COMPUTERISED PHYSIOLOGICAL TREND MONITORING IN NEONATAL INTENSIVE CARE

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This thesis is dedicated to my parents,

in thanks for their love through the years.

Declaration

This studies presented within this thesis were carried out under the guidance of Professor Neil McIntosh, Department of Child Life and Health, University of Edinburgh, and Dr. Harry Brash, Department of Medical Physics, University of Edinburgh, between August 1990 and July 1993.

The experimental work presented in this thesis has been performed predominantly by myself, as part of a research team; contributions from co-workers have been acknowledged, where appropriate, in the text. This thesis has been composed by myself.

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Abstract of Thesis

Improvements in intensive care medicine, have led to an overwhelming increase in the volume of patient information collected. Computers could help to gather and organise this data, giving healthcare workers better information and providing more time for direct patient care.

Early computers used in medicine were slow and unfriendly, and so created a generalised computer phobia. The development of faster, friendlier computers and an increasingly computer literate workforce might signal a new age for computers in medicine.

Premature and sick newborn infants require intensive medical care. An important part of the care of these frail individuals, is that maximum information should be gathered about their physiological status with a minimum of handling. Physiological information continuously gathered from patient monitors and displayed as trends over variable time periods, might improve the ability of healthcare workers to recognise physiological deterioration (and alternatively stability); thus reducing response times to possible hazards, whilst minimising handling. Critics are understandably concerned that such systems could reduce clinical acumen.

We have assessed the introduction of a commercially available computerised physiological trend monitoring network into a neonatal intensive care unit. The attitudes of staff and parents were on the whole favourable, with the majority feeling that infant care benefitted from the introduction of computers. A detailed study of the effects of computerised physiological monitoring on patient outcome in both short and medium term, showed no significant benefits. The computers improved both the

quality and accuracy of the stored infant physiological data. Artifact was predominantly predictable; it could be ignored in real time trends and removed from recorded data prior to statistical analysis.

Neonatalogy is a relatively new science, where a continuously expanding physiological data source could help to improve patient care through research. Three areas were explored: (a) Reference blood pressure ranges were established for very low birth weight infants, using more detailed information on a larger group of infants than previously possible. (b) Infants with retinopathy of prematurity, compared to those without the disease, did not differ significantly in the amount of time they spent with a continuously monitored transcutaneous oxygen greater than 12 kPa. (c) Previously undescribed blood pressure waves were identified; associated with hypoxia, they may help improve understanding of fetal autonomic development.

Although unable to demonstrate an improvement in patient outcome resulting from the introduction of a computerised physiological network (possibly due to poor entry criteria), we have demonstrated improved staff confidence, better physiological record and the opportunity for improvement in care through research. The hardware and software were reliable, though expensive. Consequently, the role of networked physiological computer systems in neonatal intensive care is not proven. Such systems would be invaluable to those specialised centres with an active interest in neonatal research, but would generally prove to be too great a demand on resources (financial and manpower) in smaller units.

Acknowledgements

I would like to give thanks to Professor Neil McIntosh for his active and positive supervision during this project. My thanks also to Dr. Harry Brash for his calm appraisal of this work, and to the two research nurses on the project (Sarah Deere and Andrew Symon), who have both worked hard to provide the optimum chances of success for the project.

My special thanks goes to the nursing and medical staff of the Simpson Memorial Maternity Pavilion, many of whom have made great endeavours to benefit from the computer monitoring, in spite of the heavy burden of clinical commitment.

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Please note:

The 'Mary' trend illustrations in this thesis have been produced as indirect copies. The computer system cannot produce screen print outs in colour, neither can they be edited and so often contain excess information than that needed to illustrate a point. I consider colour to be a very important part of computer trend monitoring and the illustrations have been created to highlight this, whilst at the same time depicting typical trends. Computer print outs on which these illustrations are based can be found in Appendix 8.

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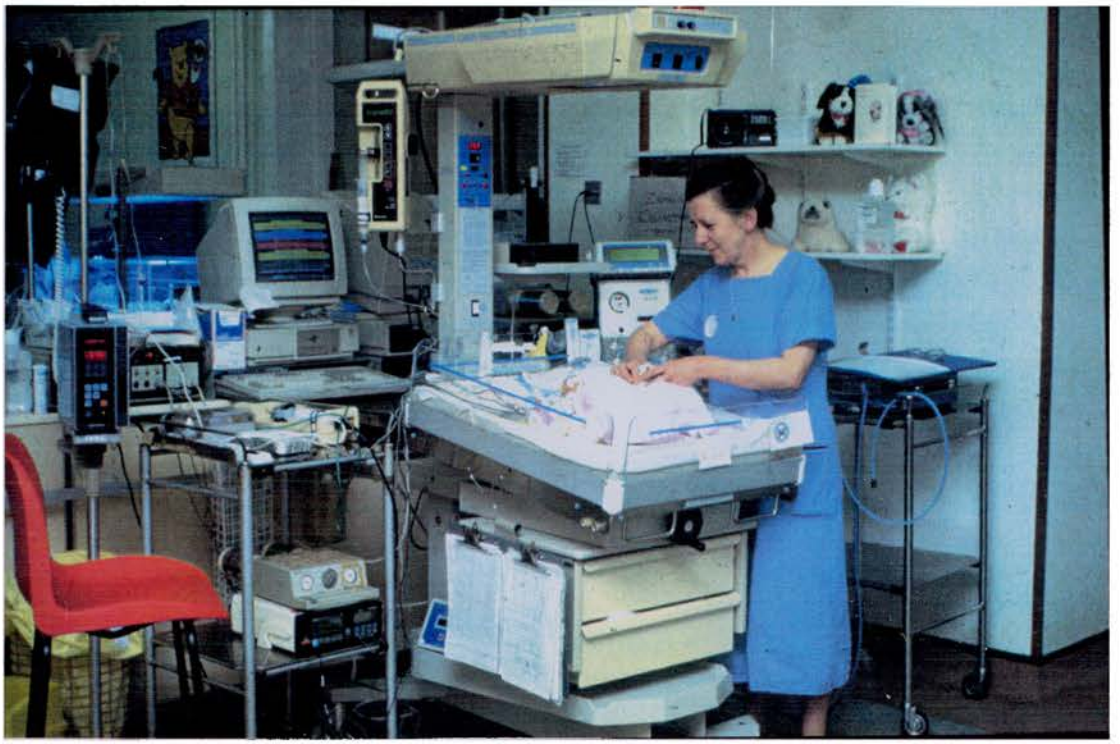
Abbreviations

Adr	adrenaline
Amp	amplitude
APH	antepartum haemorrhage
bpm	beats per minute
CPTM	Computerised physiological trend monitoring
CSF	cerebrospinal fluid
DA	dopamine
dbp	diastolic blood pressure
ICP	Intracranial pressure
iqr	interquartile range
IUGR	Intrauterine growth retardation
IVH	Intraventricular haemorrhage
kPa	kiloPascals
mbp	mean blood pressure
mls	millilitres
mmHg	millimetres of mercury
NA	noradrenaline
NHS	National Health Service
PDMS	Patient data management system
PIH	Pregnancy induced hypertension
ROP	Retinopathy of prematurity
s	seconds
sbp	systolic blood pressure
vlbw	very low birthweight (<1500g)
Δ	wavelength
°C	temperature (degrees Celcius)

Figure 1

Computerised physiological trend monitoring in neonatal ICU.



Sister Margaret Paton at the Neonatal Unit, Simpson Memorial Maternity Pavilion, Edinburgh

Chapter 1

CHAPTER 1

Introduction.

1.1 Background

Fever, for many millenia a disease entity, was first objectively measured by Philo of Byzantium in 200 BC. It was not until 1850 however, that Traube suggested to Wunderlich a systematic study of temperature patterns [Wunderlich, 1871]. The resulting temperature charts described for the first time the regular cyclical variation of temperature in enteric fever and the effects of digitalis in reducing this fever [Keele, 1963]. Similarly Sir John Floyer's 'Physicians pulse watch' invented in 1707 [Floyer, 1707], for the first time quantitatively assessed the rate of the arterial pulse, a clinical sign first described in Ancient China by Nei Ching in 2600 BC. These great contributors to medical science would be astounded by the technological ability of a modern neonatal intensive care unit, yet we continue to record temperature charts in an identical fashion to those produced by Wunderlich in 1850, alongside which Floyer's pulse rate is noted at the same hourly frequency.

In his book on medical history published in 1942 [Glendening, 1942], Logan Glendening observed that;

'Clinical medicine could not advance until it acquired objective methods of determining or measuring the nature and extent of organic disease present in a patient's body' .

Clinical medicine continues to advance; neonatal intensive care has over the last 10 years improved survival in those infants weighing less than 1500g from 55% to 71% [Cooke, 1993]. The technological and clinical skills that have evolved to enable this improvement in care are enormous. Consequently, the amount of information required about and produced for each patient has become vast. This new era of medical advancement will require new methods of objective determination of disease.

One possible method in neonatal intensive care is computerised physiological trend monitoring (CPTM).

1.2 The development of computers in intensive care

The first computer to be manufactured was produced in 1947 by Ferranti Ltd., based on the electromechanical model developed by Turing's team at Manchester University. It was bulky, slow and complicated [Hodges, 1983]. In the 1950's and 60's there was a slow but steady development of solid state electronic computers, which made computers available for use by non-physicists for the first time [Geisgow and Barret, 1987]. Computerised physiological monitoring began to be used in a short term investigative capacity [Taylor, 1965]. The combined development of the silicon chip and advanced software languages in the 1980's, produced the revolution in computers that have enabled the development of a wide range of biomedical computer applications.

Intensive care is an ideal area for the application of computers, as they enable the large amounts of data produced by intensive care patients to be condensed and simplified. Computer applications developed for

intensive care include; databases, physiological monitoring, fluid and drug management, laboratory data tabulation, nurse charting and expert systems (decision aids and artificial intelligence programmes).

Adult intensive care has had and continues to have a greater involvement than neonatal intensive care in the development of computer applications. Adult intensive care is an older medical speciality than that for neonates, and the involvement of several clinical specialities has provided a more powerful lobby for research development. Computerised physiological monitoring systems, although not as widely used as other biomedical computer applications [Stead, 1987], now form an integral part of many adult intensive care computer networks [Ross *et al.*, 1990] [Bradshaw *et al.*, 1984] [Piper *et al.*, 1991]. Adult and neonatal intensive care however are increasingly divergent specialities, where technological developments test the physiological capabilities of the human body at both extremes of age. The pathophysiological instability of an infant born 4 months prematurely is very different to that of a 70 year old man following cardiac surgery. Whilst valuable experience may be gained from the computer expertise of adult intensivists, it may be more appropriate that neonatal computer applications are developed specifically for neonatal care.

1.3 Neonatal Intensive Care Computer Survey

In September 1991, I evaluated the areas of application and the methods of development of computers in neonatal intensive care in the United Kingdom. The eight question questionnaire was sent to a consultant neonatalogist in the 47 neonatal units of the U.K. with 5 or more intensive care cots [Directory of Emergency and Special Care Units, 1990]. The questionnaire is detailed in Table 1. The responses obtained are shown as a percentage in brackets next to each question (%).

42 of the 47 questionnaires were returned answered (89%). Of these 88% used computers within their unit: 92% used IBM computers, (46% exclusively), 30% used Apple Macintosh, (3% exclusively) and 27% used BBC computers (none exclusively). Other computers, including mainframe computers were used in 14% of units (2% exclusively).

Computers were most frequently used for the collation of patient details; 100% of those units with computers kept some record of patient details. Computer databases were therefore present in at least 78% of all U.K. neonatal intensive care units (i.e. 88% of the 89% replying to the questionnaire); a figure equal to 78% patient database use, in a recent survey of all tertiary neonatal units in the USA [Slagle and Gould, 1992]. A high percentage (38%) had a fluid therapy program and 27% had the ability to tabulate their incoming laboratory data. Only 11% had the facility for any form of computerised nurse charting. Computers were used in more than half of the units for research purposes. Medical staff used computers more than any other staff group.

Methods of software development are reflected in question five; 76% of respondents who used computers had software designed by an

internal programmer (61% in the USA database survey), 59% used commercially available software and 32 % used software specifically designed by a software company. However, most neonatal units had more than one source for their software; 24% had only internally designed software, compared with 8% with just software company design and 11% with only commercially available software.

Many respondents (62%) considered computers to have been of great benefit to their neonatal unit.

Finally we asked whether consultants would like to increase the use of computers in their neonatal units; 93% wished to. There was no overall area in which development was required. Almost 50% wished to improve collection of patient details and 55% hoped to develop computerised laboratory results. Many units (43%) wished to begin computerised nurse charting. Only 26% wished to develop computerised physiological monitoring for clinical purposes and 31% for research purposes.

The survey demonstrates that neonatal consultants in the U.K., have an interest in computers and a great willingness to benefit from this new technology.

Table 1 United Kingdom Neonatal Computer Survey

1 Are computers used within your Neonatal Unit?

Yes 88% No 12%

(Answers to questions 1-6 are a percentage of those who replied yes).

2 Which members of staff use the computers?

Medical	92%
Nursing	68%
Clerks	84%
Others	27%

3 What type of computers are in use?

IBM based	92%
Apple Macintosh	30%
BBC	27%
Other	14%

SOLELY;

IBM based	46%
Apple Macintosh	3%
BBC	0%
Other	3%

Number of makes within each unit;

One type	51%
two types	38%
three types	11%

4 What principle function do the computers hold?

65%	Non Clinical / Administrative
84%	Secretarial / Word Processors
100%	Patient Details
38%	Fluid therapy program
27%	Laboratory data tabulation
24%	Clinical Physiology
11%	Nursing charts
5%	Other

Research

54%	Physiological assessment
59%	Statistical assessment

5 Who designed the Software for your computers?

59%	Commercially available
32%	Software company design
76%	Internal Programmer

SOLELY;

Commercially available	59%
Software company design	8%
Internal programmer	24%

No. of types of programming?

One 43% Two 46% Three 11%

6 How do you feel that computers benefit your NNU?

No overall benefit 0%
Some benefit 38%
Great benefit 62%

(Answers to questions 7-8 are a percentage of all respondents).

7 Would you like to increase the use of computers in your NNU?

Yes 93% No 7%

8 If yes, for what purpose?

(As a percentage of those replying yes)

29%	Non clinical / administrative
31%	Secretarial /Word Processing
48%	Patient Details
33%	Fluid therapy program
55%	Laboratory data tabulation
43%	Nursing charts
26%	Clinical Physiology
5%	Other ; State

Research

31%	Physiological assessment
38%	Statistical assessment

1.4 Neonatal Computer Applications

1.4.1 Databases

Databases are the main application of computers in neonatal intensive care. They vary from simple minimal data set collections on small personal computers using 'in house' [Winchester *et al.*, 1989] [Rao and Watkinson, 1991] or adapted commercial software [Roper, 1991] [Bash and Thorp, 1987] [van Someran, 1992], to large networks of computers processing more comprehensive data sets [Lowe *et al.*, 1992] [Lissauer *et al.*, 1991] [Franco *et al.*, 1990]. Databases may be limited to collecting only the amount of information that is required for a specific purpose, or may attempt to collect as much data as possible to enable a wider surveillance [Spencer, 1991]. The USA neonatal database survey [Slagle and Gould, 1992] demonstrated increased user satisfaction of a database if it contained a more comprehensive dataset and/or it was able to generate reports and labels.

The greatest limitation to a database is the accuracy of the data input. Accuracy may be reduced in several situations: (a) when excess information is required from individuals who are too busy with other tasks (i.e. health care workers), (b) if data is entered by staff unfamiliar with clinical terminology (i.e. ward clerks) or (c) if the data collected is not seen as valuable. Improved visual presentation of databases [Shultz and Brown, 1989], which with few exceptions[1] are poor, should encourage the bored or busy user to take a greater interest in data input and so improve the accuracy of the collected information. In the USA neonatal database survey, only 27% of responding units had a regular method of data

[1]Neo Database. Oxford Intruments Ltd, Abingdon OX14 1BZ.

checking, yet over 50% used information from databases in publications. The paper suggested that proof of data verification be given for each publication containing database derived data. This is a very reasonable proposition.

Fully configurable commercial neonatal databases, will allow adaptation of the dataset to be as small or comprehensive as desired by the attending team; enabling the database to be adapted to local requirements. It would then be possible to compare information collected at a district general hospital with that of a teaching hospital with the same software.

1.4.2 Fluid, Nutrition and Drug Management

This is an important computer application for neonatal intensive care. Premature infants have a critical requirement for adequate nutrition and are prone to large insensible fluid losses. Evaluation of fluid and nutrient intake is an essential component of care in a sick infant and one that may ultimately affect morbidity and mortality. The manual management of fluid and nutrient intake in those units without appropriate software is poor, with an error in fluid calculations of over 70% [Steckeler and Ellis, 1989]. These errors increased with smaller infants (<2kg) and less well trained junior staff [Tepas *et al.*, 1991]. Computers vastly improved the accuracy of calculations in both of these studies, without increasing the time required to make the calculations. Pharmaceutical software can help reduce the errors made in calculating the small drug dosages required by newborn infants and also help identify drug incompatibilities in complicated drug regimes[1].

[1]Personal observation of 'In House' system developed at Hammersmith and Queen Charlotte's Hospital, London.

1.4.3 Laboratory Data Collection

I have been unable to find any reports of laboratory data collection systems specifically for use in neonatal care. Adult systems collect laboratory values by direct links with the laboratories and then establish; (1) values which are outside predetermined ranges, (2) those values which are displaying important trends [Shabot *et al.*, 1990], or (3) are within a normal range but are affected by other parameters which are not (i.e. calcium and albumin) [Bradshaw *et al.*, 1989].

1.4.4 Expert Systems

Neonatal expert systems are poorly developed in comparison with those for adults. Most of the neonatal expert systems reported are 'decision aids'. In the U.K the only expert system that I am aware of in neonatal care, is the blood gas/ventilation decision aid developed in Leeds with grant assistance from the European Community[1]. Blood gas details are entered manually and the computer suggests appropriate changes in the infant's ventilation, aimed at reducing the peak inspiratory pressure. Trend detection is not yet part of the system. The programme is principally used by nurses performing blood gases and junior medical staff in their first 2-3 months on the neonatal unit. Following introduction of the aid, more consistent patterns of ventilation were reported to have occurred. A similar system was developed and assessed in Denmark. They reported that of 745 blood gas samples in 30 neonates, medical staff totally agreed with only 37.5% of the computers decisions and this decreased in infants with more severe respiratory illness [Arrøe, 1991].

'Neonate' is an expert application based on the successful 'HELP'

[1]Personal observation. Dr Peter Dear. St James' University Hospital Neonatal Unit, Leeds.

hospital information system at the University of Utah, USA [Franco *et al.*, 1990]. It generates an intelligent problem list from entries into an admission sheet, listing both probable and potential diagnoses. A separate section of the same programme has proven useful in helping junior medical staff to identify neonatal chest x-ray abnormalities [Franco *et al.*, 1991]; x-rays are interpreted by the medical staff in response to several questions from the computer. The findings are then typed into the computer, which subsequently produces a diagnosis more accurate than that reached by the junior doctor alone. Teaching provides an important function for expert decision aids. The use of computers to diagnose x-rays and ultrasound scans without encouraging clinical interpretation may dangerously undermine learning and decision making.

1.5 Physiological Monitoring Systems

The potential of computerised physiological monitoring systems within neonatal ICU is appreciated by reviewers of neonatal monitoring devices [Jenkins, 1991] [Rolfe, 1986]. However, a survey in the USA reported that only 4.8% of hospitals (both adult and paediatric) had computerised vital signs [Summers *et al.*, 1989]. I have found information about two non commercial and four commercial computerised physiological trend monitoring applications developed specifically for use in neonatal intensive care.

1.6 Non Commercial Neonatal CPTM

A four channel monitoring system with a five second sampling interval, was successfully developed in Holland on an Apple Macintosh computer [van der Weil *et al.*, 1987]. The user could change both graph and time scales and collect a few patient details. No further development of this system has occurred.

A 16 channel physiological monitoring system was developed in the USA for the study of intraventricular haemorrhage [Perry *et al.*, 1986]. Also based on an Apple computer, data was accessed from patient monitors and one minute average values were downloaded to a floppy disc hourly. Summaries were available. The system was used in a large study of intraventricular haemorrhage [Bada *et al.*, 1990]. No further developments have been reported.

1.7 Commercial Neonatal CPTM

Four general physiological monitoring systems are commercially available in addition to the 'Mary' system described in this thesis. The features of all five systems are summarised in Table 2. Two other computerised systems are available to measure oesophageal pH, apnoea and heart rate for the diagnosis of oesophageal reflux, but these do not have a general application to neonatal care [1,2].

1.7.1 *Athena Infant Monitoring System* (S &W Vickers[3])

This system is incorporated within a standard patient monitor, which reduces both size and cost.

The monitor is modular, with 6 general screens (General display, cardiovascular, ventilator interface, pneumooxybar, pneumobradybar, pneumobar) and can be incorporated into a network. Information for trend graphs is stored each minute on up to 24 channels and can be displayed over variable time scales from 15 minutes to 24 hours. Events may be denoted by an asterisk, though the exact nature of the event has to be handwritten elsewhere. Hard copies of trend screens may be printed. There is no ability to store or download information and data is lost after 24 hours. No statistical analysis of the data is possible.

Staff using a demonstration Athena, found the trend screen terminology difficult to understand and the menu system confusing. Although staff were fairly impressed by the general monitor, they infrequently used the trend screens as this involved losing many

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[1]PC Polygraf. Synectics Medical.
[2]POLY medical analysis. Research Systems BV, 1072XX Amsterdam.
[3]S&W Vickers Ltd., Ruxley Corner, Sidcup, Kent, DA14 5BL.

waveform displays.

1.7.2 *Carevue 9000* (Hewlett Packard[1])

Developed for use in adults, this network system is now also available for paediatric and neonatal intensive care. The system acts as a nurse chart spreadsheet, bringing together information on; vital signs, ventilation and blood gases, fluid intake and output, laboratory data, medication and basic patient care [Thomson, 1991].

