CATECHOLAMINE AND CARDIOVASCULAR RESPONSE TO
ELECTRO-CONVULSION THERAPY IN MAN

BY

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SUMMARY

Fourteen anaesthetized patients undergoing electro-convulsion therapy on one or more occasions were studied. Systolic and diastolic blood pressure, heart rate, and plasma adrenaline and noradrenaline levels were measured before, during and after the electric shock. With the electric shock, blood pressure and heart rate rose and adrenaline and noradrenaline levels in plasma increased steeply. These values returned to normal within 10 minutes. Asystole of about 2 seconds duration was common with application of the electric shock in patients not premedicated with atropine. With repeated electro-shocks, resting plasma noradrenaline levels decreased as did the noradrenaline response to the shock. Systolic arterial pressure was significantly correlated with circulating levels of noradrenaline in plasma.

Electrically induced convulsions produce marked cardiovascular changes indicative of strong vagal and of sympathetic stimulation with concomitant changes in plasma and urinary catecholamine levels (Griswold, 1958; Havens et al., 1959; Manger et al., 1957; Perrin, 1961; Sourkes, Drujan and Curtis, 1958; Weil-Malherbe, 1955). Two factors may reduce this sympathetic response to electro-convulsion therapy: (1) anaesthesia with barbiturates, and (2) repeated treatments (Griswold, 1958; Havens et al., 1959). This latter phenomenon is of great theoretical and possible clinical interest and required confirmation. Therefore, plasma catecholamines were measured in several patients who were repeatedly exposed to electro-convulsion therapy.

The study was also designed to show changes in sympathetic activity during and following electro-convulsion therapy by the simultaneous measurement of arterial blood pressure and heart rate, together with the estimation of adrenaline and noradrenaline levels in plasma. Since large fluctuations in catecholamine levels and in blood pressure and heart rate are known to occur during electro-convulsion therapy (Griswold, 1958; Havens et al., 1959; Manger et al., 1957; Perrin, 1961; Sourkes, Drujan and Curtis, 1958; Weil-Malherbe, 1955), we searched for correlations between these variables. It should be pointed out that the concomitant measurement of changes in endogenous catecholamine levels and alterations in cardiovascular function induced by electro-convulsion therapy has not been reported previously.

METHODS

The subjects were fourteen unselected adult patients of either sex treated with electro-convulsion therapy* for psychiatric depressions of different aetiology at this institution. The patients were taken off all medications for 24 hours prior to treatment, which was carried out in the morning. Only one patient of this series was premedicated with atropine. Under anaesthesia, a radial artery was cannulated with an 18-gauge Cournand needle, through which arterial blood pressure was sensed by a Statham transducer and displayed on a Grass polygraph. This indwelling needle also permitted the withdrawal of arterial blood samples (35 ml) for the analysis of plasma adrenaline and noradrenaline. An electrocardiogram was recorded continuously.

Thirteen patients had thiopentone-oxygen anaesthesia and required, on the average, 400 mg

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* Only modified electro-convulsion therapy is given at this institution.
for the entire procedure. Two of these patients were, on different days, also studied under nitrous oxide-oxygen anaesthesia (without barbiturate); for this the patients were given pure oxygen for 3 minutes, then nitrous oxide 7 l./min with oxygen 2 l./min. One patient received only nitrous oxide-oxygen anaesthesia for repeated treatments. Four patients received thiopentone on one occasion and light halothane anaesthesia on another. After induction of anaesthesia with halothane, a maintenance dose of 0.5 to 1 per cent halothane in oxygen was required to keep the patients asleep.

In order to eliminate the administration of suxamethonium as a variable, 40 mg of this drug were injected intravenously every time before blood was drawn and pressure recordings were made. While the response to the first dose of suxamethonium may have differed from that to subsequent doses, this design seemed preferable to one using the relaxant only prior to the electro-shock. The initial suxamethonium dose was injected and the first control sample of blood was obtained when anaesthesia was established and the cannulation was complete. Another dose of suxamethonium was then given, bilateral temporal electrodes were applied, and a shock of 120 volts, AC, lasting 0.6–0.8 seconds was delivered. About 30–60 seconds after the shock, when a full response was seen (indicated by small tonic and clonic contractions of the extremities and a rise in blood pressure) another blood sample was obtained; then 10 minutes later, with the patient still anaesthetized, the third blood sample was drawn.

