LETTERS TO THE EDITOR

Circulatory effects of fast ventilator rates in preterm infants

SIR,—Fenton *et al* have recently described the circulatory effects of fast ventilator rates in critically ill neonates.¹ These authors found a decrease in arterial oxygen tension (PaO₂) with an increase in ventilator rate and have concluded that this fall in PaO₂ was a result of the predicted theoretical fall in mean airway pressure with increasing rate.

Mean airway pressure can be calculated from the following formula:

$$(IT \times PIP) + (ET \times PEEP)$$

$$IT + ET$$

(where IT=inspiratory time, ET=expiratory time, PIP=peak inspiratory pressure, and PEEP=positive end expiratory pressure). It can also be directly measured through a transducer and should essentially reflect the area under the ventilator pressure curve. As can be seen from the above formula, if the inspiratory:expiratory ratios are kept constant and there is no significant change in peak inspiratory pressure or PEEP, then mean airway pressure should remain constant as rate is changed. A critical determinant of whether mean airway pressure will in fact change under these circumstances will be the shape of the ventilator pressure curve, which will be affected by the lung compliance and the gas flow to the ventilator.

We have tested this hypothesis by subjecting an Infant Star (Infrasonics) and a Sechrist Model IV-100B (Sechrist Industries) to the changes that were made by Fenton *et al* for rates of 30 (IT=ET=1), 60 (IT=ET=0.5), and 100 breaths/minute (bpm) (IT=ET=0.3) with a constant inspiratory (20 cm H₂O) and expiratory pressure (5 cm H₂O).

We measured mean airway pressures using an independent transducer and both ventilators were connected to a test lung with a compliance of 1 ml/cm H₂O. There was no change in mean airway pressure for the Infant Star with the ventilator flow varied between 8 and 18 l/minute. For the Sechrist, the same model used by Fenton *et al*, the mean airway pressure at 30 and 60 was 12 cm H₂O and at 100 bpm was 11 cm H₂O at a flow of 10 l/minute. If the flow at 100 bpm was increased to 15 l/minute, then the mean airway pressure was also 12 cm H₂O. Our results also confirm the observations of Greenough and Greenall.²

We believe that the fall in oxygenation associated with the higher ventilatory rates may reflect an inadequate period of time above the opening pressure of the terminal airways in infants with significant respiratory disease, as opposed to any significant change in mean airway pressure.

We believe that the fall in oxygen tensions observed in the current study reflect mechanisms other than those suggested by the authors.

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- 1 Fenton AC, Field DJ, Woods KL, Evans DH, Levene MI. Circulatory effects of fast ventilator rates in preterm infants. *Arch Dis Child* 1990;65:662-6.
- 2 Greenough A, Greenall F. Performance of respirators at fast rates commonly used in neonatal intensive care units. *Pediatr Pulmonol* 1987;3: 357-61.

SIR,—We read with interest the recent paper by Dr Fenton and colleagues but feel that certain points require comment.¹ Firstly, it is not necessary to postulate an effect on shunting to explain the rise in arterial oxygen tension when the biased flow was turned off. The more likely mechanism is via an effect on mean airway pressure. Turning on the bias flow could shorten the positive pressure plateau reducing mean airway pressure. We should be most interested to see data on mean airway pressures generated in the study.¹

Secondly, the observations on tidal volume are surprising. Field *et al* previously reported that tidal volume is maintained until inspiratory time is reduced below 0.3 seconds,² yet in this present study¹ at 60 breaths/minute (bpm) there is already a 25% reduction in tidal volume.¹ This suggests very short inspiratory times were used; this information is not given.¹

Thirdly, unfortunately, the paper of Greenough *et al* is misquoted.³ In that paper changes in positive end expiratory pressure (PEEP) were documented as not occurring with the Sechrist ventilator at rates up to 120 bpm, as this ventilator incorporates an assisted expiratory valve, which prevents inadvertent PEEP at flow rates even up to 20 l/minute.^{3 4} Increasing the flow rate at high rates restores the shape of the waveform, maintaining mean airway pressure without altering the PEEP.³ In that study of Greenough *et al* the inspiratory:expiratory (I:E) ratio was held constant at 1:1.2. It has been subsequently shown that with such an I:E ratio, inadvertent alveolar PEEP occurs in paralysed infants at rates of 100 bpm,⁵ preventing a fall in carbon dioxide at the fastest ventilation rate.³ It is likely that the difference in the results of the earlier study³ and Fenton *et al*¹ could be the use of different I:E ratios. Again, data on the I:E ratios used would be helpful.