Data is entered manually, except for physiological vital signs which are accessed from Hewlett Packard 'Merlin' patient monitors. The sampling interval for vital signs is between 15 minutes and 1 hour and each set of vital signs has to be verified by the nurse on duty. Alternatively, minute by minute vital signs may be recorded, but each minute has to be individually reviewed and selected within a 5 hour period [Skinkis, 1992]. Therefore, the physiological monitoring aspect of the Carevue 9000 offers little improvement on manual charting and the increased workload of reviewing data prior to its acceptance, increases computer charting time and reduces patient time [Kalbach and Kalbach, 1988]. As the principle function of this system is as a spreadsheet, trend display screens may not be visible for large periods of time and so trends may only be viewed when a problem arises with the patient. Events may be marked as they occur, but can not be explained. Statistical analysis of physiological data is not possible on standard Carevue models. Copies of daily summaries can be printed. Information for the whole of each patients stay is stored on two central servers (each backing up the other).

The problems of adapting adult ICU software for use in neonatal

[1]Hewlett Packard Ltd, Cain Rd, Bracknell, Berkshire, RG12 1HN.

ICU is highlighted by the Carevue fluid management programme, which poorly coordinates the small volumes of fluid required by sick neonates; large changes in fluid therapy may be made without the programme prompting a review of the input schedule[1].

1.7.3 *Patient Care Management System* (Space Labs Limited[2])

Also a modular system, incorporating both a monitor and trend information. It is available as either a stand-alone or can be networked. Software is incorporated that enables identification of the sequence of events in apneoa/bradycardia. The system can be integrated with other ICU equipment. Bedside monitors can display up to 8 channels. Trends can be observed in 5 time scales from 1 to 16 hours. Control is by infra-red touch screen. Information is stored as minute values for 24 hours. Standard systems have no facility to print summaries or store information for more than 24 hours.

I have only had the opportunity to see this model in a trade display and not whilst in clinical operation. The screen appears crowded due to the amount of information present on the screen (includes on-screen controls). Data manipulation and storage is minimal and is of little value for longer term review.

1.7.4 *System 2000* (Emtek, marketed by Siemens[3])

This is an adult system from the USA, which has been used in Paediatric and neonatal ICU. Only 4 hospitals use the system outside the USA, none in the U.K.. It functions principally as a nursing spreadsheet,

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[1]Comments of nurses working with the system in the Paediatric Cardiac Unit, Brompton Hospital, London.
[2]SpaceLabs U.K., Eskdale Road, Winnersh Triangle, Wokingham, Berkshire, RG11 5TS, U.K.
[3]Siemens Ltd, Siemens House, Windmill Road, Sunbury-on-Thames, Middlesex, TW16 7HS.

with automatic data entry from standard ICU equipment (bedside monitors, ventilators, IV pumps etc.). The system also includes automatic calculation of fluid balance and drug intake. Laboratory results and progress notes are manually entered. There are also features enabling billing and audit, and the system can prevent duplicate prescribing of medicines and laboratory tests. Vital signs have to be verified prior to acceptance, usually every 30 minutes, though they can be accepted each minute. Summaries can be printed. Data is stored permanently on central servers for up to one year. On-line statistical analysis of physiological information is not possible on standard models.

Table 2 Comparison of features of the five commercially available CPTMs

	Athena	Space Labs CPTM	Emtek 2000	Carevue 9000	Mary
Comprehensive spreadsheet	No	No	Yes	Yes	No
Incorporated within a patient monitor	Yes	Yes	No	No	No
Vital sign storage with no verification	Yes	Yes	No	No	Yes
Smallest sampling frequency	1 minute	1 minute	1 minute	1 minute	1 second
Long term data storage	Yes*	No	Yes	Yes	Yes
Central observation station	Yes	Yes	Yes	Yes	Yes
Designed for neonatal care	Yes	No*	No*	No*	Yes
On-line statistics (physiological)	No	No	Yes†	Yes†	Yes†
Event identification (Comment/Marker)	M	None	None	M	C
Number of channels	24	8	16	90	32
Number of trend time scales	8	5	5¶	5¶	22

* neonatal software for use in NICU

† at extra cost

¶configurable to more

Figure 2 Mary Network Plan

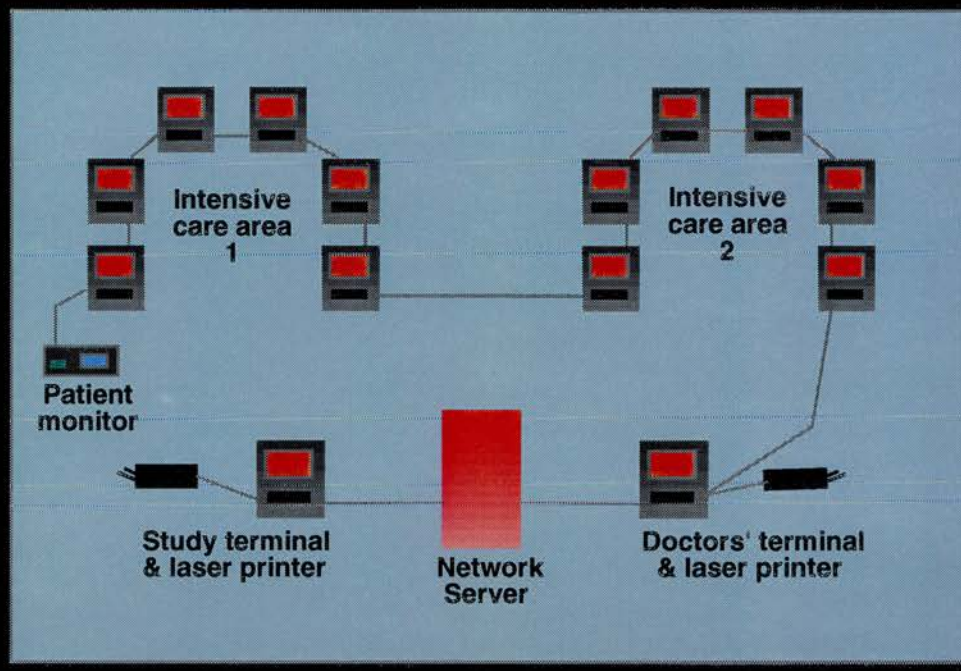
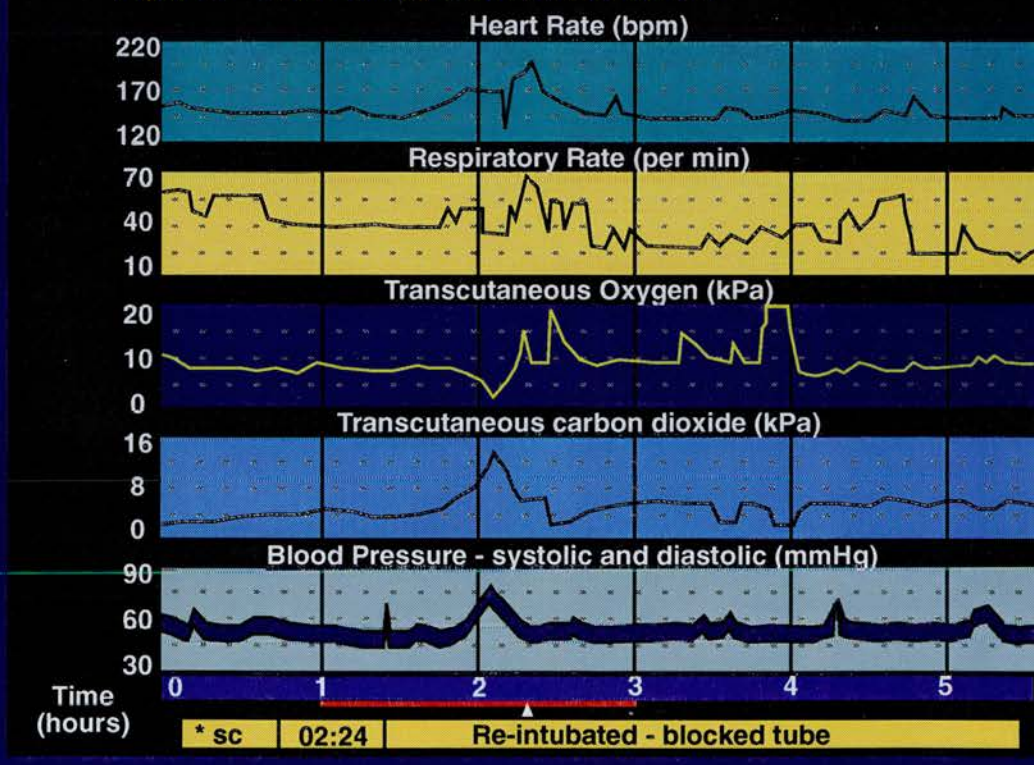


Figure 3 General Mary screen with comment



1.8 Mary Neonatal Monitoring

'Mary'[1,2], is primarily a computerised neonatal physiological monitoring system. The system has evolved from a computerised physiological monitor called MONIC [Bass *et al.*, 1986], which was developed in 1983 based on an Apple II microcomputer.

The current system (version Mary 3.4) [Bass *et al.*, 1991] was installed as a local area network into the Simpson Memorial Neonatal Intensive Care Unit in October 1990. The network installation and my post as research fellow, was funded by a research grant from the Scottish Home and Health Department, to study the clinical value of computerised physiological monitoring in neonatal intensive care. The 2 year study results are reported in Chapter 2.

The following brief explanation of Mary functions will enable an appreciation of the methods involved in the studies contained in this thesis. A more detailed explanation is contained in Appendix 1.

The Simpson Memorial Maternity Pavilion neonatal network is illustrated in figure 2. A central server (Dell 486D/25) serves both a study terminal, a doctors room terminal and two laser printers, together with 12 peripheral terminals based in two intensive care nurseries. Each terminal is a standard industry (Dell) 80386SX personal computer with colour VGA monitor and keyboard[3]. A maximum of 32 channels of data may be continuously sampled at one second intervals. Data is accessed from standard neonatal bedside monitors with analogue or RS232 output[4]. The

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[1]Mary Neonatal Monitoring. Meadowbank Medical Systems Limited, 314 Beacon Road, Loughborough, Leicestershire, LE11 2RD.

[2]'Mary' is a name adopted from the ward clerk who was initially to use the system.

[3]Each PC contains; 2 megabyte of RAM, 40 megabyte hard drive, 24 channel A-D board or RS232 serial, 8 bit Ethernet card

[4](a) Hewlett Packard neonatal multichannel recorder (78834A), (b) Ohmeda Biox 3700E pulse oximeter (c) Critikon Oxycheck monitor.

network is linked by standard ethernet cable. Data is automatically backed up each day at 0300 hours to a 500 megabyte optical disc drive. Patients may be archived from and restored to the network from these discs. Network maintenance is by myself and a research nurse assigned to the project, together with Meadowbank Medical Systems and Edinburgh University Medical Physics Department.

Mary comprises of three sections (1) patient details (2) physiological trend monitoring (3) Marystats. The system attempts to provide easy cotside access to trend graphs by staff previously untrained in computer use.

1.8.1 Patient Details

Although 'patient details' forms one section of a larger neonatal database, it is also an integral part of Mary. Patient details include information about the infant, the pregnancy, labour and delivery. An admission document and adhesive patient identification labels are produced from this information. Hospital identification number is all that is required to allow the user to begin physiological trend monitoring.

1.8.2 Physiological Trend Monitoring

Admitting a new patient to an intensive care cotside terminal will automatically begin trend monitoring. Patients re-entering the intensive care area may recommence monitoring after identification by name or hospital number from a list of active patients. Monitoring begins with 3 default graphs; heart rate, respiratory rate and transcutaneous oxygen. Data is sampled each second from standard bedside monitors and is displayed either as one minute data (denoted by blue time bar) or if selected, as one

second data (red time bar).

A maximum of seven channels (five trends graphs), in any combination of those currently monitored can be viewed. Each channel of physiological information may be changed in respect to its graph scale, time scale and relative size and position to the other graphs displayed. Graph colours may be changed.

Comments may be entered either in real time or retrospectively and it is possible to review comments with the appropriate graphs appearing above.

One second data is automatically stored for 72 hours during which time a request can be made to permanently save the one second data points. Following this time, data will be permanently stored as one minute averages. Data from any part of the infants monitored stay in the neonatal unit can be recalled.

Laser printing is available either as a screen dump or as a detailed graph print.

Help screens are available to assist users at any stage.

1.8.3 Marystats

This software enables basic statistical assessment of the trend data. Any period of trend graphs may be analysed from 1 second to 3 days. Boxes are created around data to indicate points to be included or excluded from analysis. Multiple boxes of any duration can be made. The following data are produced for each inclusion box created; mean, standard deviation, variance, median, highest and lowest values, number of data points within the inclusion box, number of data points included in the calculation, the number of points outside of artifact, high and low artifact

levels chosen (variable)(Appendix 2). Results can be printed, or placed into an ASCII file, which can be read by a commercial statistics or spreadsheet package.

1.9 CPTM as an aid in neonatal intensive care

Although reviewers of monitoring methods in neonatal ICU regard trend monitoring as a necessary advance, only 24% of UK neonatal units currently use such monitoring and only 26% hoped to do so in the future. This low usage may occur for many perceived reasons, including;

(1) prohibitive costs of hardware / software or network personnel

(2) lack of perceived clinical and / or research benefits

(3) a poor choice of trend monitoring software

(4) the possible stress placed on staff and parents by such technology

It is now possible for neonates to survive when born as early as 24 weeks gestation and weighing as little as 500 grams. The morbidity associated with such survival is potentially very significant and includes; sepsis, cerebral intraventricular haemorrhage, acute and chronic pulmonary problems (eg. blocked endotracheal tube, pneumothorax, bronchopulmonary dysplasia) and apnoea. Such events may be frequent in small, immunologically and physiologically immature infants. There is often little warning of deterioration and without immediate intervention, death or serious handicap may result.

CPTM may be more useful in the care of intensive care neonates than adults for several important reasons:

(a) the sick neonate is relatively invisible, often hidden by bubble plastic, enclosed within an incubator and discoloured by blue phototherapy units.

(b) the fragile infant should be minimally handled to ensure thermal and fluid stability [Mok *et al.*, 1991] and allow adequate rest [Murdoch and Darlow, 1984].

(c) the nurse/patient ratio in a neonatal ICU may be only 1:2 or 1:4, whereas adult ITU has a ratio of least a 1:1.

(d) deteriorations in sick neonates are often acute over seconds or minutes; partly at least because the neonatal patient cannot verbally indicate deterioration, but also because of the immaturity of neonatal homeostatic mechanisms.

In essence, because a neonatal patient is poorly visible and unable to communicate deterioration, clinical information may frequently be limited to the physiological parameters displayed on monitors. For nurses who have to cope with more than one poorly visible intensive care patient at a time, computers could assist by providing continuous informative trends of the monitored values. Trend displays could be viewed across crowded units, allowing doctors and nurses to assess physiological trends in an unstable baby, whilst at the same time performing a procedure on another baby.

Physiological trend monitoring in neonates has three main areas of use:

(1) a real time clinical tool to assist care

(2) a system to continually evaluate neonatal physiology and aid neonatal research

(3) a system that can educate staff.

The studies within this thesis have aimed to evaluate CPTM in the neonatal ICU with reference to these three areas.

Chapter 2

CHAPTER 2

The clinical value of CPTM in neonatal ICU

2.1 Introduction

Computer purchasing in the NHS has been dogged by an inadequate advice service and a lack of a coordinated combined purchasing power, from what is the U.K.'s largest single employer [Porter, 1993] [Kelsey, 1993] [BMJ News, 1993]. An enterprising software salesman may cajole an inexperienced buyer into purchasing software, that whilst attractive, may perform poorly and be wholly inappropriate for the required task [Gardner and Shabot, 1990]. The cost of purchasing and maintaining a network CPTM, is not insignificant with the current restraint on hospital finances. Despite this 26% of all major U.K. neonatal units wished to have CPTM (chapter 1). Unfortunately, independent validation of major computer systems is infrequently performed and the results limited in their availability to potential buyers [Ambroso *et al.*, 1992]. Inevitably, poor systems may flourish if they have strong commercial backing, whilst well performing, suitable software from smaller companies might flounder.

'Mary' is a network CPTM designed for use in neonatal ICU. The financial implications of possible widespread demands for such networks, prompted the Scottish Home and Health Department to fund a clinical assessment of the system, in the form of a randomised controlled trial. These are the two year study results for short and medium term infant clinical outcome. Long term outcome assessed by the Denver 2 developmental test at 1 and 2 years is not yet available [Frankenburg *et al.*, 1992].

2.2 Methods

From 1.1.91 to 31.12.92, infants entering the neonatal ICU at the Simpson Memorial Maternity Pavilion were randomised to the cot monitoring trial if they satisfied the following criteria:

(a) < 33 weeks gestation,

(b) ≥ 33 weeks gestation and ventilated for more than 3 hours or asphyxiated[1].

Neonates with major congenital abnormality were excluded. Infants were eligible for randomisation up to 4 days of age. Randomisation was by opening the next sequential sealed computer printed envelope. These were opened by nursing staff when a suitable infant was admitted and were used on an intention to treat basis. Infants were initially randomised to four groups:

A *no screen display (though data still collected)*

B *permanent screen display*

C1 *alternate 24 hour display/no display - starting with display*

C2 *alternate 24 hour display/no display - starting with no display*

The protocol lasted for seven days, following which all screens were permanently displayed.

After 18 months, randomisation was restricted to just groups A and B. Groups C1 and C2 had been incorporated to investigate possible short term variability to the presence of computers.

[1]Defined as pH <7.1 in first hour, 5 minute apgar <5, or signs of hypoxic ischaemic encephalopathy.

Demographic details about the mother, pregnancy, labour and infant were collected (appendix 3).

Each infant had a daily cranial ultrasound for the first seven days of life, performed by myself and a research nurse[1]. This was to identify intracranial pathology and included measurement of ventricular index and the resistance index of the internal carotid artery [Levene *et al.*, 1985] [Papille *et al.*, 1978]. The volume of colloid support given and the number of blood gases performed each day were noted for the first seven days. Time to discharge or death, time ventilated and requiring supplemental oxygen, and cranial ultrasound appearances were noted at discharge (appendix 4).

The day to day variability of the amount of colloid support given and number of blood gas samples analysed, were assessed in groups C1 and C2. With alternating periods of monitoring and non monitoring, one might expect to see an alternating variability in these values if CPTM were affecting them. In table 7, group C1 and C2 daily values for colloid (mls/day) and number of blood gases (per day), have been subtracted from the previous day's total.

Statistical analysis of the study was by Dr. R.A. Elton of the Medical Statistics Unit, University of Edinburgh, with clinical direction by myself and Professor Neil McIntosh. Wilcoxon rank sum and Chi squared (with and without Yates' correction) have been used where indicated.

Ethical approval for this study was obtained from the Reproductive Sub-committee of the Edinburgh Royal Infirmary Medical Ethics Committee.

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[1]Toshiba colour doppler diagnostic ultrasound machine; Sonolayer SSH 140A.

2.3 Results

The study began on 1 January 1991. By 31 December 1992, 458 infants had been appropriately randomised.

Infants spent a median of 6 days being monitored by computer (iqr 3 -11 days). This was similar for all groups. The maximum time any individual infant was monitored by computer was 185 days.

Tables 3 to 7 show the statistical analysis of the details studied in the four groups.

2.3.1 Details on entry to the study

The numbers allocated to each group and their sex, together with mean birthweight, gestation and apgar scores are shown in table 3.

The demographic details of infants entering each of the four groups were compared (appendix 3); of the 88 tests performed, nine were significantly different (higher than the 1 in 20 one might expect by chance). However, only a lower apgar score at 5 minutes in group C than group A was significant at the 0.01 level.

Table 3 Infant details in each computer group

Group	A	B	C1	C2
N =	148	155	76	79
Sex % M	59.2	56.8	52.6	55.7
F	40.8	43.2	47.4	44.3
Birthweight (g)	1740	1769	1875	1767
mean (sd)	787	836	945	935
Gestation (weeks)	31.4	31.6	32.2	31.5
mean (sd)	4.2	4.1	4.3	4.7
Apgar 5	7.7	7.6	7.2	7.2
mean (sd)	1.9	1.9	2.2	2.2

The following comparisons were significant at less than the 5% level:

Baseline comparisons

Wilcoxon	Parity	A < (C1+ C2)	p=0.017
rank sum	Apgar 1	A > (C1+ C2)	p=0.022
	Apgar 5	A > (C1+ C2)	p=0.008
	Age at transfer	B < (C1+ C2)	p=0.015
Chi squared	Fetal distress	A < B	p=0.032
	Onset	C1 < C2	p=0.044 (fewer inductions in C1)
	Fetal Distress	C1 < C2	p=0.031
	Fetal Distress	A < (C1+C2)	p=0.013
	Mode of delivery	B < (C1+C2)	p=0.039 (fewer emergency LSCS in B)

2.4 Short term clinical effects of CPTM

2.4.1 Cranial Ultrasound appearances

Table 4 shows the effect of CPTM on cranial ultrasound appearances. Maximum IVH grade attained over the whole seven day period is noted. 'Trend' is the difference in the mean value between the first 3 days and the last 3 days: a positive value indicates a predominance of the factor in the first 3 days (e.g. colloid support was greater in the first 3 days in all groups), whereas a negative trend demonstrates an increase in the factor with time (e.g. IVH increased over time in all groups).

