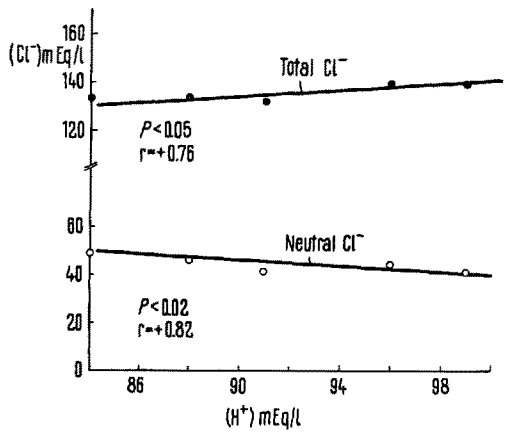

Fig. 4. Regression lines demonstrating the relationships between total and neutral chloride and the hydrogen ion concentration in gastric juice following graded insulin dosage. Each point represents the mean value of 10 rats.

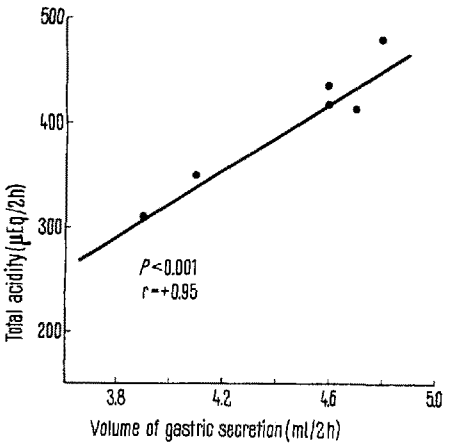

Fig. 5. Regression line demonstrating the relationship between the total acidity and the volume of gastric secretion following graded insulin dosage. Each point represents the mean value of 10 rats.

of potassium ions into the gastric juice was related to the volume rate of secretion. From Figure 4, which represents the relationship between acidity and the total and neutral chloride in the 5 groups of rats receiving insulin, it can be seen that as the acidity increases the concentration of total chloride increases also, whereas the concentration of neutral chloride decreases. This suggests that neutralization-dilution mechanisms (i.e. the 2-component hypothesis of gastric secretion proposed by HOLLANDER[22] in 1932), as well as exchange diffusion, may be operating to produce the rise in gastric acidity following insulin hypoglycemia. Finally, the close relationship between total acidity and the rate (volume) of gastric secretion following graded insulin dosage is indicated in Figure 5. This association is highly significant: $r = + 0.95$, $P < 0.001$.

From the present study it appears that maximal gastric secretory response develops with 4 U crystalline zinc insulin/100 g body weight in pylorus-ligated Shay rats. Furthermore, under graded insulin dosage, patterns of gastric juice electrolyte changes occurred supporting both neutralization-dilution and exchange diffusion mechanisms in the production of gastric secretion[23].

Zusammenfassung. Die Insulinwirkung auf die Magensäuresekretion wurde in männlichen Sprague-Dawley Ratten untersucht, deren Pylorus 2 h vorher unterbunden war. Eine Dosis-Wirkungskurve wurde aufgestellt. Maximale Sekretion von Magensäure und Magensaft wurden durch s.c. Injektion von 4 Einheiten krystallinischen Zink-Insulins per 100 g Körpergewicht erzielt. Grössere Dosen von Insulin unterdrücken Säure- und Magensaftsekretion. Das Verhalten der Elektrolyte im Magensaft spricht sowohl für die Neutralisierungs-Verdünnungshypothese als auch für die Austausch-Diffusionshypothese zur Erklärung der Magensaftproduktion.

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14th November 1966.

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Hyperbaric Oxygen and Testicular Damage and Fertility

It has been reported that male rats which survive after exposure to raised pressures of oxygen develop testicular atrophy and signs of defective spermatogenesis[1-3]. In these experiments the diagnosis of testicular damage was based on macroscopic and microscopic appearances. In the report of DE ALMEIDA[1], the experimental conditions of exposure and pressurization of rats was not made clear. In the studies of MATTEO and NAHAS[3], rats were kept continuously for periods of up to 4 weeks enclosed in aquarium tanks through which 98% oxygen at ambient pressure was circulated, the CO_2 produced being absorbed. This treatment caused the death of most rats within the first 5 days, testicular atrophy being seen in survivors. The authors rightly suggest that testicular damage by oxygen may be of importance in the therapeutic applications of inhaling enriched oxygen mixtures at ambient or hyperbaric pressures in man.