The catecholamines in plasma were assayed by the method of Anton and Sayre (1962). For the statistical analyses, two tailed paired "t" tests and calculation of the regression line and correlation coefficients were carried out (Hoffman, 1963).

RESULTS

A typical tracing of arterial blood pressure and electrocardiogram (fig. 1) shows the brief cardiac standstill, the hypotension associated with it, and the subsequent rise in blood pressure and heart rate. Average systolic and diastolic arterial pressures and heart rates are shown in figure 2, together with the duration of cardiac standstill during, and immediately following, application of the electric shock. The mean differences of systolic and diastolic pressure and heart rate between the control values (before the shock) and peak values immediately after shock were statistically highly significant (P<0.01). The mean values returned to control levels within the 10 minutes of observation. The mean differences between the peak values immediately after shock and the values recorded 10 minutes later are also statistically highly significant (P<0.01). The mean duration of cardiac standstill occurring with application of the electric shock was 1.9 seconds. The longest period of cardiac arrest lasted 7.2 seconds. When the heart rate was not slowed, or temporarily stopped, there was a question

![Fig. 1](image)

Fig. 1

Tracing of arterial blood pressure and electrocardiogram during electro-shock. The prominent disturbance of the e.c.g. started when the bitemporal electrodes were applied. Notice the drop in blood pressure during cardiac standstill and the subsequent hypertension.
whether or not the electric shock had been sufficient to elicit a convulsion. In one patient, only mild slowing of the heart with variable types of cardiac arrhythmias occurred, ranging from bigemini to ventricular premature contractions. This was the only patient who had been given a subcutaneous injection of 0.6 mg atropine sulphate 1/2 hour prior to the shock treatment.

The mean noradrenaline and adrenaline values measured in plasma before, immediately after (blood was collected within 60 seconds after the shock which lasted for 0.6-0.8 seconds), and 10 minutes after the application of the shock are shown in figure 3. The differences between the "control" and the peak "after shock" values and between the peak values and the values recorded 10 minutes later, are statistically highly significant.

In one subject, blood samples were taken simultaneously from an arm vein, and from the radial artery on different occasions during three different shock treatments. In figure 4, arterial values of adrenaline and noradrenaline are plotted against the venous values and in this patient no significant difference between arterial and venous blood, nor between the slopes of adrenaline and noradrenaline, could be found.

Seven patients were studied on two different occasions when electro-convulsion therapy was applied and the same anaesthetic was used. In all
<table>
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<tr>
<th>Patient</th>
<th>anaesthetic</th>
<th>Date</th>
<th>Systolic pressure (mm Hg)</th>
<th>Plasma noradrenaline (µg/100 ml)</th>
<th>Plasma adrenaline (µg/100 ml)</th>
<th>Duration asystole (sec)</th>
<th>Systolic pressure (mm Hg)</th>
<th>Plasma noradrenaline (µg/100 ml)</th>
<th>Plasma adrenaline (µg/100 ml)</th>
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<td>145</td>
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<td>140</td>
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<td>170</td>
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* This patient had 0.6 mg atropine sulphate 30 minutes before shock.
CATECHOLAMINE AND CARDIOVASCULAR RESPONSE TO E.C.T.

All noradrenaline and adrenaline plasma values from one patient taken at three different electro-shock treatments before, immediately after, and 10 minutes after shock. The patient had thiopentone anaesthesia on all three occasions. Arterial and venous blood samples were drawn simultaneously and are plotted accordingly.

seven patients, the control values (prior to shock) of plasma noradrenaline were higher at the first exposure as compared to the control values of the subsequent exposure. The mean difference between the first and the second exposure was 0.034 μg noradrenaline per 100 ml plasma. This difference was statistically highly significant (P<0.01). Immediately after the shock, the patient's noradrenaline values rose to higher levels after the initial exposure as compared to the levels reached after a shock treatment a week or more later. The mean difference was 0.047 μg per 100 ml of plasma (P<0.05). There were no differences in adrenaline levels.

In six patients a comparison between anaesthetics was possible. Two patients were studied once under thiopentone-oxygen anaesthesia, and once under nitrous oxide-oxygen anaesthesia. Four patients received halothane on one occasion and thiopentone on another. The data from these patients are tabulated in table I. The differences between the anaesthetics were inconsistent. Our patients objected to anaesthesia induced by mask and therefore further comparisons between anaesthetics were abandoned.