Table 4 Cranial Ultrasound appearance with computer monitoring

Group	A	B	C1	C2	Total
N=	148	155	76	79	458
IVH - grade 1 (%)	9.5	5.2	5.3	6.3	6.8
IVH - grade 2 (%)	7.4	9.0	13.2	12.7	9.8
IVH - grade 3 (%)	3.4	1.9	2.6	2.5	2.6
IVH - grade 4 (%)	4.1	2.6	3.9	7.6	4.1
Trend IVH	*-0.12 (0.41)*	*-0.13 (0.43)*	*-0.26 (0.70)*	*-0.14 (0.42)*	
Flare mean (sd)	0.16 (0.29)	0.14 (0.28)	0.12 (0.26)	0.32 (0.40)	
Trend flare	*0.08 (0.26)*	*0.05 (0.26)*	*0.01 (0.21)*	*0.04 (0.28)*	
Cyst mean (sd)	0.02 (0.13)	0.04 (0.16)	0.04 (0.17)	0.03 (0.15)	
Trend cyst	*0.00 (0.04)*	*-0.01 (0.05)*	*0.01 (0.06)*	*-0.01 (0.10)*	
Doppler mean (sd)	0.74 (0.08)	0.74 (0.07)	0.73 (0.07)	0.71 (0.08)	
Trend doppler	*0.00 (0.08)*	*0.01 (0.08)*	*0.02 (0.10)*	*0.00 (0.08)*	

The following were significant at less than the 5% level:

Wilcoxon rank sum	Flare mean	C1 < C2	p=0.001
	Flare trend	A > (C1+C2)	p=0.017
	Doppler mean	A > (C1+C2)	p=0.007
	Cyst trend	B > (C1+C2)	p=0.036
	Doppler mean	B > (C1+C2)	p=0.017

There appears to be no valid interpretation of these results in relation to the randomised groups.

2.4.2 Colloid support and blood gas assessment

The total volume of colloid support, including all synthetic and natural blood products (except platelets), was calculated for each infant from the time of birth, daily for the first seven days. We also noted the number of blood gases per day (from time of birth) for the first seven days. These results are shown in table 5.

Table 5 Colloid support and blood gas treatment by computer group

Group	A	B	C1	C2
Colloid support (mls/day) mean (sd)	6.6 (13.7)	6.9 (13.7)	7.2 (14.0)	8.4 (18.4)
Trend colloid	*5.1 (9.5)*	*6.1 (11.7)*	*8.0 (14.5)*	*5.8 (10.1)*
Number of gases (per day) mean (sd)	3.7 (3.0)	3.5 (2.4)	3.9 (3.0)	4.1 (2.9)
Trend gases	*3.0 (2.2)*	*2.5 (1.6)*	*2.7 (1.7)*	*3.4 (1.8)*

The following was significant at less than the 5% level:

Wilcoxon signed rank	No. of blood gases	B < (C1+C2)	p=0.016

2.5 Medium term outcome measures

Medium term outcome measures (appendix 4) showed no statistically significant differences (< 5%) between groups (table 6). The data for discharge ultrasound was discarded, as large numbers of early transfers from our neonatal unit made this data far from complete.

Table 6 Medium term outcome in infants by computer group

Group	A	B	C1	C2
Death * (%)	14	9	12	14
Time to death / discharge † (days)	20 (1-195)	20 (1-173)	17 (1-155)	22 (0-359)
Time ventilated † (days)	2 (0-91)	2 (0-126)	2 (0-57)	2 (0-211)
Time in oxygen † (days)	2 (0-159)	3 (0-158)	2 (0-145)	1 (0-211)

* shown as percentage, analysis by Chi-squared with Yates' correction

† shown as median (range), analysis by Wilcoxon rank sum

2.6 Effects of 24 hour alternating screen display

Short term variability in both the amount of colloid given and the number of blood gases taken per day with screens alternating on and off i.e. comparing C1 and C2, are shown in table 7. In the table, the mean values for one day are subtracted from the preceding day and compared between groups C1 and C2.

Table 7 Short term variability of colloid support and blood gases in groups C1 and C2

	Colloid support (mls) mean per day		Number of blood gases mean per day	
Day	**C1**	**C2**	**C1**	**C2**
2 minus 1	-6.4	-7.7	-3.5	-3.7
3 minus 2	-3.3	1.2	-0.4	-1.0
4 minus 3	-1.6	-3.2	-0.4	-0.8
5 minus 4	-2.3	-1.0	-0.8	-0.5
6 minus 5	-0.0	-0.5	-0.4	-0.4
7 minus 6	-2.5	-0.7	-0.6	-0.4

A pattern can be seen in the alternating values for colloid support in C1 and C2. More colloid support appears to have been given when trends were displayed, than at times when they were not (numbers in italics). However, these changes were not significantly different; Wilcoxon rank sum $p = 0.51$. No significant differences were present in the blood gas data.

2.7 Discussion

The results demonstrate no significant clinical benefit or detrimental effects of using CPTM in neonatal care. Other areas investigated as part of this assessment of CPTM are included in this thesis, and the final discussion (chapter 10) is an appraisal of all aspects of CPTM in neonatal care. The results of this study however, represent a major component of this assessment with regard to the clinical benefit of the introduction of CPTM into neonatal ICU. The study included 458 patients over a period of 2 years and assessed ICU computerisation in a randomised controlled study, something which has not been previously attempted. In retrospect, there are several areas where the study might have been improved, with a possible effect on the result.

The computer study began within 3 months of the computer network being installed. Teaching was not complete and staff remained wary of the system. Following the active teaching programme there was a longer period than expected of gaining familiarity with trend graphs (chapter 3). Both myself and the study research nurse noted a marked improvement in the appropriate use of the computer system by permanent staff, 12-18 months after the system introduction. The parent questionnaire also showed evidence that over time the doctors appeared more confident about and the nurses less in awe of, the computers. The study itself may have obstructed this learning curve. The protocol required that monitor screens be turned off for certain infants or even worse, alternated off and on. This undoubtedly prolonged learning curves and reduced reliance on the system as a dependable source of information. In addition, the rapid turnover of neonatal ICU staff further prolonged the

learning time of permanent staff, as new nurses require a period of supervision. The presence of CPTM increased staff awareness and understanding of neonatal physiology (chapter 3). There is a possibility that this may have had a carry over effect to those infants in whom CPTM was not available, further reducing the overall effect of the study.

In hindsight, our patient selection criteria and the parameters chosen as outcome measures may have been too crude. We hoped to demonstrate an improvement in outcome in ICU neonates due to the presence of CPTM, in their first seven days of life. Many infants who were 'routinely' managed in intensive care with prematurity, yet minimal or no respiratory distress were included in the study, although they were not acutely unwell. The outcome for infants in this group was already satisfactory and would have been difficult to improve upon. It was unlikely therefore that CPTM would significantly alter their course. It might have been more beneficial to concentrate on carers' reactions to the trend data during acute illness, i.e. stricter entry criteria.

Cranial ultrasound is a valuable tool in neonatal care. Intraventricular haemorrhage is a major determinant of neonatal outcome and undoubtedly physiological instability is an important cause [Perlman *et al.*, 1985]. CPTM could either help maintain physiological stability and therefore reduce the incidence of IVH, or alternatively, could have increased the incidence by promoting intervention. IVH was therefore a good outcome measure and no significant differences were noted between groups for IVH. However, flare is more difficult to define and the pathophysiology underlying flare is poorly understood [Levene, 1990]. Although intense flare is associated with infant instability and therefore possibly under some control by CPTM, lesser degrees of flare

appear to arise without undue hypoxic insult and it is less obvious how CPTM might alter its' incidence. Cysts noted in the first 7 days result from prenatal events and have no relation to CPTM [Levene *et al.*, 1985].

Seven days of protocol may have been insufficient to affect medium term outcome, especially in those extreme preterm infants requiring several weeks of intensive care.

2.8 Conclusions

Should this study accurately represent CPTM, i.e. a clinical tool without a discernible effect on outcome, then its clinical value will have to be further assessed. It may be that CPTM has a clinical role for doctors and nurses familiar with trends, when used on acutely unwell infants. The possible limitations of CPTM as a clinical tool will have to be justified to administrators budgets, although there are undoubted benefits for research. Whether or not this can justify the cost will be discussed further in Chapter 10.

Chapter 3

CHAPTER 3

Attitudes to computer networks in neonatal ICU

3.1 Parental attitudes to the presence of computers

3.1.1 The role of parents in the care of intensive infants

The care of intensive care infants has to incorporate the feelings and considerations of their parents. Optimal medical care must be given, with minimal interference to the developing relationship between the parents and their child. Having an infant in intensive care may lead to a gross disruption of the family unit [Benfield *et al.*, 1976]. This may produce a long term disorder of family relationships [Jeffcoate *et al.*, 1979], in a group of parents already at high risk for psychosocial problems [Hunter *et al.*, 1978].

One particular set of parents were articulate enough to write;

"the story of his (Andrew's) short cruel institutionalised life, is a case study of what can happen when a baby becomes hopelessly entrapped in an intensive care unit where the machinery is more sophisticated than the code of law and ethics governing its use" [Stinson and Stinson, 1981].

There is no doubt that both parents and doctors feel aggrieved that the level intensive care given to some infants is excessive [Campbell, 1982]. The introduction of ICU computer technology, may result in an

important increase in parental perceptions of 'intensiveness'. Whilst expectations of computer technology in intensive care areas are continually increasing [Clifford, 1986], we have to ensure that clinical benefits are achieved without alienating parents.

Mary monitors had a red flashing light at the bottom right hand corner of the screen to indicate one second monitoring intervals. Next to this an information bar indicated the key for 'help' information. One mother, convinced that the red light was flashing to indicate that her baby needed help, watched for 2 days before she felt confident enough to ask a nurse why her baby was in such distress.

3.1.2 Parent Questionnaire

Parents of infants enrolled into the computerised cot monitoring study, were asked to complete a 22 question questionnaire after their infant had left the intensive care nursery and was therefore no longer being monitored by computer. The questionnaires were devised by Professor Neil McIntosh, co-ordinated by the project nurse and myself, and analysed as part of the computerised cot monitoring trial by the Department of Medical Statistics (with clinical direction from myself). 244 questionnaires were answered and both the questionnaire and replies are detailed in Appendix 5. Eighty questionnaires were not returned. Questionnaires were not given to the parents of infants who had died (34 infants).

Most parents (80.3%) were aware that the progress of some of the infants were being monitored by computer. Whilst the majority (69.0%) said the equipment had been explained to them, only 23.4% were able to give a reasonably accurate explanation of the use of the computer, reflecting the difficulty parents have in coping with information following

the overwhelming experience of having their infant admitted to an intensive care unit. Reassuringly, only 10.6% of parents reported that the presence of computers in intensive care increased their anxiety. In 85.8% of parents, computers either reduced or made no difference to their anxiety. Only 2% of parents felt that the computers were just for the benefit of science, the majority of parents (91.8%) felt that the computers were for baby's benefit, or for the benefit of both baby and science. Only 1% of parents were worried by the computer monitoring of their infant.

Questions regarding the confidence of the nursing and medical staff in using the computers were either very generous, implying that the nurses and doctors were very knowledgeable/confident with the computers, or parents replied 'don't know'.

Although parents with higher levels of previous computer experience (in comparison to those with less/no experience) were better able to distinguish computer equipment, the presence of this equipment did not reduce their anxiety. These parents were also more likely to feel that the computers were as much for the benefit of science as for the baby. Overall however, parents with computer experience were more pleased about the presence of computers than parents without experience, who tended to be indifferent. This agrees with data based in an out patient department, where previous experience of computers improved patient opinion about the use of computers in medicine [Cruickshank, 1982].

Questionnaires were given to parents after their baby had left intensive care and this to some extent may have improved responses in favour of the computers, as there is a certain parental relief that accompanies the transfer of their infant to the special care nursery. Overall responses were very favourable. Identification of those parents who are

concerned would enable us to give more advice. As familiarity with the computer system increased, we felt that greater staff confidence with the computers reassured many parents. The end of the computer study and hence the use of computers as an experiment, should also help reduce anxiety amongst parents.

3.2 Nurses attitudes to CPTM

3.2.1 Nurses and technology

Technical issues often take precedent when computer technology is introduced into intensive care. Although staff acceptance is recognised as important, the concerns of staff are frequently underestimated by those whose main aim is the installation of the computer system [Kjerulff *et al.*, 1985]. New technology can fail, simply because staff acceptance and education were not approached with enough vigour and resources [Agamalian, 1987]. The majority of nurses are receptive to new technology, if introduced in the correct manner [Gilhooly *et al.*, 1991]. Intensive care nurses are more willing to accept computer technology than nurses in other specialities, and indeed they may choose their speciality [Kjerulff *et al.*, 1992] or even hospital [Sorenson, 1989] to suit their ability to cope with technology.

An estimated 45% of medical systems fail because of staff resistence [Kaplan and Duchon, 1987], causes include:

- poor development co-operation [Avila and Shabot, 1988]
- misunderstandings of the system role [Stoodley *et al.*, 1992]
- lack of appropriate teaching by trained friendly instructors [Plummer, 1987]
- computer technology anxiety [Gribbens and Marshall 1982]
- concerns that computers will diminish patient care [Sorenson, 1989]
- inappropriate software [Bailey and Rollier, 1988]
- excessive new workload with minimal benefits to the nurse or patient [Watt, 1984]

Yates [Yates, 1983] defined two extreme reactions to the introduction of computers into intensive care:

(a) ignore the patient in an attempt to cope with the technology

(b) concentrate solely on the patient and ignore the technology in an attempt to hide a lack of knowledge.

These reactions may be minimised by appropriate action in the planning stages of an intensive care computer network.

We assessed the reactions of our nursing staff to the introduction of the computer system, by means of a 37 question questionnaire. The questionnaire was devised by Professor Neil McIntosh with assistance from the Department of Psychology, University of Edinburgh. The questionnaires were administered and analysed by the project research nurse and myself. Staff were asked to complete the questionnaires after six months exposure to the computer system. 100 questionnaires were answered over two years.

Most ICU computer systems are introduced by, co-ordinated by and used predominantly for, medical staff. Whilst their was no overt aggression to the introduction of the system into our unit, there was a general feeling that the system was principally for the benefit of the doctors and research [Blum, 1986(1)]. The computer network was purchased with a research grant and the effects of the computers studied by a research team. This initial depreciation has mostly been overcome, though 11% of nurses questionned felt unreasonably pressed into using the computer and appeared to regard the system as an imposition. No attempt was made to compel nurses to use the system; the choice of graphs displayed, the number of comments entered and how much the system was used, has not been investigated on a personal level.

Only 6% of our staff had regular previous computer experience (appendix 6), and 29% had never touched a computer before. Studies in the USA have shown a higher degree of computer experience, as high as 93% in one study [Fenny and Donovan, 1989]. In another study 89% of nurses had typing skills prior to the introduction of computers [Lundsgaarde *et al.*, 1980]. Although 'Mary' CPTM aims to be user friendly, the relative lack of computer and keyboard experience in British nurses challenges this approach at its lowest level. Many nurses are initially daunted by using a QWERTY keyboard and are unfamiliar with function keys (eg F3, page up, control, ≥).

3.2.2 Staff Teaching

Teaching sessions began with the introduction of the system (though a single stand-alone Mary had been present in the unit for one year). Instruction was by myself and a research nurse. We aimed to give 3 sessions to each nurse. The first session being a basic introduction to the keyboard, starting monitoring and the ability to change graph colours, the second session included common trends and graph manipulation and the third session discussed artifact in trends and 'hot keys'. The ability to simply change graph colours is a popular and easy introduction to a computer system and gives the nurse some personal command over the computer.

73% of nurses responded that they had received personal instruction on how to use the computer, and these lessons were felt to reasonably thorough in 54% of staff (23% did not reply). The majority of nurses (65%) wanted more information after the initial sessions; this they

predominantly obtained from ITU sisters, the research nurse and other staff nurses. 57% sought only occasional help after the initial teaching session, 27% needed more frequent help. Although we are unsure how satisfied staff were with this second source of information (i.e. asking other staff), it implied an invaluable filtering down of training skills to a group of senior nurses who were continually available and readily approachable. Ideally these people would receive extra training and a core group might be identified. The vast majority of nurses (86%) used written instructions taped to the keyboards to perform functions; this is disappointingly high for a menu driven system, but the typed instructions reduced the required keyboard skills and allowed the user to identify the command required at the start, without having to search through menus. A self teach booklet has recently been produced by two of our research nurses, to help staff learn the basics of using the system at their own pace, whenever they have time.

Some nurses did not receive all 3 teaching sessions. We found it increasingly difficult to train staff without reliable training times. Urgent clinical commitments in this busy unit frequently took precedence and cancelled teaching sessions became too time consuming for the training staff. In addition the high staff turnover of intensive care nurses [Phillips *et al.*, 1982], increased teaching demands both on research and clinical neonatal staff.

The introduction of Hewlett Packard's Carevue system, is pre-empted by a large scale teaching programme co-ordinated by a retrained nurse from the unit [Duce and Harris, 1990]. It is extensive, though expensive in terms of nursing time. All nurses on the unit are trained to a basic level, with extra training for a core group of nurses who act as on the

ground experts, able to introduce new staff to the system and to solve easy problems. The 'flagship' Carevue system at the Brompton Hospital, London, still found that even this intensive teaching was difficult to provide in terms of cost and time available in a busy ICU [Thomson, 1991]. Many smaller intensive care groups could not afford this form of teaching.

Teaching therefore represents a major challenge, not only to the introduction of a computer system, but to its ongoing success. In a major project it will place a large strain on resources, and its failure may lead to the collapse of the project. Constraints on staffing seriously undermine in service training by trained computer staff. Whilst busy staff (both medical and nursing) are often unwilling to be learn by manuals or videos [Lundsgaarde *et al.*, 1989], they do need to be able to interact with the computer at times when they aren't busy. This can be on their own if necessary and at their own pace, i.e. an adult learning approach [Krampf and Robinson, 1984]. More rigid approaches to learning do not always achieve the success they expect [Lange, 1988]. Computer software designers selling to the healthcare sector, could better prepare the computer inarticulate users of their software by being encouraged to provide on-line software instruction (similar to that provided by Apple Macintosh). Trained instructors could then make a better response to the task of providing user support.

3.2.3 Staff acceptance

After 6 months of use, 93% of nurses replied that they did not feel threatened by having to use the computer, though 28% still found aspects of the computer daunting. Daunting aspects of the computer centred

predominantly on a concern that they were not using the computer to its full potential. Whilst another group believed that by their interaction with the computer they might wipe all the information off the system, despite repeated reassurances that this was not possible.

Senior nurses are fully aware that inappropriate use of new technology may lead to serious mistakes [Farmer, 1978] [Kjerulff *et al.*, 1992]. As supervisors, they have to be confident with the equipment being introduced and be aware of any problems that might arise [McIntyre, 1993]. Poor teaching may undermine this confidence and nurses will be appropriately opposed to the technology. Some authors have regarded this as age related computer anxiety [Gribbens and Marshall, 1982], though this is not generally accepted [Summers, 1990].

44% of nurses still felt unfamiliar with the system after 3 months of use, this reduced to 11% by 6 months (26% no reply). Both further teaching and time have increased familiarity. Time was an important factor in the complete acceptance of the new system. Senior members of nursing staff are now involved in system development. The involvement of nurses in research projects using CPTM data has improved clinical acceptance [Summers, 1990].

3.2.4 Affects on patient care

Doctors [Shortcliffe, 1990], nurses [Sorenson, 1989] and patients [Cruickshank, 1982], all show concerns that computers may interfere with patient care. The introduction of a computer system may improve patient records at the expense of time spent caring for the patient [Pryor, 1989] [Kalbach and Kalbach, 1988]. Although this effect may be minimised by

bedside terminals, this remains a concern of many health care workers [Hendrikson and Kovner, 1989]. Mary requires only minimum input to begin monitoring; the infants hospital number. Further infant details may be entered later. Comments describing interventions are encouraged, but these may be entered retrospectively. The ability to view data in real time and input (minimal) information retrospectively, balances the clinical and technological requirements of a computer system, without interfering with patient care [Abraham *et al.*, 1986].

Although work within an intensive care unit is stressful [Malacrida *et al.*, 1991], the majority of tasks are repetitive and boring [Melia, 1977], which may lead to mistakes and poor patient care [Daly and Wilson, 1983]. Computers could assist nurses by performing some of these repetitive tasks, thus increasing the time available for caring [Cobin, 1983]. In practice by relieving nurses of these tasks, there might be a paradoxical loss of a guaranteed period of observation, resulting in worse care for the infant [Hendrickson and Kovner, 1989]. These concerns would have to be investigated before computers could take over this role.

Patients (or in neonatal care, parents) may feel threatened by computers [Cruickshank, 1982] and this may be a strong source for resistance by nursing staff. The parent questionnaire did not reveal any strong anxieties caused by the computers, though interestingly 30% of nurses perceived parents as being more worried because of the presence of computers. Studies based in an out patient department found patient stress was not increased by the use of computers during consultations [Brownbridge *et al.*, 1985].

3.2.5 Further nursing concerns

The cost of implementing and maintaining the computer network concerns the nurses of our unit and others [Fenny and Donovan, 1989] (Appendix 7). This topic is further discussed in the final chapter, though computers account for only a small proportion of the overall ITU budget.

3.3 Doctors attitudes to computer technology

The opposition (usually by apathy) of many medical staff to the use of computer equipment is well documented [Green *et al.*, 1991] [Gilhooly *et al.*, 1991]. Shortcliffe [Shortcliffe, 1990] summarised these reactions as;

fear of loss of rapport
non acceptance of computer capabilities
suspicion of artificial intelligence
too old to learn about computer technology
fear of loss of control
distaste for data entry
fear of legal liability
inertia

The response of individual doctors to computers varies widely. We are fortunate to have a core of medical consultants who are actively interested in the clinical applications of the system [Blum, 1986(1)]. Registrars and Senior Registrars use the trends frequently in the critical management of infants. Despite this, they rarely contribute by entering comments etc [Green *et al.*, 1991]. Senior House Officers, whose primary concern is the logistics of performing numerous onerous tasks, have minimal time to become familiar with the system and only a few find it useful.

Increasing computer literacy among medical school entrants, should eventually increase the interest of medical staff in computers. In the USA, 70% of first year medical student at one school had access to computers, a five fold increase in five years; the school now wishes entrants to understand computing and computer technology [Schaad and Edfeldt, 1989]. 71% of first year entrants at another medical school also

wished to have medical informatics as part of their course [Magid and Rabold, 1988].

