis, and later in the muscles of rats and

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1 Carey, E. J., Massopust, L. C., Zeit, W., and Haushalter, E., *J. Neuropath. and Exp. Neurol.*, 1944, **3**, 121.

2 Carey, E. J., *Am. J. Path.*, 1944, **20**, 961.