Fourthly, the results of Fenton *et al* are given only as mean and standard errors, it is thus not possible to determine if all the babies studied generated the same pattern. This seems unlikely as the patients were of very varied postnatal ages (range 14-216 hours) and birth weights (720-2420 g) and of different ventilatory requirements (fractional inspiratory oxygen 0.35-1.0; peak inflation pressure 15-35 cm H₂O). In particular, it would be more informative to have the results of individual babies' tidal volumes expressed as ml/kg.

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Antiviral and antibacterial lipids in human milk and infant formula

SIR,—We read with great interest the recent article by Isaacs *et al* in which they conclude that the antiviral and antibacterial activities of lipid extracts from gastric aspirates in infants probably result from intragastric lipolysis by lingual lipase to monoglycerides and fatty acids from the triglycerides of the original feeds.¹ Lingual lipase hydrolyses medium and short chain triglycerides at a higher rate than longer chain fats.² In the study by Isaacs *et al*, at least 50% of the fat content of both formulas was medium chain triglyceride if the additional coconut oil is taken into account. Hydrolysis of milk fat by lingual lipase produces a large amount of monolauryl glycerol, which has been shown to have appreciable antibacterial, antiviral, and antifungal activities.³

We have recently shown a similar effect in mice, where by modifying the mother's dietary fat intake we were able to change the fatty acid composition of their milk. The offspring were inoculated orally with EDIM rotavirus. In those young mice fed on milk naturally enriched with lauric acid (C12) and other medium chain fatty acids, the onset of diarrhoea was delayed and the stool excretion of rotavirus was appreciably reduced by comparison with mice fed on milk of different fatty acid composition (unpublished observations).

At least in mice, therefore, and contrary to the assertion of Isaacs *et al*, the protective effects of milk fatty acids appear to operate against non-enveloped viruses as well as enveloped viruses and bacteria. We cannot, of course, rule out the possibility that other mechanisms such as secondary variation in trypsin secretion could be responsible for our observations,^{4 5} but we think that this is inherently unlikely.

It is becoming increasingly clear that milk fat, whether human or of animal origin, has important protective value against intestinal infection. Skimmed milk should not be used as a food source for young children unless there is a strong medical reason for the withholding of fat, and this policy should be followed particularly in countries with a high incidence and severity of gastroenteritis.

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- 1 Isaacs CE, Kashyap S, Heird WC, Thoramar H. Antiviral and antibacterial lipids in human milk and infant formula feeds. *Arch Dis Child* 1990;65:861-4.
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Dr Isaacs comments:

I certainly agree with Professor Dodge and Dr Sagher that milk lipids may provide important protective effects. Further, I find their observation that alterations in the medium chain fatty acid composition of mouse milk may reduce the severity of infection from rotavirus, a non-enveloped virus, extremely interesting. We, of course, did not determine the effect of the stomach contents of infants fed the various formulas on non-enveloped viruses. Rather, our statement that milk fatty acids and monoglycerides have antiviral activity against enveloped viruses but not non-enveloped viruses was based upon the results of a number of studies by us and others showing that only enveloped viruses are inactivated by milk lipids or purified lipids.

In the early studies of Welsh *et al* enveloped Semliki Forest virus and herpes simplex virus type 1 (HSV-1) were inactivated by milk lipids but enterovirus coxsackie B4, a non-enveloped virus, was not.¹ In addition, we found that human milk inactivated the enveloped measles virus, vesicular stomatitis virus and HSV-1 but not the non-enveloped vaccinia virus and poliovirus.² Milk lipids also have been shown to inactivate dengue virus³ and mouse mammary tumour virus⁴; these are both enveloped viruses.

In *in vitro* studies it has been found that purified free fatty acids and their derivatives inactivated the enveloped Sendai virus, Newcastle disease virus, influenza A virus, Sindbis virus, West Nile virus, HSV-1, and a number of enveloped bacteriophages but not the non-enveloped SV40, polio or encephalomyocarditis viruses (ECMV).^{5,6} This antiviral effect appeared to be due to the destruction of viral envelopes.⁷

These multiple findings suggest that the apparent protective effect of milk lipids against rotavirus infection observed by Dodge and Sagher is unlikely to be due to direct inactivation of the non-enveloped rotavirus. However, milk fatty acids may prevent the binding of rotavirus and other non-enveloped viruses to receptors or interfere with viral uncoating. These suggestions are supported by the observations of JFE Newman (Institute for Virology, Sandringham, South Africa), reported at the recent VIIIth International Congress of Virology (Berlin, 1990), that fatty acids with chain lengths of 12-15 prevent uncoating of some non-enveloped viruses, for example, bovine enterovirus and ECMV, but not others, for example, poliovirus type 1, coxsackie B5, and human rhinoviruses 1B and 14. It would, therefore, be interesting to see the results of an *in vitro* study examining the effects of medium chain fatty acids found in mouse milk on rotavirus infectivity.