As with nurses, doctors computer confidence reflects their degree of computer use [Martin, 1983]. However, confidence may also increase frustrations with limitations of the software [Nolan-Avila and Shabot, 1987], in spite of real savings in time produced by the system (labels, admission and discharge letters).

Concerns that computers are detrimental to the physician-patient relationship appear to have been overestimated [Legler, 1990]. The majority of patients accept that computers are an inevitable development [Cruickshank, 1984]. Whilst patients do not belief that computers (in an out patient department) make the physician patient relationship more impersonal [Pringle *et al.*, 1984], the form of the relationship does appears to become more medical and less socially orientated [Pringle *et al.*, 1985 (1)] [Pringle *et al.*, 1985 (2)]. Potter demonstrated that approximately 20% of patients were worried about computers in medicine [Potter, 1981] [Cruickshank, 1984]. Computer literacy and increasing expectations of computers by the general public, should decrease these concerns with time. Overall, the individual personality of the doctor and how the computer is used and presented, are thought to be more important than the presence of computers in determining the physician-patient relationship [Cruickshank, 1985].

Chapter 4

CHAPTER 4

The assessment of computer usage by time lapse video

4.1 Introduction

The influence of CPTM on the actions of neonatal staff is difficult to evaluate. The parent and nurse questionnaires just described, provided subjective evidence that the presence of CPTM affected the actions of both nursing and medical staff. The objective computer study (chapter 2) failed to note any influence of CPTM on patient outcome. In order to gain further objective evidence, we attempted to evaluate the effects of CPTM on infant handling using time lapse video recording. It is possible that knowledge of CPTM data might have either increased or decreased infant handling. We assessed this possible difference using video recordings of the daily care of infants in the intensive care nursery.

4.2 Methods

A time lapse video camera and recorder[1] were fixed at ceiling level in one of the intensive care nurseries. The camera position enabled two cots to be continually monitored. 3 hour video cassettes were used to record 120 hours of infant care on time lapse mode (approximately one frame per second). Time lapse video enables real time events to be condensed, in this case from 120 hours to just 3 hours (the appearance is of rapid continual movement of people). An internal clock notes both date and time (to the nearest second) on the video recording. Thus enabling a rapid review of a long time period. Any events can be quickly identified and timed. The camera once in-situ required no further involvement. The video cassettes were changed every fifth day. Allocation of infants within intensive care nurseries was decided by the nurse in charge and was not influenced by research staff.

The first two weeks of recordings were discarded, to allow time for nurses to adjust to the presence of the camera. Observations were then made on any infant that entered either cot space, who fulfilled the entry criteria for the computer study (chapter 2). Due to the high level of activity stabilising an infant on entry to the neonatal unit, observations were not commenced until 6 hours of age. From 6 to 30 hours after birth (i.e. 24 hours), we noted the time and duration of each intervention. An intervention was defined as the opening of the incubator portholes, with hands entering, for any reason. Any intervention occurring within two minutes of a previous intervention was counted as the same intervention (this commonly occurs during a single procedure). Medical and nursing

[1]Panasonic time lapse video recorder (AG-6720) and system camera (WV-F15E)

interventions were not differentiated. Interventions for research studies or due to parental handling were not counted.

For each infant, we calculated the total number of interventions (in the 24 hour period) and the median, iqr and maximum duration of all interventions.

We then matched each infant observed, with the next infant to enter a video cot space that was of the same approximate gestation (within 2 weeks), and in the alternate computer group i.e. match group A (no screen display) with group B (permanent screen display). The number and duration of interventions were then compared.

The diurnal distribution of the duration of interventions was also assessed. Each intervention was sorted into hourly time periods according to the time of day that it occurred i.e. 1300-1400 hours. The time periods were then combined for all infants in group A and compared with the combined time periods for all infants in group B. Interventions covering 2 time periods were separated and the appropriate amount of time allocated to each period. The combined time periods in the two groups were compared using the paired t test.

4.3 Results

Four pairs of infants were recruited and observed over 24 hours. Perinatal details of the four pairs of infants are contained in table 8. A comparison of the number and duration of interventions in the four pairs of infants can be seen in table 9.

Table 8 Perinatal details from the four pairs of video infants

Pair	Group	Gestation (weeks)	Birthweight (g)	Ventilated (days)	Oxygen (days)	IVH grade
1	A	26	553	7 *	7 *	0
	B	28	929	38	130	left 2
2	A	31	1820	0	0	0
	B	32	1020	0	0	0
3	A	31	1103	0	0	0
	B	30	1563	1	9	0
4	A	31	1800	8	35	0
	B	31	1334	1	2	0

* neonatal death at 7 days

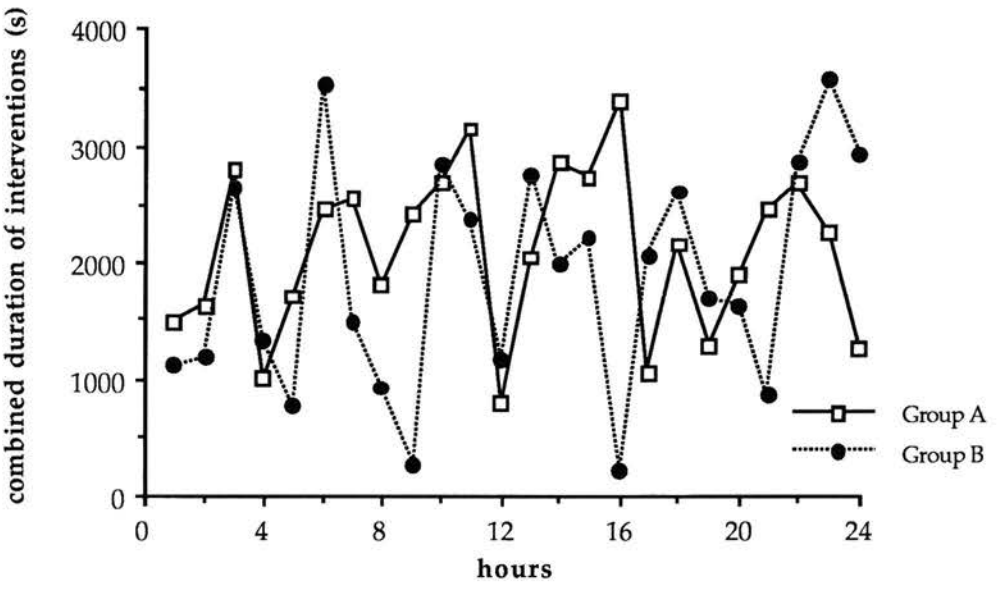
Table 9 demonstrates that the number of days of ventilation and supplemental oxygen required by the infants, related to the total number of interventions but not the duration of the interventions. This was independent of study group. In this small study, CPTM did not appear to influence either the number of interventions or the duration.

Table 9 Interventions over a 24 hour period in the four pairs of video infants

Pair	Group	Gestation (weeks)	Number of interventions	Median duration (s)	IQR duration (s)	Maximum duration (s)
1	A	26	59	105	31 - 288	1733
	B	28	71	65	21 - 180	1485
2	A	31	46	91	38 - 245	1028
	B	30	42	109	50 - 364	2116
3	A	31	38	177	53 - 348	888
	B	32	36	98	18 - 319	3294
4	A	31	68	137	61 - 366	1159
	B	31	32	166	61 - 382	1960

Figure 4 shows the distribution of the combined duration of interventions when combined in the two groups. Again no discernible differences could be determined to suggest that CPTM influenced either the time that interventions took place or had more of an effect on any particular nursing shift. A paired t test demonstrated no statistically significant difference between these two groups, $p=0.325$.

Figure 4 The diurnal distribution of duration of handling interventions in groups A and B



4.4 Discussion

The concept of using video recordings to assess behaviour is not new, but the use of this method in medicine is uncommon. In particular, I have found no reports in the medical literature of the use of time lapse video to assess the effects of a new technique. Real time video has been used in general practice as a method of determining the behavioural effects of a new form of structured consultations [Verby *et al.*, 1979]. Another general practice study used video to assess how the introduction of consulting room computers affected the content of the consultation [Pringle *et al.*, 1985]. These studies achieved their aims reviewing relatively short periods of video recording.

Video recording is an excellent form of surreptitious surveillance; unfortunately, this in part explains the difficulties we encountered beginning this study. Some members of the nursing staff were extremely angry that they were to be 'spied' upon and that 'their' actions were going to be scrutinised and publicised (possibly criticised). The start of the video assessment was delayed on many occasions because of the unwillingness of staff to be videoed in their workplace. We had many meetings with members of staff to appease their fears, explaining both the purpose of the study and the technique of time lapse video (with an example filmed in the unit). Many were satisfied following this explanation and the example video recording. Some nurses needed more persuasion, but eventually we were able to start, only to be delayed by faults with the equipment. Consequently, this has not been a very successful assessment. Despite continuous video recordings over 11 months, we have accrued only four pairs of infants; limited also by matching criteria and the presence of chronically sick preterm infants in the allocated cot spaces.

The data provides an interesting insight into the handling of preterm infants, but provides little clear objective evidence that CPTM influences behaviour. The range of illness in preterm infants, even at specific gestations, means that a much larger study would be necessary to detect any real difference between groups. With the advent of the end of the computer study this is no longer possible in this unit, as all screens will be on permanent display in all infants.

Chapter 5

CHAPTER 5

Comparison of nurse and computer charting of vital signs in intensive care

5.1 Introduction

The evolution of computer applications in intensive care has met with mixed success, up to 50% fail [Cotrell *et al.*, 1982]. Computers are however becoming progressively more powerful, and seem to be the ideal method of storing and manipulating data for our increasingly complex intensive care management. Computer collection of physiological parameters occurs in 4.8% of USA hospitals [Summers *et al.*, 1989] and in our survey of U.K. neonatal intensive care units, 24% used computers to assess clinical physiology and 26% wished to do so in the future (chapter 1). The automated recording of physiological parameters would give greater control of this data and could liberate nurses from this routine task [Melia, 1977], increasing time available for them to perform other duties. Gardner observed that in a thoracic ICU, 19% of nurse time was spent on charting [Gardner *et al.*, 1989]. He summarised the limitations of the hand written record as [Gardner and Shabot, 1990]:

(a) it may be physically unavailable

(b) it is often poorly organised and illegible

(c) ICU instruments have their data only periodically hand written onto a chart

(d) data retrieval for research is time consuming and cumbersome.

In addition, the reliability of manual written data decreases as patient instability increases and nurses become too busy with clinical management [Kari *et al.*, 1990]. The manual charting of physiological parameters by nurses is therefore, time consuming, inflexible, open to inaccuracy and limited in its sampled frequency.

The paucity of published studies validating computerised collection of physiological parameters in intensive care has been noted in a review by Sittig [Sittig and Gardner, 1990]. Turner compared computer monitoring of intracranial pressure (average of 720 data points each hour) with a single nurse hourly observation and found it to be comparable [Turner *et al.*, 1988].

Three other studies have noted the inaccuracy of intermittent handwritten nursing observations when compared with computerised physiological monitoring. Aukburg found that computers enabled a two and a half fold increase in the detection of adverse physiological events in post anaesthetic intensive care [Aukburg *et al.*, 1989]. Kari compared intensive care nursing charts to computerised monitoring and demonstrated that one significant haemodynamic event was missed every two days [Kari *et al.*, 1990]. Another study showed a 32% increase in the detection of secondary insults in head injured patients using computerised recording [Corrie *et al.*, 1993].

We have evaluated the bias and precision of the hourly hand written observations of four physiological parameters by intensive care nurses, when compared to the same four parameters collected by CPTM, thus assessing whether routine data collection could reasonably be performed by computers in intensive care areas.

5.2 Methods

98 consecutive infants receiving intensive care were studied for their first 48 hours of life (or until death/transfer from ICU). We assessed values for heart rate, mean blood pressure, transcutaneous oxygen and central temperature[1].

The computers take information each second (subsequently averaged to one minute values), from the same bedside patient monitors from which the nurses also note a single value each hour (see chapter 1). We retrospectively compared the hourly value noted by the nurse to an hourly median calculated by the computer[2]. Median values were calculated as they would be minimally influenced by temporary changes in physiology during procedures or instability. The nurse may note the hourly value at any time within each hour, although it is usually at a specific time within the hour. The precise time depends on the number of other infants cared for by the nurse. Even the most unstable infants have a value recorded at some time during the hour.

The parameters measured on the bedside patient monitor are dependent on the degree of illness of that infant; whilst virtually all infants have heart rate and transcutaneous oxygen measured, only those infants expected to require more intensive therapy have continuous temperature and blood pressure measurements. This accounts for the differences in the number of data points for figures 5-8 and 9-12. If the parameter was being monitored then it was available as a computer trend. The four parameters investigated are routinely monitored and displayed in intensive care infants.

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[1]Study performed by myself and Sarah Deere (study research sister).
[2]Statistical assistance from Dr. R.A. Elton, Senior Lecturer, Dept. of Medical Statistics, Edinburgh.

Prior to the computer calculation of the hourly median any values due to artifact were removed, some artifact was automatically excluded by the computer for being outside predefined limits (appendix 2), other non-physiological artifact was removed manually by trained observers noting periods of invalid data, which were then excluded from further analysis (see chapter 6). Invalid data would include those times when e.g. an arterial line measuring blood pressure was closed for calibration or sampling (figure 14), or the re-calibration of a transcutaneous blood gas probe (figure 13).

The study was performed retrospectively. Nurses were not informed of the study as this may have altered their usual behaviour.

5.3 Results

A total of 6.9% of data was excluded as artifact from the hourly computer medians. 0.6% of this data was excluded automatically for being outside predefined limits (Appendix 2) and 6.3% of the data was excluded manually. The difference between the hourly nurse reading and the computer hourly median was calculated for every hour observed. Figures 5-8 show the hourly differences between nurse and computer for each of the four parameters. Each point represents the difference between the nurse and computer for a single hour on each baby. The figures illustrate both the variation between infants as well as the hourly differences for each infant. The mean and standard deviation of these differences were then calculated for each patient. The average values for all patients are shown in table 10; the average mean difference is in column **(1)** and the average standard deviation of the differences is in column **(2)**.

Table 10 Mean difference between nurse and computer observations

	Mean difference between nurse and computer: For all patients		Mean of all computer sd's for minute data within each hour
	mean	**sd**	
	(1)	**(2)**	**(3)**
Transcutaneous oxygen (kPa)	0.23	1.18	0.88
Heart rate (bpm)	3.85	8.48	7.21
Mean blood pressure (mmHg)	0.38	3.81	2.80
Central temperature (°C)	0.59	0.47	0.21

The mean difference indicates the average **bias** between the nurse and computer. All are statistically significantly different from zero (expected if there were no difference) (t test $p<0.001$ for all four parameters). Our nurses tended to chart higher. The differences are small enough (with the exception of temperature) to be clinically unimportant . The standard deviation of the mean nurse - computer differences is a measure of **precision** (table 1 column 2), indicating how variable the differences are from hour to hour (note the spread of points in vertical columns of figure 1). For comparison, table 1 also shows the standard deviation of the minute by minute computer readings for each hour (column 3). These should be similar to the nurse - computer standard deviation difference if the nurses were accurately recording a random minutes' reading; the computer sd recordings (column 3) are actually

somewhat smaller, confirming that other sources of inaccuracy exist between nurse and computer.

Comparing data before and after the manual exclusion of artifact (6.3% data) produced little difference in the results, although as expected the results showed less precision when artifacts were included. Figures 9-12 show that although most values were unaffected by the manual exclusion of artifact, occasional large differences were found. Many of these extreme outliers in tcpO2 (figure 9) are explained by calibration of the transcutaneous pO2 probe taking longer than 30 minutes of one hour and account for only 3.9% of observations. The extreme outliers in figure 10 are mostly due to persistent lead fault or electrical interference and account for 0.5 % of observations. In figure 11, deviations in blood pressure were mainly due to blocked or damped arterial lines and in figure 12, the single extreme outlier was due to a dislodged temperature probe.

