



**Trial of ventilatory support with
INhaled Nitric Oxide versus
Ventilatory support withOut
inhaled nitric oxide**

Newsletter No 2

August 1998

GOOD NEWS FROM THE MRC

The MRC has agreed to support an extension of the pilot recruitment until the end of July 1999. Funding is also assured for the paediatric assessment at one year (corrected) of all babies entered into the trial, and for the analysis of this data. Over this next crucial year we need to show the MRC that a definitive trial is feasible. We will be guided by the advice of the independent Data Monitoring Committee which will look at a confidential interim analysis in the Spring.

RECRUITMENT

Slow and steady

July best month ever

48 BABIES NOW RECRUITED

Best recruiter Leicester

Best improver St Mary's, Manchester

CLINICAL UNCERTAINTY

There is widespread uncertainty about which babies could benefit from nitric oxide. We are convinced that there is insufficient evidence from trials to recommend treatment with inhaled NO until it has been evaluated. The short term benefits in improved oxygenation shown by some babies when treated with NO, and the reduction in the need for ECMO shown in the NINOS trial for mature babies, may be counter-balanced by adverse longer-term problems, including potential toxic effects. No convincing follow up information is currently available.

In recognition of the range of clinical uncertainty, centres are deciding their own criteria for considering whether babies are candidates for this phase of The INNOVO Trial. Some centres are only entering babies of <34 weeks into the trial and treating term babies (= 34 weeks). The data collected at entry about gestational age and disease severity of babies recruited by March 1999 will give better information on which a sample size for the main trial can be calculated.

Of the 24 centres currently 'on-line' in the trial, the following 10 centres are only treating with nitric oxide in the context of the trial

Erinville Hospital, Cork	Royal Victoria Hospital, Newcastle
Hillingdon Hospital, Middlesex	St Mary's Hospital, Portsmouth
Leicester Royal Infirmary	South Cleveland Hospital, Middlesbrough
Liverpool Women's' Hospital	Southmead Hospital, Bristol
Northwick Park Hospital, Middlesex	University of Wales Hospital, Cardiff

NEW CENTRES

Now that we have the multi-centre research ethics committee (MREC) approval the following new centres have recently made a We will be setting up new centres until the beginning of March

1999. We will provide centres with the documentation needed for making applications to the local REC and give appropriate technical support.

TECHNICAL SUPPORT

Roger Smith, respiratory technician from Leicester is our new Research Technician who has taken over from Richard Crook from this August. He will provide technical support and advice to centres “on-line”. He will be focusing on new centres installing delivery systems giving advice and visiting centres to give practical demonstrations and run teaching sessions. Please make initial contact via the trial office.

DATA COLLECTION

Many thanks to everyone who is involved in completing and returning the trial datasheets. We are aware that this creates some additional work, but so far the rate of return has been extremely high. We will remain in regular contact with all recruiting centres to ensure that we have a complete dataset for the interim analysis next Spring.

PATHOLOGY

The pathology sub-study is an important adjunct to this trial as mortality is likely to be quite high. We are now in regular telephone contact with each centre when a baby is recruited and will remind neonatal co-ordinators about asking for a post-mortem if appropriate.

OUTCOME AT ONE YEAR (CORRECTED)

The one year assessment of the first few babies in the trial is being conducted as part of the routine follow up in the paediatric outpatient clinic. Some babies are also receiving a detailed respiratory assessment in one of two specialist centres.

TOXICOLOGY

A great deal of in-vitro (bench top) work has been going on. The aim has been to establish techniques capable of identifying evidence of lung damage or changes induced by exposure to exogenous NO. It

is important that we can differentiate such an effect from those of natural/endogenous NO exposure. Any units wishing to contribute samples to the toxicology studies please contact:

David Shuker, MRC Toxicology Unit, tel: 0116 252 5573 fax: 0116 252 5619 email: degs1@le.ac.uk or Sailesh Kotecha, Department of Child Health, tel: 0116 252 3262/5818, answering machine: 0116 252 3266, fax: 0116 252 3282 or email: sk43@le.ac.uk, both at University of Leicester.

SUPPLIES OF NITRIC OXIDE

BOC have written to centres within their donation programme indicating their intention to start charging for supplies of nitric oxide. They have taken this decision after a two year period in which they supplied the gas free of charge. We are pleased to inform you that BOC have agreed, however, to continue to support the INNOVO trial by giving nitric oxide free for babies entered into the trial.

TEACHING PACK

The teaching pack was one of the suggestions made at the Study Day held for neonatal nurse co-ordinators in March. In September, we will be sending centres a set of overheads giving the background to the study, eligibility criteria and trial procedures.

INNOVO TRIAL PROJECT MANAGEMENT GROUP

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