considered to represent decay of xenon from extracerebral structures. The tension of CO_2 in the end tidal air was monitored continuously, by means of a Beckmann infrared analyser.

The subjects were allowed to rest on a couch for between 10 and 15 min before baseline readings were obtained. The procedure was explained to them in detail, and every attempt was made to allay anxiety. During the cerebral blood flow measurement, which takes some 50 min, frequent recordings of heart rate and blood pressure (obtained with a sphygmomanometer) were made.

A dose of clonidine (2 μg/kg body weight) was then administered intravenously over a period of 2 min. Ten min later a further cerebral blood flow study was performed. This dose of clonidine caused an initial bradycardia and a significant fall in mean arterial blood pressure, the fall in systolic blood pressure being the most marked. The majority of subjects complained of drowsiness and a dry mouth, and initially appeared very pale. There was a mean fall in cerebral blood flow of 30% ($P<0.001$) and also a highly significant increase in calculated cerebrovascular resistance. There was also a small but significant reduction in the CO_2 tension of end tidal air. It is unlikely, however, that the fall in cerebral blood flow can be ascribed to this; or indeed to the fall in arterial blood pressure. The acute intravenous administration of clonidine in man would appear to cause cerebral vasoconstriction.

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Interaction between intravenous alcohol and some sedatives and tranquillizers

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Interactions between alcohol and various soporific agents are assuming greater importance in our present social climate. It is agreed that these potentiate the effect of alcohol, but it is not clear whether the potentiation is an intensification or prolongation of its action. Chlordiazepoxide appears to be the exception since it is reported to have no such effect on the action of alcohol (Goldberg, 1964; Kissan, 1967).

Most data have been obtained from animal experiments or following ingestion of alcohol in man (Benor & Ditman, 1967; Forney & Hughes, 1968). A re-evaluation of alcohol as an intravenous anaesthetic (Dundee & Isaac, 1969) provided an opportunity to study some interactions under controlled conditions. Drugs were given intramuscularly, with 0·6 mg atropine as premedication, and alcohol was infused as 8% w/v solution at 80–150 ml/min as required to a maximum of 700 ml. This study was based on patients anaesthetized with ethanol alone, without a barbiturate supplementation.

Previous studies (Dundee, 1970) showed that it is more meaningful to express average dose as mg/kg per $\sqrt{\text{min}}$ and demonstrated that arterio-venous equilibrium is completed 3–4 min after rapid infusion. Blood samples taken at this time are

more reliable than arterial samples at the end of infusion. Since the blood level required to induce sleep increases with infusion time this was standardized to 4-6 min.

In Table 1 the findings with different doses of some drugs are pooled, since these were similar within the range used. After chlordiazepoxide, more ethanol was needed to produce sleep ($P<0.01$). This increase was associated with increased concentrations of ethanol in the venous blood ($P<0.005$). After pentobarbitone, although less ethanol was needed to produce sleep, the difference was not significant. Blood alcohol concentration was significantly less ($P<0.05$). The decline of ethanol concentration in the blood following 0·8 g/kg was not affected by chlordiazepoxide.

TABLE 1. *Average amount of alcohol required to produce sleep after rapid infusion of 8% w/v and venous blood levels taken 3–4 min after loss of consciousness*

Premedication: atropine (0·6 mg) plus:	Average dose of alcohol required to produce sleep		Blood ethanol concentration (mg/100 ml)		
	No. of observations	mg/kg per $\sqrt{\text{min}}$	No. of observations	Average	Range
—	31	274±13	14	186±12	111–270
Chlordiazepoxide 100–140 mg	43	393±11	14	291±16	207–459
Diazepam 10–30 mg	44	295±16	12	187±11	147–282
Pentobarbitone 100–120 mg	28	256±14	11	150±14	97–194
Promethazine 50 mg	32	301±5	17	186±10	124–305
Cyclizine 50 mg			12	176±18	90–286

Thus, this drug appears to induce true cerebral tolerance to alcohol while clinical doses of pentobarbitone have the opposite effect.

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The promotion of phenolic alcohol formation in man by reserpine and ethanol

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Reserpine (Sandler & Youdim, 1968) and ethanol (Smith & Gitlow, 1966; Davis, Brown, Huff & Cashaw, 1967a) administration in man promote the formation of 4-hydroxy-3-methoxyphenylglycol (HMPG) at the expense of 4-hydroxy-3-methoxy-