Figure 5 Difference between nurse and computer for heart rate

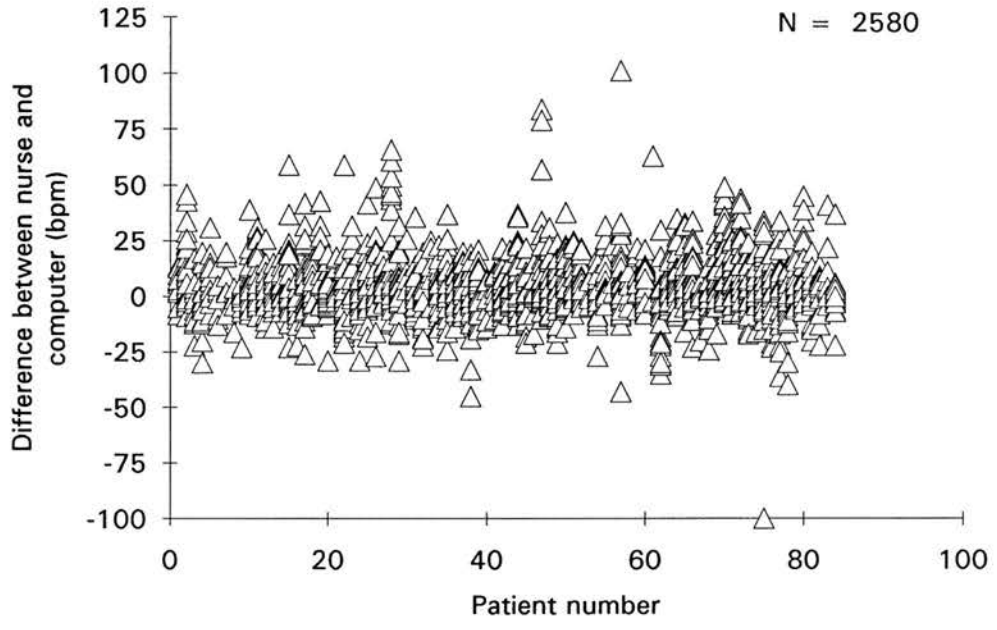


Figure 6 Difference between nurse and computer for transcutaneous oxygen

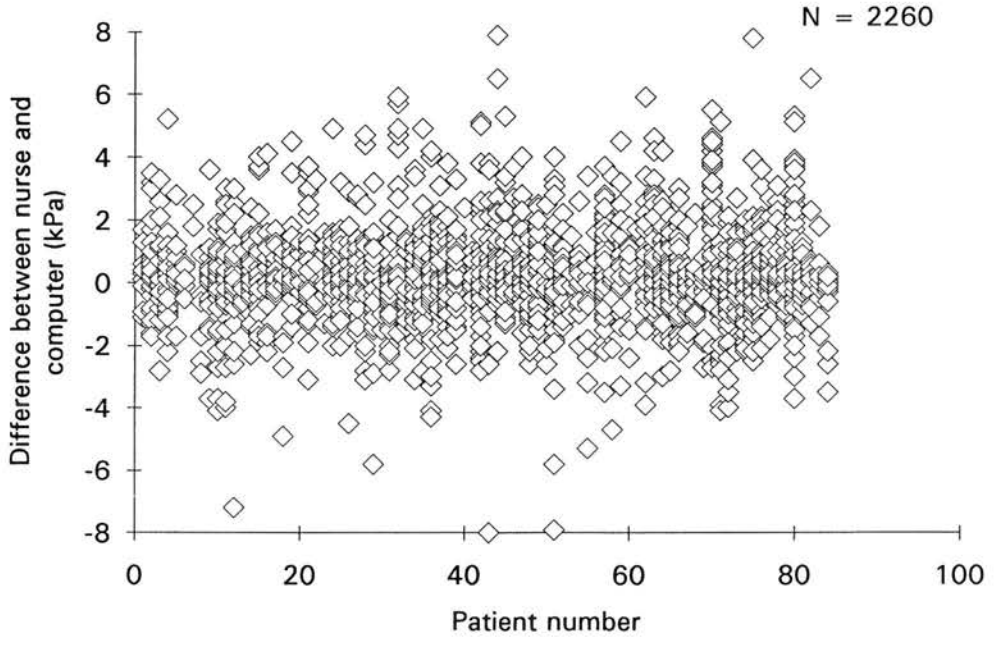


Figure 7 Difference between nurse and computer for mean blood pressure

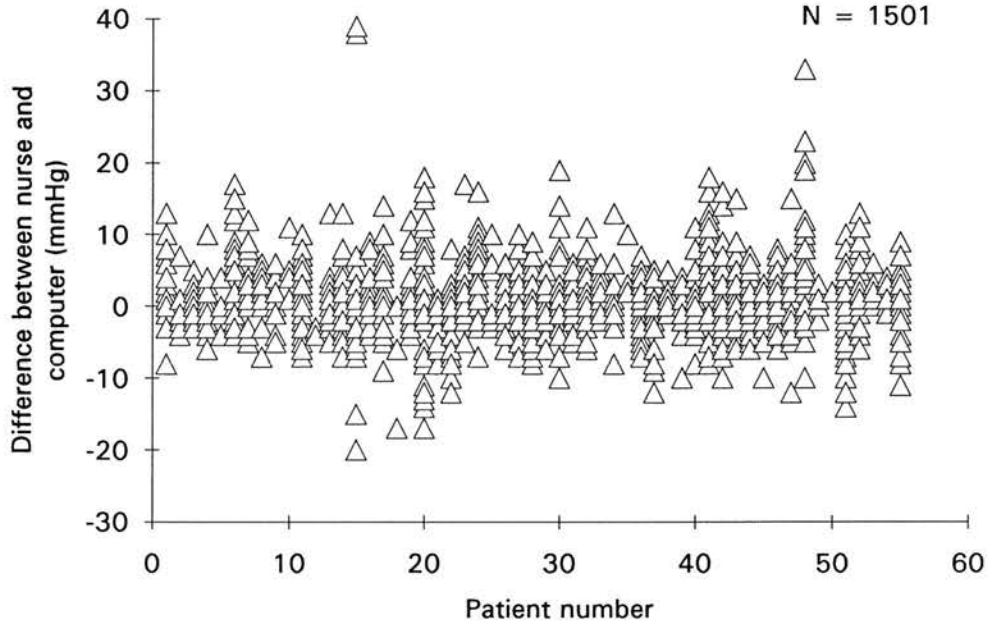


Figure 8 Difference between nurse and computer for temperature

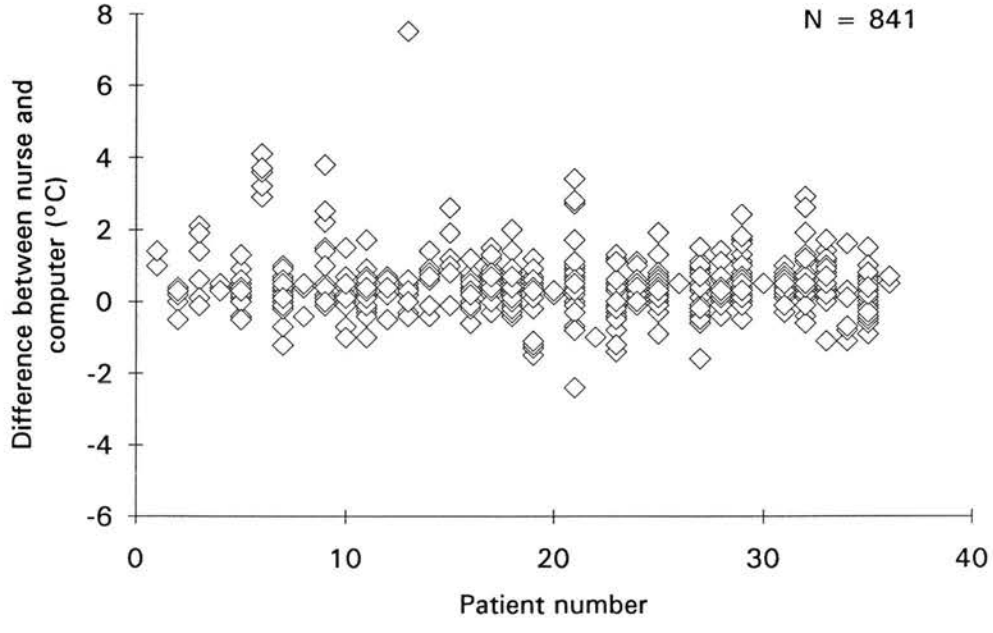


Figure 9 Effect of artifact on heart rate

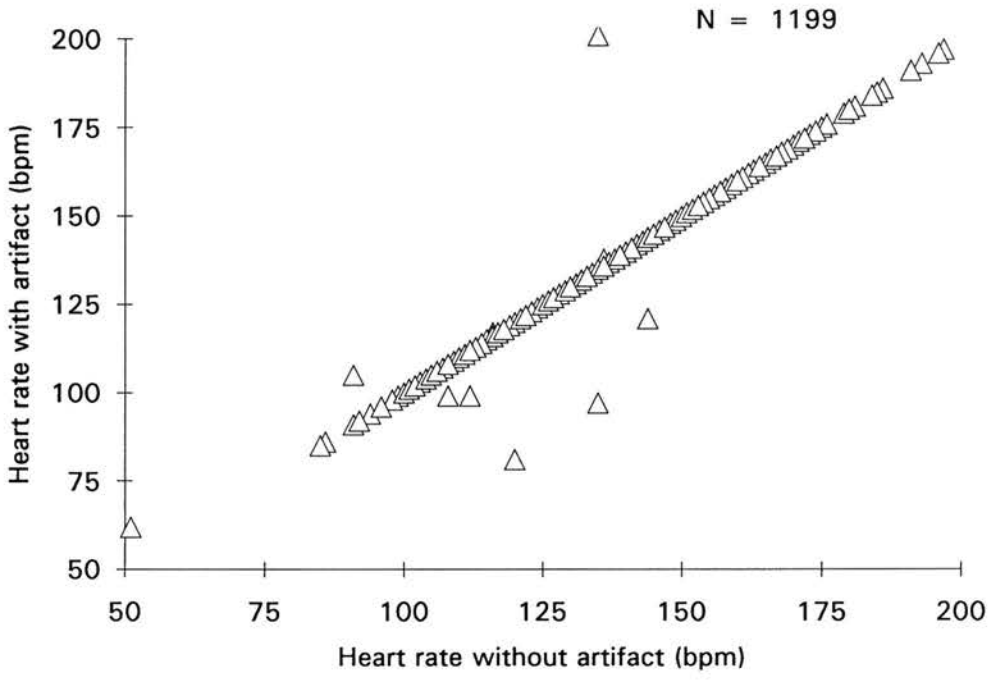


Figure 10 Effect of artifact on transcutaneous oxygen

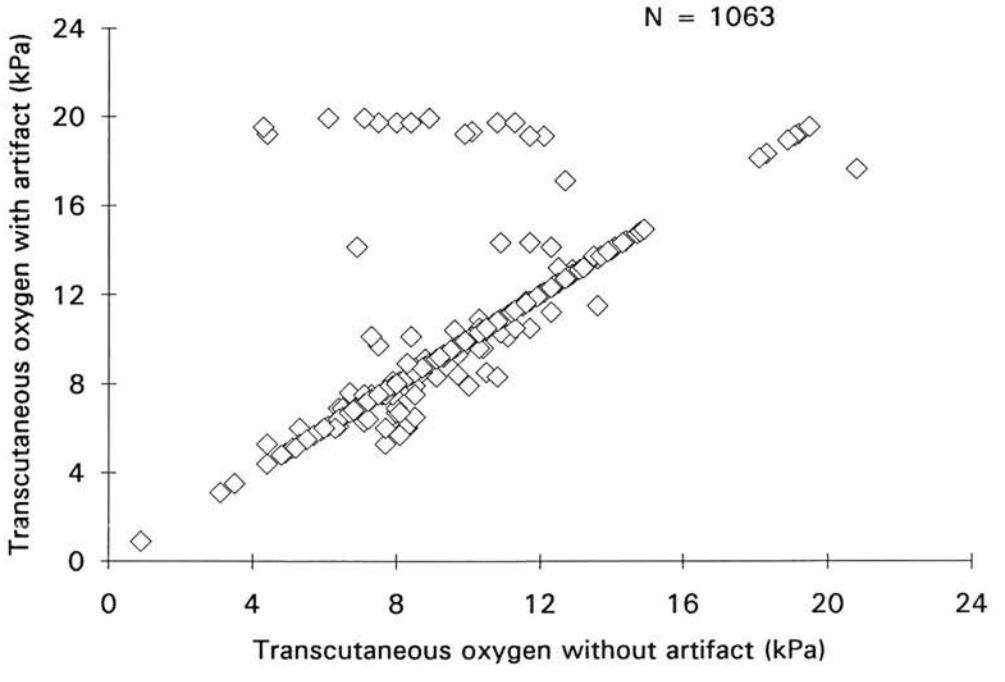


Figure 11 Effect of artifact on mean blood pressure

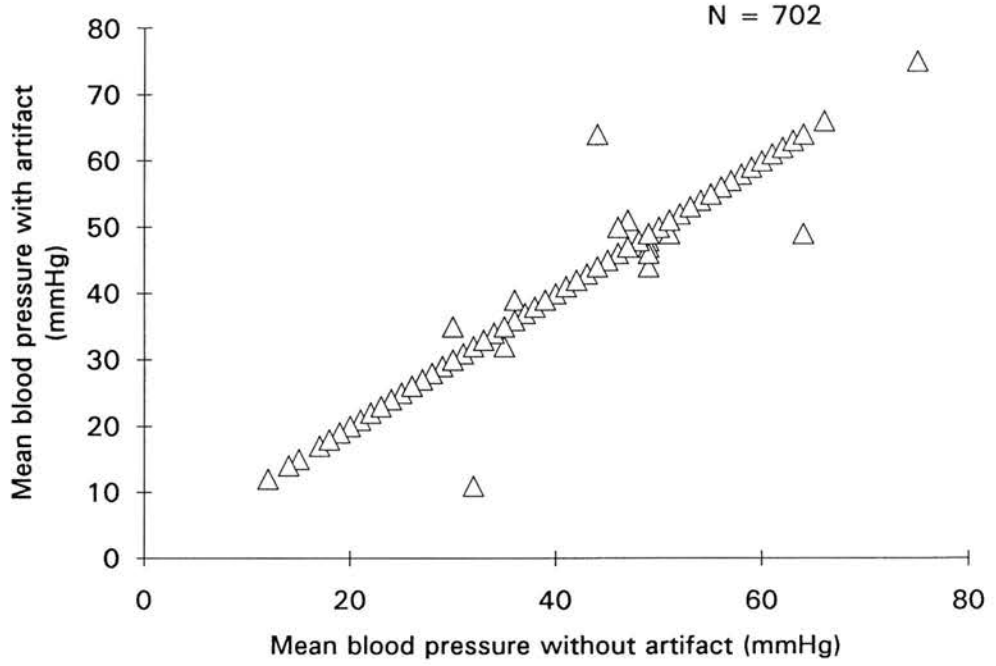
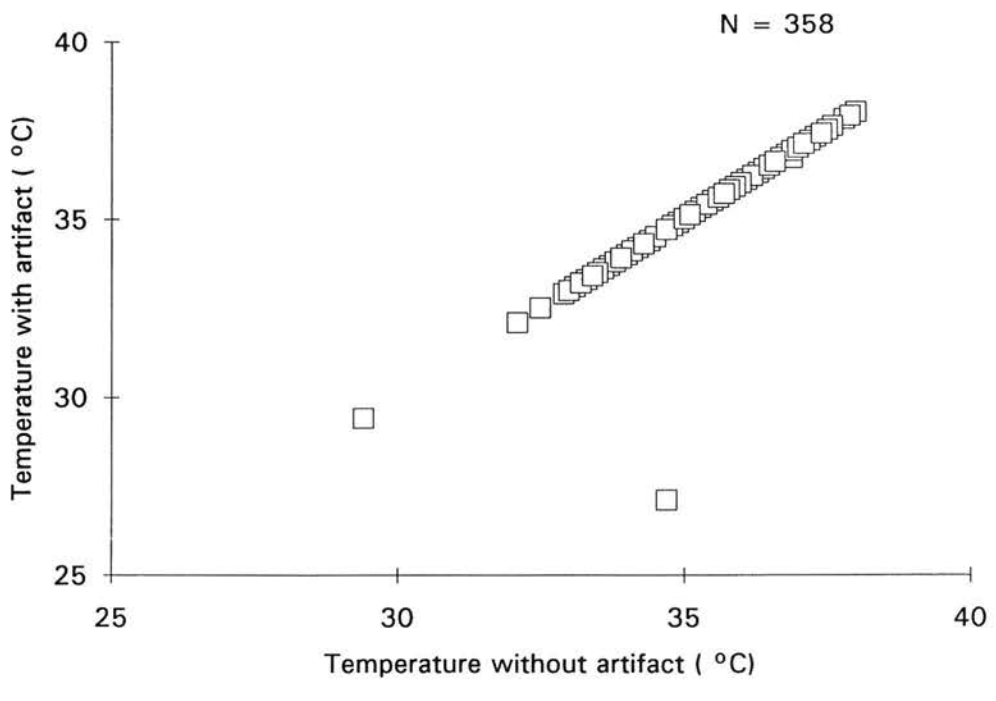


Figure 12 Effect of artifact on temperature



5.4 Discussion

Bedside computer data should not only be accurate, but should improve the accuracy of collected data [Colvin and Kenny, 1988]. The mean differences between nurse and computer, although of large statistical significance, are of little clinical importance (with the exception of temperature) (table 10). The standard deviation of these differences are clinically more important e.g. mean blood pressure 2 sd = 7.62mmHg. Intensive care infants show considerable variability of their physiological vital signs each hour; this is demonstrated in table 1 (column 3) by the standard deviation of the minute by minute computer values within each hour. This variability cannot be represented by the single hourly value noted by the nurse. If the nurse were to choose a single random data point (from the 720 possible) to represent the hour, then because of this variability, the value chosen may not accurately summarise the infant's physiological state. We have demonstrated that nurses do not simply note a single random value each hour (comparison of column 2 and 3 in table 10), other factors must therefore influence the nurse.

The computer collects all data points each hour, including those during procedures and periods of instability. The nurse may recognise that temporary changes in vital signs are untypical for that infant and might choose to ignore them. If she does, then in order to note an hourly value the nurse could either await a period of stability or might estimate an representative value for that hour. All three of these possibilities (random choice, await stability, estimate), will occur to a different extent in handwritten observations depending on the level of training and expertise of the nurse. It is impossible when reviewing handwritten trends to

determine how the hourly value has been derived. The errors resulting from these inconsistencies of nursing data entry, have been previously anecdotally described [Gardner *et al.*, 1992]. The computer is more consistent. The median value it produces is based on all data points and will be little influenced by temporary changes. It is not subject to observer variation and is independent of the level of training or expertise of the nurse caring for that infant [Clemmer and Gardner, 1992].

We have demonstrated that nurses tend to chart higher and feel that this may be a subconscious effort by the nurse to present a stable picture of her infant; waiting until patient physiology stabilises following a procedure or period of instability before writing down the hourly values. Procedures and instability frequently produce a decrease (hypoxia [Cassana, 1984] [Long *et al.*, 1980], bradycardia [Cordero and Hon, 1971], hypothermia [Mok *et al.*, 1991]) or large fluctuation (blood pressure [Perlmann *et al.*, 1983] of values in intensive care infants.

The large mean temperature difference noted between nurse and computer is of concern, as an incubator may have its temperature adjusted to compensate for a 0.5°C difference in infant temperature. We feel however, that the lower mean temperature noted by the computer, indicates that the computer is more accurate in monitoring minor fluctuations in temperature due to opening of incubator doors for procedures, etc [Mok *et al.*, 1991]. The standard deviation of the nurse/computer temperature difference is small and trend graphs would clarify clinical decision making with regard to temperature control.

Artifact may significantly reduce the reliability of data produced by computers. A nurse is able to identify erroneous data and can ignore this when making decisions about the infant. We manually removed artifact

from data during this study, however artifact cannot be removed from data prior to its trend display in the intensive care unit. The display of real time trends containing artifact might be confusing and could possible lead to inappropriate intervention. Only a small amount of our collected data was artifact (6.9%). Figures 9-12 demonstrate that most values were unaffected by the removal of artifact and of those values affected by artifact, the majority showed an extreme difference that would be easily identified on trend monitoring.

Humans have a better capacity to assimilate data displayed as graphs rather than numbers [Cole, 1990] [Cole and Davidson, 1989]. Graphical trend data presentation has been praised by Green [Green *et al.*, 1991], and the introduction of an ICU computer system in Aberdeen [Ross *et al.*, 1990], was criticised for its poor trend display [Gilhooly *et al.*, 1991]. The trend data for our patients is always visible, with computer screens continually displaying physiological trends at each cotside. Others have also found this to be the optimum method of data presentation in ICU [Shabot *et al.*, 1986]. The information is stored permanently and is highly flexible, allowing trends to be displayed over variable time scales both in real time and retrospectively. Thus the computer network, in addition to ease of data collection and increased accuracy, confers advantages to the clinician over and above the handwritten record [Lowe *et al.*, 1992].

The introduction of computers into ICU has been of variable benefit, some studies have shown a reduction in direct patient care as a result of the introduction of ICU computers [Pryor, 1989] [Bradshaw *et al.*, 1988] [Clifford, 1986]. Whilst computers have an undeniable role in ICU, their influence should be carefully evaluated to ensure that they are of benefit, without increasing workload and reducing patient care [Cobin,

1983]. Computer software that reduces routine paperwork without a time consuming computer input requirement, would allow nurses more time for direct patient care [Cook, 1982]. The method we have assessed compares a single value noted by the nurse with a single value calculated by the computer; this method is not only comparable to hourly nurse observations but also of greater accuracy. The computer data however is more flexible, with the ability to observe minute by minute trends and the standard deviation of these trends each hour. We have demonstrated that nurses could be released from manual charting of vital signs by automatic computer data collection (i.e. no input time), leading to greater accuracy and possibly increasing time available for direct patient care.

Chapter 6

CHAPTER 6

Artifact in CPTM

6.1 Artifact definition

CPTM, in accumulating large volumes of 'raw' clinical data, is inevitably corrupted by artifact; data that does not represent the true state of the patient. Artifact is detrimental to both the accuracy and visual presentation of the collected data [Clemmer and Gardner, 1992]. Artifact in diminishing the true trend [East *et al.*, 1992 (1)], may reduce staff confidence and produce an unwillingness to rely on the system as a reliable source of information. Data used for clinical decision making and statistical analysis, may be unreliable if there is an unknown quantity of artifact present [Clemmer and Gardner, 1992].

Two types of artifact may be present;

6.1.1 Physiological artifact

This artifact occurs as a result of induced physiological changes in the infant; it may be iatrogenic or patient induced. Physiological artifact is difficult to define, as it is subjective and dependent on what exactly is to be observed. For example, if the physiological effects of endotracheal suction were being observed, then the suction procedure itself would not be described as artifact. Whereas, if one wished to determine the normal heart rate of intensive care infants over a 24 hour period, then the rise in an infant's heart rate during endotracheal suction might be regarded as iatrogenic artifact, and therefore not 'normal'. Alternatively, endotracheal suction might be regarded as a 'normal' part of life for an infant in intensive care and therefore not artifact. This topic is discussed later in this chapter in the '3 observer study'.

6.1.2 Non physiological artifact

This artifact arises at some point between the generation of the signal at the patient and presentation of the data; it is often predictable and therefore identifiable [Gardner *et al.*, 1986]. Non physiological artifact accounts for the majority of artifact in CPTM data and may arise due to problems at any stage in signal processing; system electrical supply, patient monitor, patient monitor to computer connections, computer software or hardware, patient movement.

6.2 Methods of reducing non physiological artifact

Large computer systems should have a ***back up electrical supply***, to minimise artifact due to interruption of electrical supplies.

Patient monitors that supply data to computers may produce artifact by incorrect signal generation or output configuration. It has been suggested that patient monitor manufacturers, should take a greater role in reducing the artifact produced by their monitors [Gardner *et al.*, 1992].

Electrical ***connections*** may introduce artifact if they are loose or damaged. High quality connections are an essential part of both individual PCs and local area networks. The harsh environment of an ICU will soon expose poor interconnections; finding the problem isn't always easy.

Artifact arising from ***computer hardware and software*** increases with the age of the system. Quality hardware and rigourously tested software reduce the problem, but regular maintenance is still essential.

Poor signal generation due to ***patient movement*** is a frequent cause of artifact in neonatal ICU. Sedation of infants reduces, but does not abolish this artifact. Sensitive instruments i.e. non invasive blood pressure monitoring probes have been used successfully in adults and anaesthetised children [Wong *et al.*, 1992], but have limited use in neonates because of excess movement artifact [Cunningham and McIntosh, 1992]. More research is needed by manufacturers of neonatal monitors to reduce movement artifact to acceptable levels.

Figure 13 Artifact due to calibration of transcutaneous gas probe

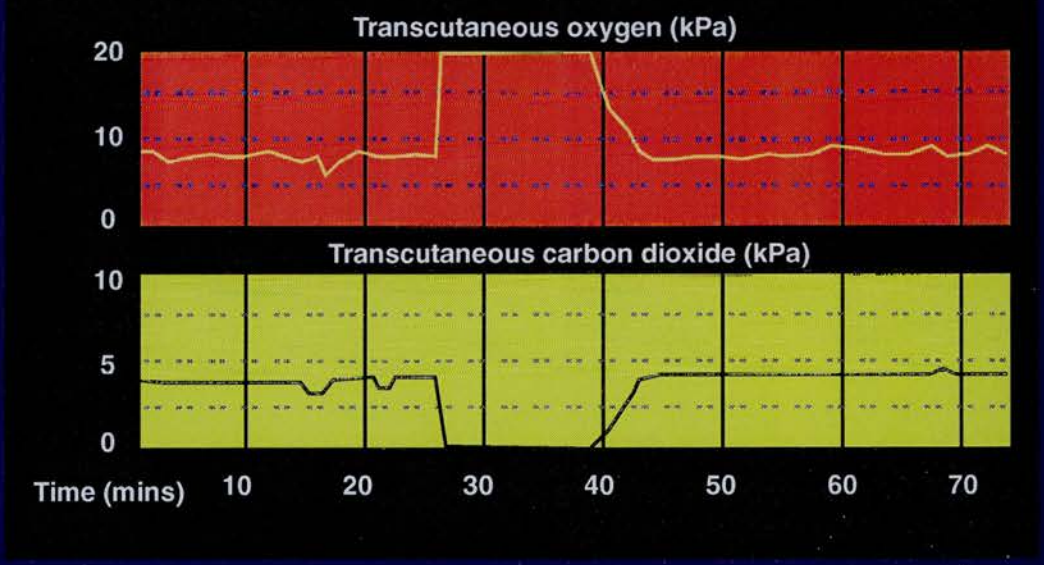
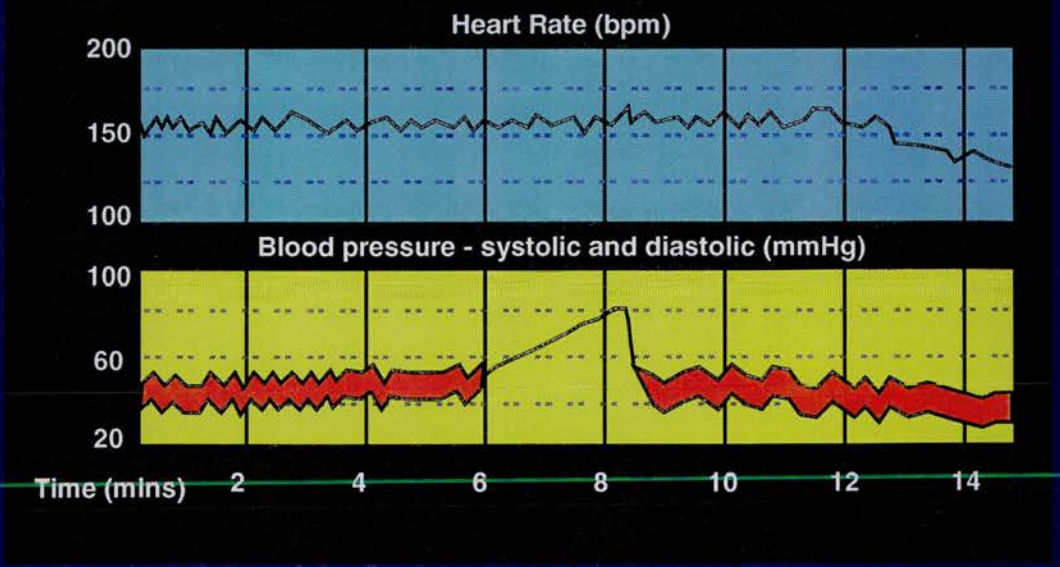


Figure 14 Artifact due to arterial line sampling



6.3 Artifact Identification

The adoption of the methods described above may reduce artifact, but they will not eradicate it. Further attempts at artifact identification/ removal must involve computer programmes and/or trained observers. In attempting to reduce the effects of artifact on data two main approaches exist;

(a) attempt to remove all artifact from data; an onerous, complex and probably impossible task.