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Group	Treatment in HPO	Acute effect of treatment	Testes and sperm	Fertility
I. 24 rats (50–200 g body weight)	1 h in 4–5 atm	Convulsions in all rats during exposure. Dyspnoea, lung damage and death in 14 rats	No abnormality seen in 14 animals dying in HPO nor in 10 survivors killed 1–6 weeks after HPO	Not tested
II. 6 rats (130–170 g)	30 min at 4 atm followed by 1 h at 3 atm repeated 6 times over 3 weeks	3 rats died from HPO toxicity during treatment	No abnormalities in rats dying from HPO toxicity or in survivors 6 weeks after HPO	Not tested
III. 10 rats (67 ± 3 g)	3 h at 3 atm on first day and $1^1/_2$ h at 3 atm on 2nd and 3rd days respectively	(a) 2 rats died during treatment in HPO (b) 8 rats survived and gained weight	(a) Normal testes and sperm (b) 2 rats killed on 28th and 31st day; normal testis and sperm	(a) – (b) 5 weeks after HPO, 6 rats mated[a] with 12 normal fertile females → 12 litters (7.3 normal offspring/litter)
6 rats (65–100 g)	Not exposed to HPO	Surived	–	6 unexposed rats mated[a] with 12 normal fertile females → 12 litters (5.7 normal offspring/litter)
IV. 8 rats (180–250 g)	30 min at 4 atm first day, 15 min at 4 atm on 2nd, 3rd, 4th, 5th and 8th days	6 rats convulsed during first exposure, 1 died after first exposure	Normal testis and sperm in non-survivors and in 3 rats sacrificed after 3rd exposure and 2 and 4 weeks after HPO	4 rats mated[a] 4 weeks after HPO with fertile females. All females produced normal litters

[a] Each treated male rat mated with 2 fertile unexposed female rats.

To provide further data concerning the possible damaging effects of acute and subacute exposures to hyperbaric oxygen on the testis and its function, rats have been subjected to single or repeated treatments with hyperbaric oxygen (HPO) at 3–5 atmospheres absolute pressure. Evidence of testicular damage was determined by (1) histological studies at various times up to 6 weeks after exposure of rats to HPO, (2) examination of the sperm by phase contrast microscopy for motility and viability, and (3) by mating HPO exposed male rats with non-exposed fertile normal females, to assess their fertility and whether abnormalities are produced in any of the offspring. The animals were divided into 4 treatment groups. The results are shown in the Table.

In these experiments, single or repeated exposures to HPO were used which produced a significant incidence of oxygen toxicity in respect to pulmonary damage and convulsions, and even death. However, no significant histological changes were produced in the testes of these animals; also, the fertility of survivors was unimpaired and the offspring appeared normal and healthy at birth and during subsequent post-natal development. These findings are considered of sufficient significance to reduce anxieties which may be entertained as to defective spermatogenesis resulting from the use of single or repeated *acute* exposures to HPO of short duration as a therapeutic measure in man.

Some authors[4] have claimed that at cellular and subcellular levels the biological actions of raised oxygen pressure resemble those of ionizing radiations. However, studies in this laboratory[5,6] have failed to substantiate such hypotheses. There is no evidence that the types of cellular lesions primarily produced by ionizing radiations (i.e. chromosomal damage, changes in DNA and its synthesis, and defective cell division) are also primarily produced by raised oxygen pressure[5–7] or predominate in causing cellular and tissue damage by this modality. Indeed, the clinico-pathological changes resulting from oxygen poisoning in mammals largely differ from those produced by ionizing radiations. The resistance of testis to damage by HPO is a further example of this dissimilarity, and the relative inefficiency of raised oxygen pressure in producing chromosomal damage and abnormalities of cell division in vivo and in vitro.

The testicular atrophy observed to occur in rats exposed continuously to 98% oxygen at ambient pressure in the experiments of MATTEO and NAHAS[3], would seem to be an abscopal effect, not primarily related to acute oxygen toxicity and the damage produced at a cellular level by raised oxygen pressure in tissues such as lung and in the central nervous system. This view is also supported by their observations[3] that treatment of rats with sodium bicarbonate before exposure to oxygen reduced mortality and pulmonary damage, whilst the testicular atrophy was not affected by this increase in the basic content of the body tissues.

Zusammenfassung. Männliche Ratten zeigen nach einmaliger oder wiederholter stark erhöhter O_2-Zufuhr (3–5 at) Krämpfe und Lungenschäden und zum Teil Absterben. Schädigungen der Spermatogenese oder der Fertilität traten nicht auf.

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Radiobiological Research Unit, Cancer Institute, Melbourne (Australia), 16th September 1966.

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