increase in adrenal cholesterol. Thus it appears that the prevention of dextran oedema by chloroquine is not dependent on the adrenal hormonal secretions.

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Phenazine Methosulphate in Cyanide Toxicity

The blocking action of cyanide ion on cellular respiratory enzyme cytochrome oxidase is of considerable biological importance. *In vitro* action of phenazine methosulphate[1] (PMS) appears somewhat similar to that of the terminal respiratory enzymes in the cell. The following experiments would suggest that PMS might be effective, *in vivo*, as a temporary substitute of the cyanide-blocked respiratory enzymes.

Adult albino rats and mice of either sex were used. All substances were dissolved in water and used within 3 h. PMS solution was protected from light by thick black paper. Respiratory arrest in animals was taken as the end-point.

The dose of PMS (15 mg/kg) used in these experiments was apparently well tolerated by rats and mice. Sodium cyanide (10 mg/kg) alone invariably killed all animals. In mice, 15 mg/kg of PMS proved more effective than 7·5 mg/kg. Increasing the interval between PMS and cyanide injections from 0·25 min to 4 min decreased the protecting action of PMS. Those animals which PMS or nitrite failed to protect against cyanide lived longer than the ones receiving only cyanide. PMS solution lost considerable activity after 3 h exposure to daylight. Animals protected by PMS or nitrite against cyanide often suffered brief unconsciousness followed by sedation. Animals surviving for 2 h usually recovered completely. In rats, PMS given by the intraperitoneal route 3 min after subcutaneously injected cyanide could protect 69 per cent of animals.

Table 1. Survival of Mice and Rats after Cyanide Treatment, with and without Protective Pre-treatment

First drug (mg/kg)	Interval between first and second drug (min)	Second drug (mg/kg)	No. animals died and average survival time (min)	No. and % of animals protected against cyanide
		Mice		
NaCN, 10	Nil	Nil	24 (3)	Nil (0%)
PMS, 15	0·25	NaCN, 10	8 (35)	22 (73%)
PMS, 15	4	NaCN, 10	5 (19)	1 (17%)
PMS, 7·5	0·25	NaCN, 10	6 (24)	4 (40%)
PMS, 15*	0·25	NaCN, 10	7 (35)	Nil (0%)
$NaNO_2$, 80	4	NaCN, 10	4	11 (73%)
		Rats		
NaCN, 10	Nil	Nil	20 (15)	Nil (0%)
NaCN, 10	3	PMS, 15	8 (29)	18 (69%)

* PMS solution in glass container exposed to daylight for 3 h.
NaCN injected into rats by the subcutaneous route. All other injections by the intraperitoneal route. Room temperature 16°–34° C.

Sodium nitrite, the well-known antagonist of cyanide *in vivo*, was used for comparison. It acts by converting haemoglobin into methaemoglobin; the latter forming the comparatively stable complex cyanmethaemoglobin. Unlike PMS, nitrite was effective when injected 4 min before cyanide. This suggests that its mode of action is different.

Survival of 73 per cent of mice and 69 per cent of rats ingesting what is otherwise an invariably fatal dose of cyanide is considered significant.

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Nitrogen Oxides in Tobacco Smoke

Because of their considerable pharmacological significance, the presence of nitrogen oxides in tobacco smoke has been the subject of a number of reports in the past few years[1–4]. In general, the choice of experimental techniques has been such that the relative amounts of the principal components, nitric oxide (NO) and nitrogen dioxide (NO_2), in cigarette smoke have not been clearly established.

Although NO and NO_2 are both readily absorbed in the human lung, their physiological action is reported to be quite different. NO is found to be approximately five times less toxic than NO_2 (ref. 5), and recently it has been found that NO is approximately six times less active as a mammalian ciliastatic agent[6]. These considerations made it desirable to develop an analytical technique which would provide quantitative estimates of the amount of each oxide in tobacco smoke. With such a technique it is found that almost all of what had previously been considered as a mixture of oxides is, in fact, the less active nitric oxide.

Although NO undergoes oxidation to NO_2 by the well-known termolecular reaction $2NO + O_2 \rightarrow 2NO_2$, the rate of conversion is found to be relatively slow at the concentrations existing in cigarette smoke. It is calculated that approximately 500 sec would be required in undiluted smoke, and more than 5,000 sec would be required in the more dilute system within the human lung, for the oxidation of half the NO to NO_2. Since these times are very much greater than those available during the inspiration, absorption and expiration of a puff of smoke, NO can be considered as an independent agent in its pharmacological action.

Because of the considerable difference in volatility of NO (B.P. −151° C) and NO_2 (B.P. 21° C), a cold adsorption trap can effectively be used to separate these gases. Following such a separation the NO is allowed to oxidize to NO_2, and the concentrations of both are individually estimated by the Saltzman procedure[7]. Our smoking and smoke collection system consisted of a train containing an efficient particulate smoke filter, a flow-limiting orifice, a small U trap, and an evacuated terminal gas collection flask. The functions of the filter, orifice and terminal flask have been described elsewhere[8], and it is necessary to note here that they provide a means of withdrawing a single 40-ml. puff of smoke of normal duration from a lighted cigarette, and of separating the gaseous mixture from the entrained smoke particles. The 55-ml. terminal collection flask both provides the suction necessary for puffing and also serves as a quantitative container for the gas mixture and its component NO during the reaction with 10 ml. of the Griess–Ilosvay reagent contained therein. The 7-ml. U trap, which is packed with glass helices and 1·0–1·5 grams of silica gel deactivated with 20 per cent H_2O, is cooled to dry-ice temperatures. This trap largely retained such NO_2 as is present, which subsequently can be estimated by elution and reaction with Griess–Ilosvay reagent.

Experiments with pure gases and mixtures of NO and NO_2 each diluted with nitrogen to the approximate level of nitrogen oxides in cigarette smoke were performed. It