(b) try to identify only events that are of interest, therefore ignoring all other data that might possibly be corrupted by artifact.

A combination of both methods are used by the developers of current physiological expert systems (see later).

6.3.1 Computer methods of identifying of artifact

Artifact identification by computers uses a wide variety of methods, indicating the complexity of the task and the enormous diversity of the input signals. Many of the methods developed have been specific to one particular type of signal. Artifact created by the computer itself, cannot be removed unless the computer forms part of a self regulating network.
(1) ***Exclusion of values outside preset limits.*** Values that fall outside predefined limits of acceptable normals in health and disease are excluded. Although simple to programme, there must be the ability to incorporate data from the occasional patient who legitimately falls outside the chosen limits e.g. a patient with heart block may have a 'non-physiological' heart rate [Arrøe, 1991] [Bradshaw *et al.*, 1989].

(2) ***Smoothing of data by Box Filter.*** The filter attempts to 'damp' a roving variable by assessing the mean of a number of points within a predetermined time period. If the time period is too long then the sensitivity to rapid change is lost, if it is too short then artifact may not be sufficiently damped out [Gardner *et al.*, 1992].

(3) ***Wave form analysis of oscillatory signals.*** This method analyses wave forms, to assess their frequency, amplitude and duration. If these values are outside acceptable normal ranges then they are excluded (the 'comb filter' technique) [Brusil *et al.*, 1980].

(4) ***Rate of change of individual parameters.*** Non physiological artifact frequently produces a rapid change in a parameter. Physiological changes are usually smoother and slower. An assessment of rate of change may therefore help identify artifact [Avent and Charlton, 1990] [Sittig *et al.*, 1992].

(5) ***Identifying parameters associated with artifact.*** Values with a physiological velocity change might be excluded if they were associated with a parameter containing artifact i.e. exclusion of respiratory values when movement artifact affects heart rate values derived by chest lead impedance. Alternately, tcpCO2 might not be excluded if there were no associated changes in tcpO2 (with a combined probe)[Shabot *et al.*, 1990].

6.3.2 Operator methods of identifying artifact.

(1) ***Education of system users*** enables real time artifact to be identified and noted [Clemmer and Gardner, 1992]. CPTM does not increase the amount of artifact present in physiological data, but in displaying that artifact within trends it may predispose data to misinterpretation. Alternately, trend graphs may be of value in detecting artifact, i.e. when individual values appear plausible and only the trend helps to identify them as artifact e.g. a partially blocked arterial blood pressure line. The majority of artifact is predictable and therefore education can help staff identify and disregard it. Comments entered at the time of an event or problem can be of significant value in later assessment.

(2) ***Retrospective analysis***, with identification and removal of artifact by a computer operator can be both time consuming and subject to interobserver variation [Piper *et al.*, 1991]. For many users however it represents the only dependable method of artifact removal.

Exclusion of artifact by retrospective analysis is too time consuming to be adopted as a technique for reviewing all data. Extraneous value exclusion and box filtering of data are of limited value. The comb filter techniques are limited to oscillatory signals i.e. respiration, and are therefore superseded by the velocity change method, which may also be applied to oscillatory signals.

6.4 The velocity change method of identifying artifact and events.

The most successful artifact and event identification techniques have been very specific, and include: cardiac arrhthymia detection [Ritz, 1984], EEG derangement [Panych *et al.*, 1989], intracranial pressure monitoring [Avent *et al.*, 1987] [Allan, 1983] and more recently cardiotocograph pattern recognition [Neilson *et al.*, 1988 (1)] [Neilson *et al.*, 1988 (2)].

CPTM can collect data on a large variety of parameters, from a number of different sources. Consequently, new methods of artifact identification and rejection have had to be developed.

6.4.1 Velocity change models

In 1991 we devised a series of models for the exclusion of artifact. The models were based on the identification of defined velocity changes in associated parameters, e.g. a combined transcutaneous oxygen and carbon dioxide probe change (figure 13) [Cunningham *et al.*, 1991]. The predictable nature of this commonly occurring artifact makes it an ideal candidate for exclusion. The removal of the probe from the skin causes a rapid rise of tcpO2 to 21kPa and a simultaneous fall in tcpCO2 to zero (that of room air). Both the rise in oxygen and fall in carbon dioxide occur at a rate of change that exceeds all physiological events. A second model was devised for endotracheal tube blockage, based on changes in heart rate, transcutaneous oxygen, mean blood pressure and transcutaneous carbon dioxide.

The models have not been implemented however, as both the programming time and computer handling time required for this process

must be received, processed, matched to models and a reaction made if necessary, before the next signal arrives i.e. in one second for 'Mary' CPTM. This is too great a task (at present) for a small local network run on PC's. It is estimated that this process requires up to one hundred times the computational time of other processes in an intensive care computer monitoring system [Factor *et al.*, 1990].

Sittig and his colleagues at Yale University, USA, have developed a system to detect both physiological trends and artifact using a parallel software architecture in a hierarchical 'process trellis' [Factor *et al.*, 1990] [Sittig and Factor, 1990]. The system attempts to match incoming data with 5 states of change; steady, slope, step and slope, step, and transient change. Any one or a combination of these states can be used to create a model that will describe a physiological trend or artifact. The system operates with bedside PCs, that receive data and then distribute it to possibly thousands of central processing units, each of which assesses a portion of the signal. The authors describe the detection of cardiovascular and respiratory instability, though no details of the equipment or detection success were reported. This expensive approach appears to be the best current way to tackle the problem and costs should become more reasonable within the next few years. This method enables both artifact and physiological trends to be detected using the same computer hardware and software. Whereas statistical assessments of data are possible using much less computational power, these methods are limited in their application e.g. comb filters. The Yale system increases the flexibility of the data, widening its range of uses; artifact and trend detection (possibly even patient specific), dynamic linkage of therapeutic interventions eg. dopamine infusions to patient physiology, and the use of intelligent warning alarms.

6.5 The effects of manual removal of artifact on computerised physiological data.

'The 3 observers study'

6.5.1 Introduction

The removal of artifact by expert systems will not be a real possibility in standard computerised physiological monitors for many years. The effects of artifact on physiological data therefore needs to be assessed:

(1) what constitutes artifact?

(2) how much artifact is present in data?

(3) can independent observers accurately identify and remove similar artifact ?

(4) does the inclusion of artifact significantly alter the results?

To answer these questions, we assessed the results of three independent observers removing artifact from the CPTM data of three infants - 'the 3 observers study'.

6.5.2 Methods

Three independent observers removed artifact from the CPTM data of three typical low birth weight intensive care infants. Each infant had 7 complete days of data for the four physiological parameters assessed. These were; heart rate, respiratory rate, tcpO2 and systolic blood pressure. For each parameter, 6 hourly sections of one minute values were analysed over the first seven days of life i.e. 28 time periods (n.b. the first period was from the time monitoring started until 6 hours of age). Six hourly time periods were chosen as they represent a typical time period for assessing long term changes in physiology. Short term changes i.e. drug effects, are usually assessed over a few minutes and most non-physiological artifact can usually be prevented during brief studies. For each six hour time period the computer generated a median and a mean value from the available data points. Values outside predefined limits were automatically excluded (appendix 2) and remained unchanged throughout the study.

Each of the three observers then removed what they considered to be artifact from the data of the three infants. The observers were all familiar with trend monitoring (Professor of Paediatrics, myself and the Computer Research Nurse). Observers were told the time periods from which artifact should be removed, but no instructions were given as to what would constitute artifact. Observers were not able to discuss the study until it had been completed. Following the manual removal of artifact by each observer, the computer calculated a second median and mean value for each 6 hour period. We compared the respective median and mean values before and after this subjective removal of artifact. The percentage of data removed as artifact was calculated in all cases (table 11).

Table 11 **Percentage of data removed as artifact for 6 hourly assessment in the first 7 days of life.**

	Infant	Observer 1	Observer 2	Observer 3	All observers
Transcutaneous oxygen	a	9.1	11.9	7.5	
	b	9.8	10.4	6.0	
	c	8.6	14.2	8.7	
	total	*9.2*	*12.2*	*8.4*	***9.9***
Systolic Blood Pressure	a	6.1	11.8	5.2	
	b	3.9	10.1	3.2	
	c	16.9	22.9	15.4	
	total	*9.0*	*14.9*	*7.9*	***10.6***
Heart Rate	a	0.3	5.6	0.7	
	b	0.1	8.4	0.2	
	c	0.6	5.3	0.6	
	total	*0.4*	*6.4*	*0.5*	***2.4***
Respiratory Rate	a	2.4	6.3	4.5	
	b	0.8	3.7	1.2	
	c	1.1	4.1	0.8	
	total	*1.4*	*4.7*	2.2	***2.8***
Totals		**5.0**	**9.6**	**4.8**	**6.5**

6.5.3 Results

Each of the three observers removed what they believed to be artifact from the computer monitored data. The percentage of data removed from the parameters by each of the observers is shown in table 11. The percentage of data removed as artifact is greater for observer 2, than the other two observers in all cases. Observers 1 and 3 consistently removed similar volumes of data. Whereas heart rate, respiratory rate and tcpO2 had consistent volumes of data removed from infant to infant (< 4% difference), sbp showed a marked inter-patient variability (12 - 13%).

The combined results for all observers demonstrate that sbp (10.6%) and tcpO2 (9.9%) required a substantial amount of data to be excluded, whereas both heart rate (2.4%) and respiratory rate (2.8%) had much less data removed as artifact. The average amount of data removed by all the observers in the three infants was 6.5%.

The effects of artifact removal from the 6 hourly time periods in each of the three infants is shown in Table 12;

N, represents the number of episodes where there was no difference between the calculated median or mean before and after observer removal of artifact.

Mean difference, is the mean difference between the corresponding median/mean values before and after observer removal of artifact.

Range of difference gives the range of values by which the corresponding median/mean values vary before and after observer removal of artifact.

Table 12 Effects of artifact removal on statistical results in 3 infants.

variable	infant	observer	N (28)	mean difference	range of difference	N (28)	mean difference	range of difference
				median			**mean**	
transcut-	a	1	23	-0.03	-0.2,0	5	0.06	-0.21,0.62
aneous		2	23	-0.04	-0.4,0	3	0.03	-0.27,0.45
oxygen		3	26	-0.01	-0.2,0.1	20	0.05	-0.21,0.46
(kPa)	b	1	5	0	-1.6,1.4	1	0.14	-1.23,1.51
		2	5	0	-1.6,1.5	1	0.14	-1.15,1.49
		3	5	-0.01	-1.6,1.5	1	0.14	-1.23,1.50
	c	1	22	0.01	-0.1,0.1	2	0.03	-0.10,0.34
		2	21	0.01	-0.1,0.4	3	0.04	-0.15,0.38
		3	28	0	0,0	20	0.04	0,0.40
average		**all**	**18**	**0.01**		**6**	**0.07**	
systolic	a	1	27	-0.11	-3,0	7	-0.10	-4.09,1.34
blood		2	24	-0.07	-2,0.5	6	-0.17	-4.31,1.56
pressure		3	27	-0.09	-2.5,0	23	-0.10	-3.95,1.33
(mmHg)	b	1	24	-0.13	-4,1	3	-0.12	-2.48,0.53
		2	20	-0.23	-4,1	1	-0.01	-2.02,0.75
		3	25	-0.14	-4,1	11	-0.13	-2.45,0.48
	c	1	26	1.61	0,44	5	1.90	-0.32,50.91
		2	17	1.89	-1.5,44	1	2.14	-1.08,50.91
		3	26	1.61	0,44	21	1.9	-0.08,50.91
average		**all**	**24**	**0.48**		**9**	**0.59**	
respira-	a	1	26	-0.61	-18,1	17	-0.37	-17.99,1.21
tory rate		2	21	-1.98	-54,1	8	-1.00	-28.65,1.61
(breaths/		3	27	1.68	-47,0	26	-0.94	-25.33,0
min)	b	1	26	-0.07	-1,0	22	-0.21	-5.31,0.09
		2	25	-0.04	-1,1	9	-0.21	-5.20,0.89
		3	26	-0.07	-1,0	23	-0.24	-5.26,0.09
	c	1	25	-0.09	-1,0	20	-0.11	-1.72,0.04
		2	22	-0.13	-1,0.5	10	-0.26	-3.03,1.06
		3	27	0.02	0,0.5	25	-0.03	-0.63,0.11
average		**all**	**25**	**-0.15**		**18**	**-0.37**	
heart	a	1	28	0	0,0	23	0.03	-0.13,1.19
rate		2	21	0.34	0,3	9	0.46	-0.25,2.28
(bpm)		3	28	0	0,0	28	0	0,0
	b	1	28	0	0,0	0	0.51	-7.97,18.79
		2	17	-0.3	-2.5,1	0	-0.04	-9.41,18.78
		3	27	-0.04	-1,0	0	0.49	-7.97,18.79
	c	1	28	0	0,0	17	0.05	-0.13,0.53
		2	24	0	-1,1	2	-0.31	-1.45,0.38
		3	28	0	0,0	23	-0.02	-0.21,0
average		**all**	**25**	**0**		**9**	**0.13**	

Median Values: The overall effect of the extra removal of artifact by observer 2 on the median values (**N**) was minimal and the mean difference showed little variation between observers. Median values correlated best between observers 1 and 3. Overall 24 or 25 of the possible 28 median values did not change following the removal of artifact (except for tcpO2 where an average of 18 remain the same).

Mean values: Artifact removal had a greater effect on mean values. There was a better correlation between observers 1 and 2, than between observers 1 and 3, despite the fact that similar amounts of data were removed by observers 1 and 3. Again the mean difference was persistently small and consistent between observers (observers 1 and 3 being closest). Overall, 6-9 mean values did not change following artifact removal, (except respiratory rate, where 18 values remained the same).

Mean values were calculated to two decimal places and so were more sensitive to change than median values: a change of only 0.01 bpm for heart rate or 0.01 kPa for tcpO2 after artifact removal would produce a disagreement in mean values.

Average changes: Table 12, gives an average value of both **N** and mean difference for each of the four parameters. Blood pressure changes with artifact removal were clinically the most important with a median/mean difference; sbp (0.46/0.59 mmHg). Heart rate (0.00/0.13 bpm) and tcpO2 (0.01/0.07 kPa) had a negligible change and respiratory rate was minimally affected (-0.15/-0.37 per min) by the removal of artifact. Only sbp changes were felt to be clinically important.

6.5.4 Discussion

During the study we deliberately avoided establishing rules that might have altered the 3 observers' perceptions of what constituted artifact, as this was one of the questions to be answered. After the data had been collected, we held a 'post mortem' of the results. We discussed the methods each of us had used to identity artifact and compared printed trend graphs (over 7 days) from one infant, onto which we had individually marked areas that we considered to be artifact. A section from one time period (with large amounts of artifact) is illustrated in figures 15 and 16, which compare artifact removal by the 3 observers for both tcpO2 and combined (i.e. systolic) blood pressure. Data that was removed as artifact, has been shaded in red in figures 15 and 16. As has been demonstrated in the tables, observer 2 removed more data than either observer 1 or 3. Whereas observers 1 and 3 removed similar areas of data, observer 2 in addition removed data where there was a transient physiological change in that parameter.

It transpired that there had been a philosophical difference of opinion of what constituted artifact. Observer 2 had removed both non-physiological artifact and also physiological values he deemed to be iatrogenic (e.g. during routine procedures). Timed comments by nurses assisted in the identification of these events. The remaining two observers did not exclude these values, because in their opinion these events were a normal part of life for ICU neonates. Thus observers 1 and 3 removed only non-physiological artifact [Clemmer and Gardner, 1992]. These differences of opinion accounted for most of the inconsistencies caused by the increased data removal by observer 2.

Figure 15 Artifact removal by 3 Observers from transcutaneous oxygen (kPa)

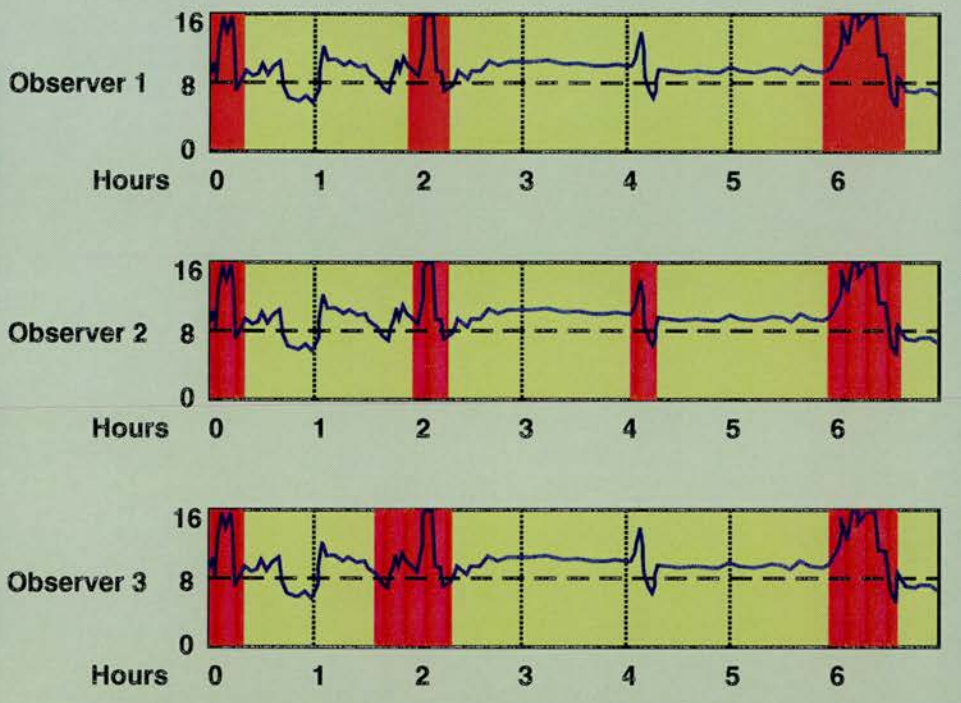
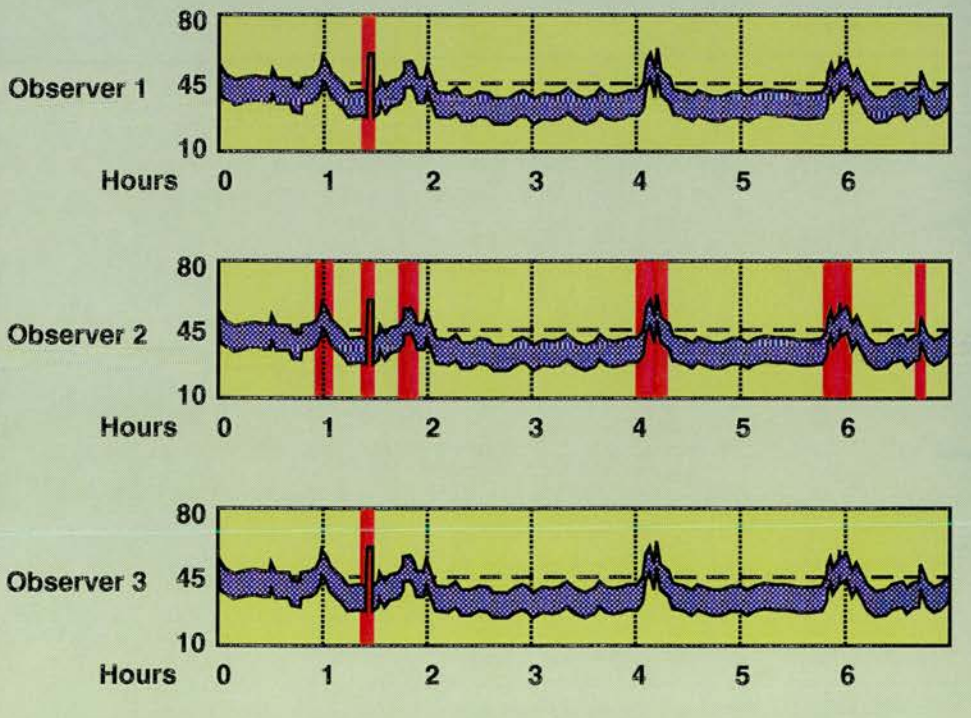


Figure 16 Artifact removal by 3 Observers from systolic (and diastolic) blood pressure (mmHg)



Non-physiological artifact arises at some point between signal generation and presentation of the data. Physiological artifact is more difficult to define, it might be due to iatrogenic intervention (i.e. handling), or due to changes in patient physiology e.g. activity. What constitutes artifact depends on what one wishes to define. If one wished to observe the effects of a treatment on physiology, then both non-physiological and patient induced physiological artifact might be removed. To establish a 'normal' or resting physiological reference range, non-physiological artifact would always be removed but it can be debated whether physiological artifact should be removed. The type of artifact removed from physiological data is therefore important when interpreting results. Observers 1 and 3 had broad agreement of what constituted artifact and removed similar percentages of data in all cases. This would suggest therefore, that removal of artifact by trained observers with agreed artifact rules is consistent, with minimal inter-observer variation.