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Fluorescein dilaurate test of exocrine pancreatic function in cystic fibrosis

SIR,—I read with interest the paper by Drs Dalzell and Heaf,¹ particularly as we had a very similar study published in the *Archives* four years previously (to which no reference was made!).² In both studies the index cases and controls were similar in age and number, but we prescribed double the dose of fluorescein dilaurate than did Dalzell and Heaf. Our study also demonstrated significantly different fluorescein dilaurate excretion ratios between patients with cystic fibrosis and normal subjects, with the ratios being significantly reduced in patients with cystic fibrosis ($p < 0.01$). An additional component to our study was to compare the fluorescein dilaurate test with faecal chymotrypsin estimation. We found a positive correlation between the two tests ($R = 0.69$, $p < 0.02$).

Although the fluorescein dilaurate test appears to detect exocrine pancreatic insufficiency, in practice it is of limited value as it is in capsule form and not suitable for the age group in which the presentation of cystic fibrosis is most prevalent. We did explore the possibility of the test being used to titrate pancreatic supplement administration. If cholesterol ester hydrolase, which is responsible for liberating the fluorescein from fluorescein dilaurate, was incorporated into a pancreatic enzyme supplement, it may be possible to use the fluorescein dilaurate test to determine the most effective dosage of pancreatic enzyme for individual patients. Unfortunately this enzyme does not appear to be present in any of the commercially available preparations.

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Hospital admission—a missed opportunity to immunise

SIR,—We agree with the conclusion of Ferson's study that there is poor documentation of a child's immunisation status on admission to hospital.¹ In 66% of the children admitted to our hospital and verified to have incomplete immunisation the 'medical record of immun-

isation' was absent or in so shortened a form as to be meaningless.

Using information from the district computer we determined the immunisation status of children from Salford district who were admitted to a general paediatric ward in a teaching hospital during November 1989. We also obtained details about the children verified to have incomplete immunisation, including the recorded immunisation history, from the hospital notes.

There were 139 admissions of 133 Salford children during the month. The children's ages ranged from 7 days to 15 years with 113 under 5 years of age. Using the immunisation schedules recommended at that time, information from the district computer showed that 70 children were fully immunised and 47 incompletely immunised; 16 were not traced by the computer.

Information from the hospital notes suggested that in five children there was a contraindication to immunisation and three children had received the necessary immunisation within the two weeks before admission. The hospital notes for six children were not available. The remaining 33 children could have been offered: triple antigen ($n = 14$), oral polio ($n = 14$), combined diphtheria-tetanus ($n = 1$), measles-mumps-rubella ($n = 22$), tetanus ($n = 3$), and pertussis immunisations ($n = 12$).

Using Ferson's classification of the 'medical record of immunisation' in the hospital notes,¹ in 27 of the 41 notes (66%) documentation was absent or unclear. In two (5%) it was clear but incorrect, and documentation was correct and clear in only 12 (29%) of notes.

At our children's hospital, sited in a district with poor immunisation uptake, the opportunities for immunisation in a single month on one ward are considerable. To immunise in hospital we need accurate information on previous immunisations. Parental recall and medical recording of immunisation provide inadequate data. Two possible solutions are improving access to immunisation information held on district computers and using parent held child health records.

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Effects of overweight on lung function

SIR,—We were very interested in the paper by Dr Fung and colleagues on overweight and lung function,¹ but we have some queries about their approach and conclusion.

To investigate the association between body mass index and lung function in children, the authors included subjects up to 20 years of age. In table 1 they show that distribution of height for the sexes was unequal: 45% of all girls were taller than 150 cm but only 12% were taller than 159 cm. This suggests that most of these females had reached their adult height: at age 13, when 75% of Hong Kong girls reach menarche, the median height is 151 cm.² On the other hand, 31% of all boys were taller than 159 cm with no skewed distribution, suggesting that most boys had not reached adult height yet.