Attempts to correlate levels of circulating or urinary catecholamines* and heart rate or cardiac standstill were futile. Plotting plasma adrenaline levels against systolic or diastolic pressure also did not suggest any correlation. A plot of all plasma noradrenaline values against all systolic blood pressure readings, however, shows the correlation seen in figure 5.

DISCUSSION

Both noradrenaline and adrenaline levels rose in plasma by more than 100 per cent in the patients in this study. While the direction of the changes and the rapid return of the plasma levels to normal control values were in good agreement with the published reports (Griswold, 1958; Weil-Malherbe, 1955), the catecholamine levels rose higher in our patients who received modified electro-convulsion therapy than in those anaesthetized and premedicated patients reported on by Weil-Malherbe (1955) and Griswold (1958). Reasons for this discrepancy may lie in the type or level of anaesthesia, the timing of the sampling or the catecholamine assay.

Barbiturates (Griswold, 1958; Havens et al., 1959; Manger et al., 1957; Perrin, 1961; Sourkes, Drujan, Curtis, 1958; Weil-Malherbe, 1955) and halothane (Anton, Gravenstein, Wheat, 1964) appear to decrease the liberation of catecholamines into plasma during electro-convulsion therapy and surgical stress. These data allow no conclusion about the effects of nitrous oxide in this regard. No indication was found that the vagal stimulation, as measured by duration of asystole, was modified by any of the anaesthetic agents.

Although Griswold's interesting observation of a decline of circulating noradrenaline levels in patients with successive exposures to electro-convulsion therapy was confirmed, the rise in adrenaline with repeated treatments as reported by Havens and associates was not obtained. The progressive reduction in circulating noradrenaline levels in psychiatric patients treated with electric

* Because of inconsistent results from urinary catecholamine determinations (also noted by Sourkes, Drujan and Curtis, 1958), they have not been included.
shock may be an effect of electro-convulsion therapy, or an effect of the hospital environment and the other therapy which the patients received. This observation is of practical and theoretical interest. It may mean that certain mentally depressed patients prior to shock therapy react to strong, non-specific challenges with a larger than normal sympathetic discharge or that in these, and perhaps in all patients, repeated challenges of this or other types cause either an adaptation or a decreased ability to respond with a sympathetic discharge. Since the observed differences in noradrenaline levels amounted to up to 50 per cent of the resting level and were quite consistent, these differences observed in the course of electro-shock therapy may be associated with important biological consequences.

The duration of asystole with electro-convulsion therapy in patients who have not been premedicated with atropine is of clinical importance. It is undoubtedly necessary to protect all patients with atropine against excessively long cardiac standstills (Clement, 1962; Hargreaves, 1962). The patient who had a standstill of almost 7.2 seconds also had subsequently the highest rise in circulating catecholamines observed in any patient studied by us. The noradrenaline plasma values rose from 0.124 to 0.614 μg per cent, and adrenaline plasma values from 0.074 to 0.874 μg per cent.

It was hoped to find correlations between heart rate, blood pressure and both catecholamine levels in plasma, because the mean value of these measurements increased and decreased simul-
taneously in our fourteen patients. No correlation was found, however, between adrenaline and any of the cardiovascular measurements. Since atropine was not used and since strong vagal activity was suggested by the period of cardiac standstill, a complex interplay of sympathetic and parasympathetic influences further modified by anaesthesia may have obscured any correlation between adrenaline levels and the circulation. On the other hand, a statistically highly significant correlation between systolic blood pressure and noradrenaline levels was found. This demonstration supports the classic concept that acute changes in blood pressure may be mediated by the sympathetic nervous system and particularly noradrenaline liberation.

Mean noradrenaline levels rose parallel with mean adrenaline levels in plasma; yet there was no correlation between the individual changes of these two amines. The authors have shown, in contrast to this, that in surgical patients noradrenaline and adrenaline change together (Anton, Gravenstein and Wheat, 1964). Whether the type of challenge, the duration of stimulation, the time of sampling or the patient population was responsible for the described difference is unknown.

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LES CATECHOLAMINES ET LA REPONSE CARDIOVASCULAIRE A LA SISMOTHERAPIE CHEZ L'HOMME

ZUSAMMENFASSUNG