The artifact removed from sbp trends was mainly due to intervention with arterial lines (i.e. sampling) or poor signal quality due to 'damping' of the arterial pressure signal [Cunningham *et al.*, 1993]. Damping of the arterial pressure trace is unpredictable and accounts for the large patient to patient variation in the amount of blood pressure data removed as artifact. TcpO2 probes are calibrated every 4 hours (taking 20 minutes) and are occasionally dislodged from the skin, therefore artifact in tcpO2 data is more predictable. Due to the large volumes of data removed as artifact in these parameters and the effects this removal had on statistical results, it would seem appropriate to remove artifact present in both sbp and tcpO2 data prior to statistical assessment. In contrast, heart

rate and respiratory rate had only small amounts of data removed as artifact (especially by observers 1 and 3 who removed only non-physiological artifact). Both these parameters had a small mean difference and generally a good agreement in mean and median values before and after artifact removal (table 12). Thus it would not seem as critical to remove artifact present in heart rate and respiratory rate data. The minute mean averaging of our data prior to data storage, may have masked transient artifact in heart rate and respiratory rate, but artifact lasting longer than 10 seconds would usually produce a notable change in the one minute mean that could be identified in the CPTM trends.

Until automatic computer exclusion of artifact is available to the majority of intensive care CPTM users, manual exclusion of artifact will continue. We have demonstrated consistent artifact removal from CPTM data, when trained observers have similar ideas of what constitutes artifact. Our results suggest that once rules identifying the type of artifact to be removed are agreed, inter-observer variability should be small. Artifact in tcpO2 and sbp data may significantly distort results and so should be removed.

Chapter 7

CHAPTER 7

Reference blood pressure values for vlbw infants in the first seven days of life

7.1 Introduction

Intensive care of the extreme preterm neonate is a relatively new science. Small numbers of very low birth weight infants born in individual neonatal units, limit the opportunities for investigation and consequently many aspects of care are based almost on anecdote. Extrapolating management from term neonates, children and adults, can be inaccurate [Versmold *et al.*, 1981]. Preterm delivery is not a normal event and preterm physiology is neither that of a fetus, nor a term infant. Many philosophical and practical difficulties exist in establishing what is 'normal' for these infants. CPTM has the ability to permanently store large volumes of continuous physiological data and so provide an accumulating archive, from which physiological 'normality' may be assessed.

The inability to accrue continuous data in a large number of vlbw neonates and the difficulties in defining normality for these infants, have prevented the satisfactory assessment of representative blood pressure ranges [BAPM, 1992]. Both hypotension [Fujimura *et al.*, 1979] [Szymonowicz *et al.*, 1984] and hypertension [Cabal *et al.*, 1986] [Wimberley *et al.*, 1982] have been associated with considerable morbidity and mortality in these infants, in particular as a cause of intraventricular haemorrhage

and periventricular leukomalacia. However, definitions of normo, hypo and hypertension vary and whilst considerable effort is made by individual clinicians to maintain (what they perceive as) 'normotension' by the use of colloid supporting agents and inotropes, the benefits to the infant from such treatments are poorly understood [Moscoso *et al.*, 1983] [Lister *et al.*, 1984] [Bignall *et al.*, 1989].

Using data accumulated over 2 years on our CPTM system, we have assessed the intra-arterial blood pressure of 141 vlbw infants during their first seven days of life. The perinatal factors which most influence blood pressure and the relationship between blood pressure and outcome have been assessed.

7.2 Methods

The study retrospectively assessed all infants admitted to our neonatal intensive care unit between October 1989 and January 1993 whose birthweight was $\leq$ 1500g. Those infants with more than 24 hours of intra-arterial blood pressure monitoring in the first 7 days of life were included in the study. Infants with serious congenital malformation were excluded.

The physiological parameters assessed in this study were the mean blood pressure (mbp), systolic blood pressure (sbp), diastolic blood pressure (dbp) and heart rate.

The decision to monitor intra-arterial blood pressure in these infants was a clinical one; usually performed in those infant's who were expected to require ventilation for greater than 24 hours. 3.5/5.0 french gauge umbilical or 24 gauge peripheral arterial catheters were used,

through which 0.9% heparinised saline was infused at a rate of 1ml per hour. Arterial pressure monitoring was by pressure dome transducer using a Hewlett Packard Neonatal Monitor (78834A). The pressure transducer was placed at the height of the infants' mid chest and calibrated to atmospheric pressure every 24 hours. The dynamics of this monitoring circuit have been demonstrated to have an acceptably small effect on blood pressure [Evans *et al.*, 1986]. Mean blood pressure was calculated by the Hewlett Packard monitor from the area under the pulse pressure curve. Heart rate was derived either by chest lead impedance or from the arterial line pulse pressure trace.

Trend data for each infant, was assessed in 12 hour periods for the first 48 hours and thereafter in 24 hour periods until 7 days of age (i.e. 9 periods). All time periods related to time of birth; consequently the first time period was from the time that arterial access was established until 12 hours of age. Any values affected by non-physiological artifact were removed; including damped systolic and diastolic arterial traces and also the mean blood pressure if it appeared to be affected by the damping process [Cunningham *et al.*, 1993]. The computer does not store the arterial pressure waveform and therefore damping was defined as a sudden reduction in pulse pressure to < 8 mmHg; this is associated with loss of the dicrotic notch on the pressure waveform (personal observation). In those infants who died, the trend data for the 4 hours before death was not analysed.

For each time period the computer calculated the following values from the available data points, after the removal of artifact; mean, standard deviation, and maximum and minimum values. These data files were placed onto ASCII files and transferred to SPSS for statistical

assessment. Artifact removal and preparation of the ASCII files was performed by two trained observers[1], with the above definitions agreed to prior to the start of the study.

Perinatal factors that might influence blood pressure were assessed retrospectively from casenotes (table 13). Sixteen individual factors of infant, maternal and perinatal care were considered, together with a further seven factors that were assessed temporally in relation to the 9 blood pressure time periods, (ventilation, dopamine, colloid support, blood transfusion, pancuronium, dobutamine, IVH). Daily cranial ultrasound scans were performed for the first seven days [Papille *et al.*, 1978].

Infants were assessed in two birthweight strata: < 1000g and 1001 to 1500g. Non-parametric tests (Mann-Whitney, Kruskall Wallis or Spearman rank correlation as appropriate) were used to examine associations between daily blood pressure values and other factors recorded at birth or measured daily during the first week. Multiple linear regression was used to test whether sets of factors significantly predicted daily blood pressure when adjusted for one another. Trends in blood pressure over the week were examined by unbalanced mixed model analysis of covariance, using BMDP 5V software. This allowed incorporation of both factors measured only at birth and those which changed from day to day. Centiles for mean mbp over the first week were calculated, by fitting a quadratic regression to all points and adding or subtracting two residual standard deviations[2].

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[1]Myself and Andrew Symon, Research Nurse on the project for the final year

[2]Statistical analysis of ASCII data was by R.A. Elton and Changqing Zhu, (Dept of Medical Statistics, University of Edinburgh), under my clinical direction.

Table 13 Details from 141 infants in the reference blood pressure study.

Birthweight group (g)	≤1000	1001-1500		≤1000	1001-1500
N =	76	65		76	65
Birthweight (g)	799 (127)	1245 (135)	Apgar 1	4.0 (2.0)	5.0 (2.0)
Gestation (weeks)	26 (1.8)	29 (1.8)	Apgar 5	7.4 (1.7)	7.9 (1.4)
Maternal age (years)	28 (5)	28 (6)	Umbilical artery catheter	59	53
Pregnancy induced hypertension	16	40	Dopamine	17	10
Antenatal steroids	38	27	Colloid support > 10ml/kg	52	32
Antepartum haemorrhage	10	20	Blood transfusion	68	60
Anti-hypertensives	15	8	Pancuronium	24	17
First haematocrit	0.47 (0.07)	0.48 (0.07)	Dobutamine	3	1
Fetal distress	17	15	Ventilation	75	61
Asphyxia*	17	4	Neonatal death	23	7

Numbers in table are either shown as mean (sd) or as number of infants out of total (N).
*Defined as pH<7.10 at birth or 5 minute agpar of ≤5 or signs of Hypoxic ischaemic encephalopathy.

7.3 Results

141 infants had sufficient blood pressure data. Of these 76 had a birthweight ≤ 1000g and 65 had a birthweight between 1001 and 1500g. Of the original cohort, 15 infants ≤ 1000g and 51 infants in the 1001-1500g group had insufficient bp data. Infant details for the two groups are contained in table 13.

Of the factors at birth listed in table 13, only birthweight ($p<0.001$), gestation ($p<0.001$), maternal hypertensive treatment ($p<0.01$), colloid support ($p<0.001$) and dopamine ($p<0.05$), were significantly associated with mean mbp during the first twelve hour period. Multiple regression showed that birthweight ($p<0.001$), colloid support ($p<0.01$) and dopamine ($p<0.05$) gave a significant independent prediction of mean mbp.

Values for mean mbp, dbp, sbp and heart rate in the nine time periods over the first 7 days are shown in table 14 for those infants ≤1000g, and table 15 for those infants between 1001 and 1500g. Mbp was analysed in two groups: Group A includes all time periods in all infants. Group B values excluded those time periods when dopamine or colloid support (>10ml/kg) were given. Colloid support included both 20% albumin and fresh frozen plasma. 10ml/kg of colloid support (in any one time period) was chosen as an exclusion point, as blood pressure has been shown to have a poor response to small volumes of colloid support [Bignall *et al.*, 1989] [Barr *et al.*, 1977] [Gill and Weindling, 1993]; of the 76 infants <1000g, 17 received colloid support < 10ml/kg during the seven days, and only 9 of those with a birthweight of 1001-1500g. Of the 878 time periods analysed for group A values, 229 were then excluded for group B calculations. The values shown for sbp, dbp and heart rate include all time periods.

Table 14 Arterial blood pressure and heart rate values in infants ≤1000g birthweight.

		Hours				Days				
		0-12	13-24	25-36	37-48	3	4	5	6	7
Mean mbp* (mmHg) Group A	m	33.1	33.0	34.8	36.4	36.9	37.2	37.5	37.3	37.3
	sd	4.5	5.0	4.2	5.9	5.5	5.1	4.8	5.9	5.8
N =		69	74	67	66	57	51	47	45	40
Mean mbp* (mmHg) Group B	m	34.7	34.8	35.5	37.3	38.0	37.3	38.6	38.9	38.5
	sd	3.9	4.4	3.8	4.8	5.8	4.1	4.2	5.7	5.3
N =		34	50	51	47	38	38	34	30	32
Minimum mbp	m	22.9	24.6	25.6	28.2	22.8	23.8	24.4	23.1	24.1
Maximum mbp	m	46.5	47.3	46.8	48.3	54.1	56.1	55.2	57.8	57.5
SD of mbp† (Gp A)	m	3.61	3.39	3.06	2.95	3.42	3.77	3.69	5.26	3.56
Mean sbp (mmHg)	m	36.9	37.2	39.0	40.4	40.2	42.1	42.2	42.2	40.9
	sd	5.6	5.5	5.1	6.5	8.8	6.6	8.0	7.7	8.5
Mean dbp (mmHg)	m	30.0	30.0	31.5	32.9	32.9	33.5	33.3	34.0	32.3
	sd	4.8	4.6	4.1	5.8	6.3	4.5	5.5	6.2	6.3
Mean Heart rate (bpm)	m	145.8	143.9	149.4	154.0	155.4	152.7	153.6	153.4	153.3
	sd	9.1	10.9	10.6	11.5	10.3	9.0	9.1	9.4	9.3

*Mean mbp is the mean of all mbp values during each time period (i.e. mean of 720 {minus artifact} mbp data points) The mean (m) and standard deviation (sd) of these values for all patients are then shown.
†SD of mbp is the sd of mbp during each time period, the mean (m) of all patients is then shown. It is this sd of mbp that is associated with IVH (see results).

Table 15 Arterial blood pressure and heart rate values in infants birthweight 1001g to 1500g.

		Hours				Days				
		0-12	13-24	25-36	37-48	3	4	5	6	7
Mean mbp* (mmHg) Group A	m	35.6	35.4	36.8	38.4	38.9	40.1	42.3	41.1	38.8
	sd	4.5	4.9	4.5	4.5	4.8	5.7	7.7	7.6	3.9
N =		54	61	59	54	47	33	24	19	11
Mean mbp* (mmHg) Group B	m	36.4	35.8	37.0	38.5	39.0	39.5	42.0	41.9	38.8
	sd	4.1	4.7	4.4	4.8	5.0	4.8	7.8	7.5	3.9
N =		37	48	51	44	34	30	23	17	11
Minimum mbp	m	25.2	26.9	28.4	29.2	25.2	26.5	30.8	30.4	22.0
Maximum mbp	m	49.1	48.9	49.2	52.4	57.0	61.2	60.2	59.1	59.3
SD of mbp† (GpA)	m	3.82	3.30	3.15	3.51	3.69	3.76	3.92	3.79	3.93
Mean sbp (mmHg)	m	40.8	40.8	42.5	44.3	45.7	48.2	49.3	47.0	48.2
	sd	5.3	5.5	5.3	5.4	5.7	6.3	8.4	12.0	4.6
Mean dbp (mmHg)	m	32.2	31.6	32.7	34.3	34.3	35.3	37.3	35.4	33.7
	sd	4.4	4.7	4.6	5.1	5.3	6.1	7.9	9.6	4.4
Mean Heart rate (bpm)	m	145.5	142.3	146.6	150.5	153.2	154.1	153.9	155.0	155.3
	sd	10.5	11.6	10.6	11.2	12.8	10.4	8.5	7.8	8.2

*Mean mbp is the mean of all mbp values during each time period (i.e. mean of 720 {minus artifact} mbp data points) . The mean (m) and standard deviation (sd) of these values for all patients are then shown.

†SD of mbp is the sd of mbp during each time period, the mean (m) of all patients is then shown. It is this sd of mbp that is associated with IVH (see results).

Blood pressure increased over the seven day period (tables 2 and 3). This increase was greater in infants of higher birthweight (and gestation). Blood pressure increased to a maximum on day 4 to 5 and then fell slightly on day 6 and 7: a quadratic term for time in the analysis of covariance was significant at $p<0.05$. Quadratic centile charts for mean mbp are shown in addition to the tables. Figure 17 demonstrates mean mbp in all infants < 1000g and can be compared with figure 18, which shows mean mbp following the removal of those time periods when dopamine or colloid (>10ml/kg) were given. Figures 19 and 20 show the corresponding trends for those infants weighing 1001 to 1500g. Blood pressures increased by different rates over the first week; sbp increased greater than mbp, and dbp increased least of all, i.e. increased pulse pressures. The standard deviation of all blood pressures (mean sbp, mean mbp & mean dbp) increased over the first 6 days but were lower on day 7, i.e. blood pressure differences between infants increased over the first week. Heart rate also increased in the same manner as blood pressure, though differences between weight groups are small.

The mean minimum mbp fell to less than two standard deviations of the mean mbp in seven (<1000g) and four (1001-1500g) of the nine time periods (groups A and B), and the mean maximum mbp was greater than two standard deviations above the mean mbp (both <1000g and 1001-1500g) in all nine time periods (groups A and B). These results would suggest that infants frequently have a mbp that is temporarily outside this reference range. It has been suggested that instantaneous hypertensive peaks in blood pressure may produce IVH [Cabal *et al*, 1986] [Wimberley *et al.*, 1982]. We only demonstrated a significant association between high maximum mbp on day 2 and IVH on day 3 ($p=0.008$). There was also a

significant association between low minimum mbp on day 2 and IVH on day 3 ($p=0.027$) and a low mean mbp on day 1 and IVH on day 2 ($p=0.018$). A much stronger association existed between mbp variability (as the sd of mbp, tables 14 and 15) and IVH. A large sd of mbp on day 1 was associated with IVH on days 3 to 7; on day 2 was associated with IVH on any of days 1 to 7; and on day 3 was associated with IVH on days 4 and 5 (all $p<0.05$). There was also an significant association between sd of mbp on day 7 and neonatal death ($p<0.05$).

In figures 17 and 19, open circles represent those infants removed for the calculation of group B values.

The figures (17-20) show the mean and (+/-) two standard deviations for mean blood pressure.

Figure 17 Mean mean blood pressure over 7 days in infants ≤ 1000g (Group A)

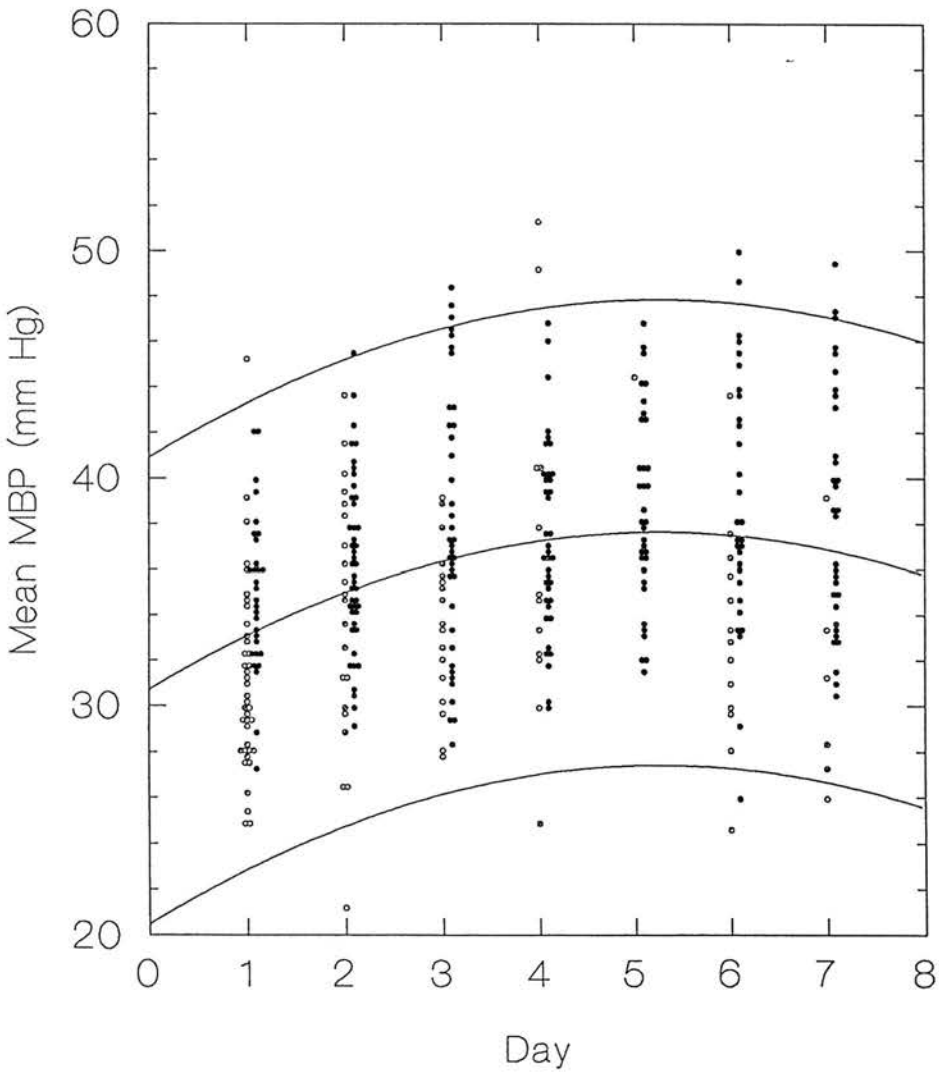


Figure 18 **Mean mean blood pressure over 7 days in infants ≤ 1000g (Group B)**

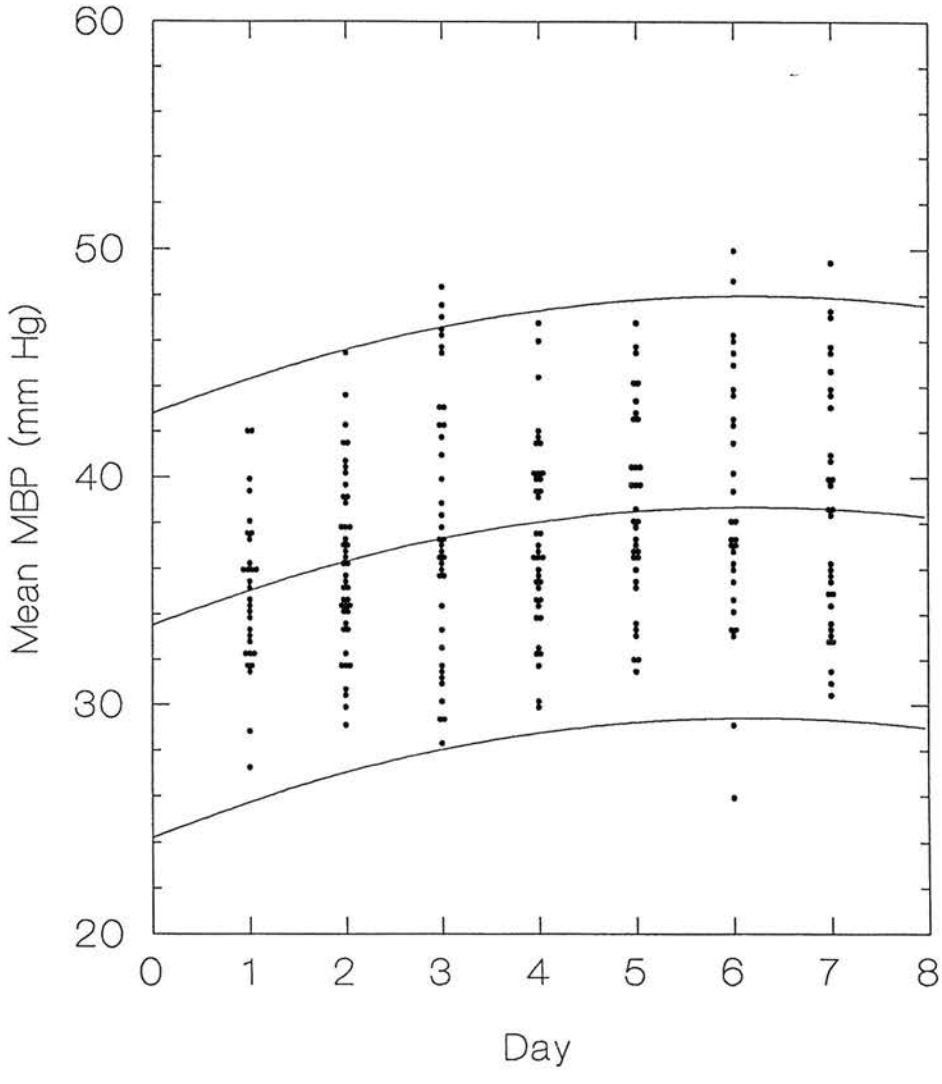


Figure 19 Mean mean blood pressure over 7 days in infants 1001-1500g (Group A)

