thetia. Blood gases showed PaCO_2 well in excess of 60 torr. A check of the anaesthesia circuit demonstrated a large leak around the sensor due to a damaged T connector, causing an inadequate fresh gas inflow to the circuit.¹ All connectors checked subsequently have shown the same defect at one time or another.

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REFERENCE

- 1 Bain JA, Spoerel WE. Flow requirements for a modified Mapleson D system during controlled ventilation. *Can Anaesth Soc J* 1973; 20: 629–36.

have shown may be of academic interest but are of no clinical significance.

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REFERENCES

- 1 Zsigmond EK, Winnie AP, Barabas E, Wang XY. The inhibitory effect of glycopyrrolate on human plasma cholinesterase. *Can Anaesth Soc J* 1985; 32: 20–2.
- 2 Mirakhur RK, Dundee JW. Glycopyrrolate: pharmacology and clinical use. *Anaesthesia*, 1983, 1195–1204.

Glycopyrrolate and human plasma cholinesterase

To the Editor:

I read the paper by Zsigmond *et al.*¹ with great interest, as I have been involved in many clinical studies with glycopyrrolate.² The extrapolation of their results to speculation about possible prolongation of the effects of succinylcholine or local anaesthetics is too far fetched. The IC_{50} of glycopyrrolate on plasma cholinesterase was shown to be 1.0 mM. With the molecular weight of 398 a 1.0 mM concentration of glycopyrrolate would be equivalent to 0.398 mg or 398 $\mu\text{g}\cdot\text{ml}^{-1}$.

Commonly used doses of glycopyrrolate in premedication range from 0.2–0.4 mg. Maximum plasma concentrations of glycopyrrolate in volunteers using a sensitive radio-immunoassay technique were about 35 $\text{ng}\cdot\text{ml}^{-1}$ after 0.4 mg IV (personal communication, C.J. Jones, A.H. Robins Co. Ltd., Horsham, England). Thus the IC_{50} of 1.0 mM demonstrated *in vitro* is over 11,300 times the maximum plasma concentration in man after 0.4 mg glycopyrrolate IV. Such concentrations would not be attained even with relatively larger doses (10–15 $\mu\text{g}\cdot\text{kg}^{-1}$) of glycopyrrolate used at the time of antagonism of neuromuscular block. Glycopyrrolate has been used in many thousands of cases without any reports of prolonged action of succinylcholine or ester-type local anaesthetics.

The results Dr. Zsigmond and his colleagues

REPLY

Dr. Mirakhur is correct in that the results of our studies have "academic interest," but he can not deny that the findings may also have clinical importance as we succinctly stated that: "Glycopyrrolate and atropine possess low inhibitory effect on human PChE, therefore it is unlikely that PChE *in vivo* would be inhibited to an extent that interferes with the hydrolysis of succinylcholine and/or local anaesthetics of the ester-type." Indeed, their experience concurs with our own observations that no clinically recognizable interactions take place between glycopyrrolate and succinylcholine. Nonetheless, only experiments involving the combination of glycopyrrolate with succinylcholine or procaine can scientifically answer this question.

Contrary to Dr. Mirakhur's claim that we extrapolated the *in vitro* inhibitory effects of glycopyrrolate to the clinical effects of succinylcholine and local anaesthetics, we are well aware of the studies of Foldes and Smith.¹ Those studies showed that extrapolation to the *in vivo* anticholinesterase effect from its *in vitro* inhibitory effect is not permissible, since the I_{50} values of other anticholinesterases used in the management of myasthenia gravis demonstrated no correlation to their *in vivo* therapeutic effectiveness.

At the other extreme, hexafluorenum, which markedly inhibits PChE *in vitro*, causes a predictable and potent inhibition of the *in vivo* hydrolysis of succinylcholine and is, therefore, employed to prolong its effect for muscle paralysis.² Moreover, in anticholinesterase poisoning, the large atropine doses required, e.g., 0.2–1.0 g daily, might lead to a marked *in vivo* PChE inhibition as predicted from its *in vitro* anticholinesterase effect also corroborated by Radic.³

PChE is present as "reserve cholinesterase" in other cholinergic transmission sites.⁴ Surprisingly, we find complete inhibition of the reserve cholinesterases by fractions of the I_{50} of several anticholinesterases in the

humain brain slices by histochemical methods.³ Based on these findings, and with the inadequate level of current knowledge on the actual number of active enzyme receptors and substrate concentrations in vivo at distinct cholinergic receptor sites, one cannot rule out the practical clinical value of this "academic" finding of a moderate PChE inhibitory effect.

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REFERENCES

- 1 Foldes FF, Smith JC. The inhibition of human cholinesterases with anticholinesterases used in the therapy of myasthenia gravis. *Ann NY Acad Sci* 1966, 135: 287.
- 2 Foldes FF, Molloy RE, Zsigmond EK, Zwartz JA. Hexafluorenum: its anticholinesterase and neuromuscular activity. *J Pharmacol Exp Ther*, 1960, 129: 400.
- 3 Radic Z. Effect of atropine on esterases of human blood and pig liver. Abstract #4 p. 43, VI. Balkan Biochemical and Biophysical Days, Plovdiv, April 15-19, 1985. Bulgaria.
- 4 Koelle WA, Koelle GB. The localization of external or functional acetylcholinesterase at the synapses in autonomic ganglia. *Progr Brain Res* 1971, 34, 371.
- 5 Foldes FF, Zsigmond EK, Foldes VM. The distribution of acetylcholinesterase and butyrylcholinesterase in the human brain. *J Neurochem* 1962, 9: 559-72.

Nuffield Department of Anaesthetics, Oxford

To the Editor:

A scientific meeting will be held in Oxford from 23rd-25th July, 1987, to celebrate the Fiftieth Anniversary of the founding of the Nuffield Department of Anaesthetics. This meeting will follow the Second World Congress on the History of Anaesthesia, which is to be held in London from 20th-23rd July, 1987.

Anaesthetists and others who have had connections with the department are invited to write to:

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enclosing their full name and postal address so that they may be circulated with further particulars.

Professor M.K. Sykes
University of Oxford

Transtacheal ventilation

To the Editor:

I was interested to read the report by Ravussin and Freeman on transtracheal ventilation.¹ Two points are worth raising, firstly that high frequency ventilation is not necessary to produce oxygenation. A simple hand-operated trigger device such as the Sanders bronchoscope injector can be used in most instances equally well^{2,3} and is more likely to be available in the emergency situation.

Secondly, in the interests of safety, I would like to stress the importance of a clear upper airway to allow the inflated gases to escape. This is best achieved with the patient's neck in the extended position (as for thyroidectomy). In my experience (in 60 cases) the surgeon can easily flex the head and neck while working on the lower jaw for example, resulting in obstruction of the gas escape pathway. Extra vigilance is necessary when using transtracheal ventilation, to prevent the occurrence of high pressure in the lower airways, leading to possible pneumothorax and emphysema.

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REFERENCES

- 1 Ravussin P, Freeman J. A new catheter for transtracheal ventilation and resuscitation. *Can Anaesth Soc J* 1985; 32: 60-4.
- 2 Layman PR. Transtracheal ventilation in oral surgery. *Annals of the Royal College of Surgeons* 1983; 65: 318-20.
- 3 Layman PR. Bypassing a problem airway. *Anaesthesia* 1983; 38: 478-80.

REPLY

We thank Dr. Layman for his letter. He points out two major aspects of great importance: (1) that when transtracheal jet ventilation is used, a clear upper airway is