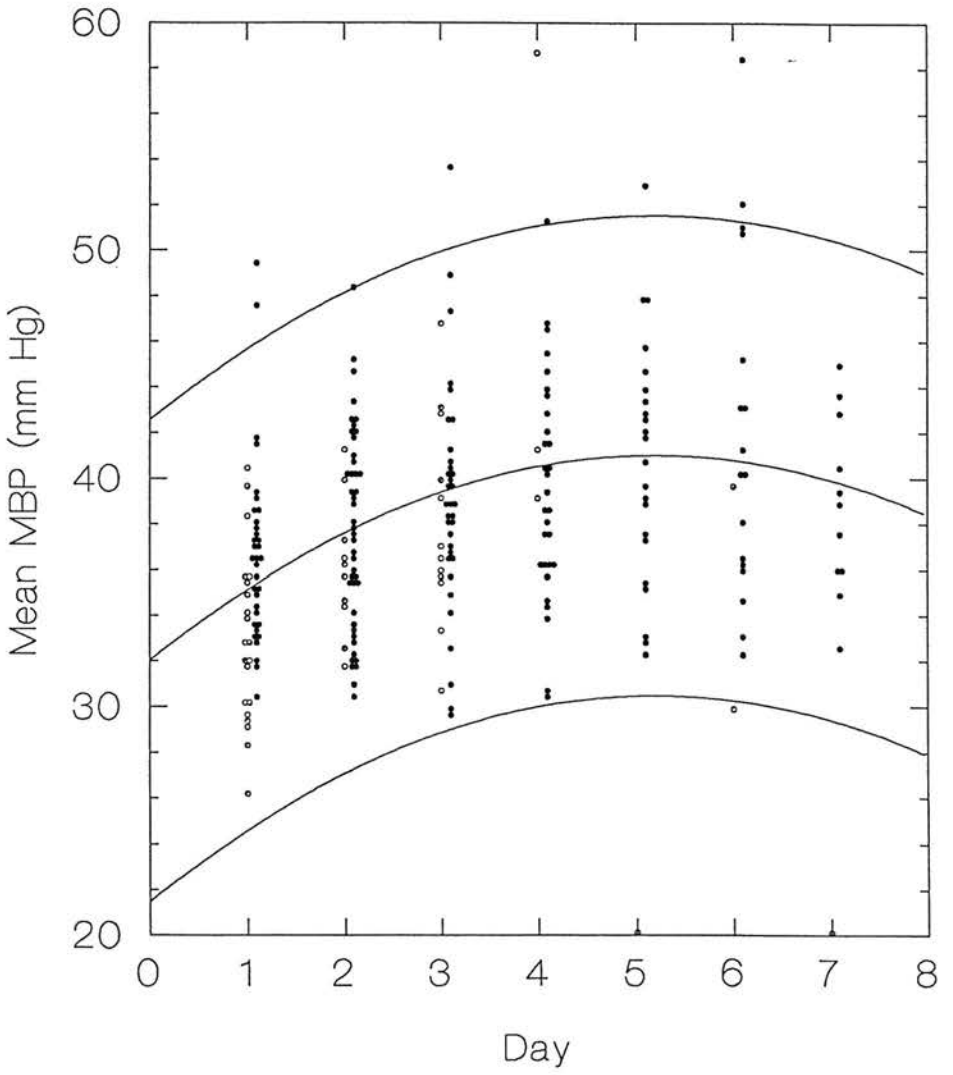
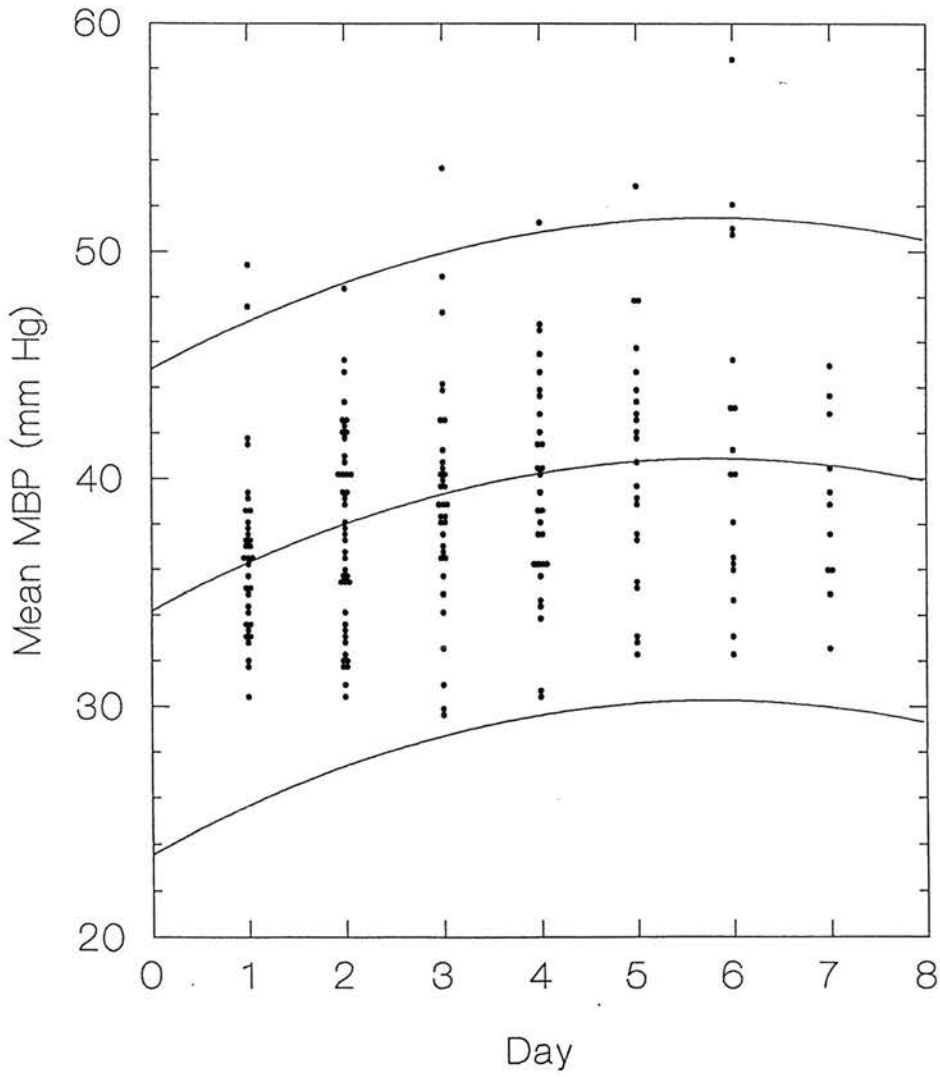


Figure 20 Mean mean blood pressure over 7 days in infants 1001-1500g (Group B)



7.4 Discussion

Intra-arterial blood pressure monitoring is a routine part of the care of many vlbw infants, which despite its disadvantages [Tooley, 1972] [Butt *et al.*, 1985], has the undeniable benefits of continual blood pressure measurement and arterial (sampling) access [Greenough, 1993]. Intra-arterial monitoring is therefore the preferred method of blood pressure monitoring for vlbw infants in the majority of neonatal units [Greenough *et al.*, 1992]. Although 'damping' of the arterial pressure waveform reduces the reliability of sbp and dbp measurements, the mbp continues to be reliable [Weindling, 1989], so reference values for blood pressure in vlbw infants are often quoted for mbp. Some groups have collated vlbw reference data using indirect methods and quoted values for sbp [Greenough and Emery, 1993] [Bucci *et al.*, 1972]. These measurements are only available intermittently at present [Wong *et al.*, 1992], and are not as accurate as intra-arterial measurements [Broberger and Sonesson, 1989] [Diprose *et al.*, 1986] [Savage *et al.*, 1979]. Indirect sbp reference values therefore, are limited in use to those infants in whom arterial access is not possible (only 2% of such infants [Emery and Greenough, 1992]) or in those vlbw infants who do not require arterial monitoring.

7.4.1 Comparison of results with those from other studies.

Invasive bp reference ranges produced by other groups have been based on either small numbers of infants [Powell *et al.*, 1992], or only the first few hours of life [Moscoso *et al.*, 1983] [Kitterman *et al.*, 1969] [Versmold *et al.*, 1981]. This is the first study to derive reference blood pressure values from continuously monitored and collated one second

data, over the first seven days of life in vlbw infants. With the exception of Moscoso, our reference values for mbp (group A and B) are lower than those for all other vlbw studies. Moscoso quoted average mbp in infants <1000g over the first day, that were more than 3 mmHg less than gestation [Moscoso *et al.*, 1983]; far lower than any other group. Watkins studied vlbw infant blood pressure over the first four days using retrospective subjective data (we have found this unreliable - see chapter 5) and obtained results persistently greater than ours (groups A and B) [Watkins *et al.*, 1989]. Adams collated computerised continuous mbp data over the first 24 hours in vlbw infants and obtained values similar to ours [Adams *et al.*, 1983].

Three studies have assessed systolic blood pressure in vlbw infants by indirect methods [Bucci *et al.*, 1972] [Tan, 1988] [Greenough and Emery, 1993]. In all three, the values obtained were higher than those we have shown. Interestingly, although our collection methods and levels differ from Tan [Tan, 1988], he also demonstrated a peak in blood pressure on day 4 (with a subsequent nadir on day 10). Our results have also demonstrated a peak in both weight groups on day 5 with a slight fall on days 6 and 7. Whilst the demonstrated changes in heart rate might account for some of these variations in blood pressure, adjustments in cardiac output and peripheral vascular resistence must also be important.

7.4.2 What is 'normal' blood pressure in preterm infants?

This study has collated the continuous blood pressure recordings of 141 vlbw infants. They were not 'well' vlbw infants; such infants do not require intra-arterial pressure monitoring. The values shown represent reference values for infants who required the level of intensive care,

whereby intra-arterial pressure monitoring was seen as an advantage in patient management. Consequently, there is a dilemma; those vlbw infants who do not require intensive care management ('well') are seen as normal, and reference blood pressure values obtained from this group, might be referred to as the 'normal' desired blood pressure range. However, this group do not have arterial lines from which to evaluate reference values and indirect methods would not give a comparable satisfactory mbp. Even if it were possible to measure mbp accurately in these infants, would this truly represent the infants in whom arterial pressure monitoring is required. What is 'normal' ?

7.4.3 The effects of blood pressure supporting agents

Two sets of reference blood pressure data have been given for mbp; group A and B (tables 14 & 15, figures 17-20). Group A data applied to all infants during all time periods, whereas group B excluded those time periods during which dopamine and/or colloid support (>10ml/kg) were given. It is usual for studies of blood pressure in preterm infants to exclude values when dopamine or colloid were given, although it is unclear whether this is because blood pressure is 'abnormally' low in these infants, or because these interventions might raise blood pressure above 'normal'. 92% of infants <1000g received colloid support during their first week of life (table 13); it would therefore be incongruous to exclude all infants receiving colloid support from our calculations. Both dopamine and colloid support were strongly associated with mbp. Those infants receiving dopamine had on average a mean mbp of 0.87 mm Hg less than other infants and those infants given colloid support had a mean mbp of 1.0 mmHg (per 20ml of colloid) less than average mean mbp.

Dopamine raises blood pressure in many but not all infants [Gill and Weindling, 1993] [Driscoll, 1987], however the ability of colloid to raise blood pressure in preterm infants is poor [Moscoso *et al.*, 1983] [Bignall *et al.*, 1989] [Barr *et al.*, 1977]. As a precise value for 'hypotension' was not known for our infants, the decision to give either colloid or inotropes was not based on a clear definition and was dependent on the views of the attending clinician. Infants receiving either of these therapies therefore, had a mbp that was perceived as either lower than average, or worryingly low, and were given a treatment with a possibly variable response, that was used to treat a blood pressure that if left untreated might not have harmed the infant. We therefore chose to provide information based on the whole population cohort (group A), to enable the reader to appreciate the range of blood pressures that occur in these infants as a group. Reference intra-arterial mbp values for 'well' vlbw infants would, we presume, be higher than those for 'sick' vlbw infants. Our reference mbp values are for those infants who require intra-arterial pressure monitoring. In this group, we have also attempted to identify deviations in blood pressure that might cause increased morbidity and mortality.

7.4.4 Intraventricular haemorrhage and mean blood pressure.

Intraventricular haemorrhage is the largest single cause of possibly preventable morbidity and mortality in preterm infants. The precise pathogenesis remains unclear, although undoubtedly blood pressure is a factor [Szymonowicz *et al.*, 1984] and many of our efforts to stabilise blood pressure are because of a fear of possible IVH. Hypertension, hypotension and blood pressure variability have all been implicated. Hypertension is most popularly associated with IVH: it has been postulated that

hypertensive peaks in blood pressure can burst the fragile germinal matrix vessels [Lou *et al.*, 1979]. Clinical evidence to support this claim is fairly weak and has been based on only small numbers of infants [Milligan, 1980] [Wimberley *et al.*, 1982] [Perry *et al.*, 1990]. However, methods of determining intermittent hypertension in preterm infants are generally poorer than those for hypotension. Hypotension as a cause of IVH has been proposed by a number of studies containing larger numbers of infants [Fujimura *et al.*, 1979] [Szymonowicz *et al.*, 1984] [Watkins *et al.*, 1989]. Goddard-Fiengold demonstrated the effect of ischaemia-reperfusion injury on intracranial vessels, with a consequent increased potential to haemorrhage [Goddard-Feingold *et al.*, 1982]. We have found only weak evidence to support either of these theories. Some authors found blood pressure variability to be the most significant factor associated with IVH [Perlman *et al.*, 1985] [Bada *et al.*, 1990], others were unable to demonstrate this [Miall-Allen *et al.*, 1989]. In this study, mbp variability was a significantly better predictor of IVH, than either low mean, low minimum or high maximum mbp. Infant death was associated with the standard deviation of mbp on day 7 only.

In demonstrating an association between mbp variability and IVH, we have been unable to provide what many neonatologists would desire i.e. a safe lower limit for blood pressure below which morbidity and mortality substantially increase. This may either be due to a deficiency of the methods incorporated in this study, or because blood pressure alone is not a substantial enough factor in the development of IVH and or neonatal death.

Chapter 8

CHAPTER 8

Transcutaneous oxygen levels preceding retinopathy of prematurity

8.1 Introduction

Debate continues about the role of oxygen in the development of retinopathy of prematurity (ROP). The condition was first described 50 years ago [Terry, 1942], prior to the widespread use of oxygen for the treatment of neonatal respiratory distress. The majority of reports during the first 'epidemic' of ROP in the early 1950's, laid blame clearly on excess oxygen as the cause [Kinsey, 1955] [Campbell, 1951] [Lanman and Dancis, 1954] [Patz *et al.*, 1952]. Many of these studies however were, in retrospect, of poor design and the results of doubtful significance to modern neonatal ICU [James and Lanman, 1976]. Subsequent withdrawal of oxygen produced a reduction in ROP but also an appreciable increase in neonatal morbidity and mortality [James and Lanman, 1976]. The care given to neonates in the 1950's and 60's was far removed from current practice in neonatal ICU. Before the association between oxygen and ROP was recognised, preterm infants were routinely prescribed a constant 70% incubator concentration of oxygen for up to two months [Lanman and Dancis, 1954], with no ability to monitor blood gases. Once the association was recognised, it was recommended that infants were given a maximum

of 40% oxygen, for episodes of cyanosis only. Both approaches appear extreme in view of todays technological advances, with accurate transcutaneous/intraarterial oxygen monitoring and on site microsample blood gas analysis.

Interest in retinopathy of prematurity remains high, with leading articles on the subject published in the Lancet [Anon. Lancet, 1991], New England Journal of Medicine [Phelps, 1992], Archives of Disease in Childhood [Fielder and Levene, 1992] and British Medical Journal [Holdström, 1993] within the past 2 years. Despite calls for a further assessment of the role of oxygen in ROP using continuous oxygen monitoring [Anon. Lancet, 1991] [Lucey and Dangman, 1984], only one such study has been performed [Flynn *et al.*, 1992].

Using CPTM, we have accumulated continuous transcutaneous oxygen data on a large number of infants at risk of developing ROP. In conjunction with Dr. Brian Fleck[1], I have assessed the role of oxygen in the development of grade 3 ROP in 12 infants matched with controls.

8.2 Methods

Since October 1990, all infants admitted to our neonatal ICU have had continuous collection of monitored physiological parameters (including tcpO2) by CPTM. Between November 1990 and October 1991 (inclusive), twelve infants developed grade 3 ROP.

Eye examinations were performed by one ophthalmologist (Brian Fleck) using the CRYO-ROP study protocol [CRYO-ROP study, 1990]. Babies

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of <32 weeks gestation and/or birthweight <1251g, were examined 4-6 weeks after birth and thereafter at 2 weekly intervals until the retinae were fully vascularised. If retinopathy of grade 2 or more was detected, weekly examinations were performed. Binocular indirect ophthalmoscopy of the peripheral retina was performed at each examination, using an eyelid speculum and scleral indentation. Examination findings were documented using the international classification of ROP [International ROP classification, 1984]. Cryotherapy was applied if "threshold" disease developed: 5 contiguous or 8 cumulative clock hours of grade 3 retinopathy with "plus" disease [CRYO-ROP study, 1990].

Hewlett Packard neonatal tcpO2 probes are heated to 44 °C, at which temperature they correlate well with arterial oxygen (r = 0.88) [Pollitzer *et al.*, 1980]. Alarm limits for the tcpO2 probe are usually set at 6 and 10kPa, though they may be adjusted if arterial blood gases indicate a calibration error.

We attempted to match each index case with two controls; (a) within 10% of birthweight, (b) of the same gestation. To be eligible, controls had to have survived to more than 40 weeks post conceptional age without developing grade 3 ROP.

For each index case and its two controls we assessed the number of days that tcpO2 data was available on the computer, and analysed the lowest common denominator, to a maximum of 21 days, i.e. if 2 infants had 19 days of data and the third had 21 days, then 19 days would be analysed for all three. A maximum of 21 days after birth was chosen for two reasons, (a) because this represents the period of maximum instability in most preterm infants, and (b) after 21 days large discrepancies appeared in the amount of tcpO2 data that was available, in both cases and controls.

We then assessed the number of minutes each day that the tcpO2 rose above 12 kPa. A tcpO2 of 12kPa was chosen because it has been determined in two studies, as the upper limit of normal arterial oxygen in preterm infants [Orzalesi *et al.*, 1967] [Thiebault *et al.*, 1966]. Any values due to artifact (e.g. probe calibration) were excluded. This is demonstrated in figure 13, where tcpO2 and tcpCO2 trend graphs are shown. The simultaneous rapid rise of oxygen and fall of carbon dioxide at about 20 minutes indicates a probe change; the 5 minutes before and 15 minutes following this change were excluded from analysis, as data during this time period may be unreliable. Values greater than 12 kPa at times when an infant was nursed in air, were identified separately (i.e. iatrogenic added oxygen could not be a factor). Seven indicators of illness severity were also investigated, including the association between steroid therapy (as treatment for bronchopulmonary dysplasia) and ROP; recent publications have both implied and rejected an association [Sobei and Phillips, 1992] [Batton *et al.*, 1992]. Dexamethasone treatment was given to our infants according to the protocol suggested by Avery [Avery *et al.*, 1985].

All analyses were by Wilcoxon signed rank test, except for the analysis of dexamethasone treatment where McNemar's test was used. When two controls were present for a single index case in the Wilcoxon signed rank test, the mean value of the two controls was compared to the index case value.

To determine whether there was any temporal change in the control of tcpO2, we calculated a regression coefficient for each infant, plotting the total time each day (in minutes) that tcpO2 was > 12kPa, against the infants age (in days).

8.3 Results

16 controls were found for the 12 cases; 8 cases had only one control and 4 had two controls. For one index case there were no suitable surviving infants within 10% of birthweight, for 3 index cases there were no surviving infants of the same gestation, and for 4 index cases the matched controls had less than 48 hours of tcpO2 monitoring on computer. Of the 16 controls, 7 were matched for birthweight and 9 for gestation. We compared birthweights in the gestation matched group and found a trend towards a lower birthweight in the index cases; median (iqr) for the index cases was 864g (709 - 949), and controls 980g (834 - 1012). This difference was not statistically significant (Wilcoxon signed rank p=0.066). In the birthweight matched group we found a statistically significant higher gestation in controls; the median (iqr) gestation for the index cases was 26 weeks (25 - 27), and the controls 27 weeks (26 - 29), (Wilcoxon signed rank p = 0.018). The birthweight matched controls were predominantly small for gestation.

A median of 19.5 days (iqr 11.5 - 21 days) of tcpO2 data were analysed in the 12 cases and 16 controls. All 12 cases had grade 3 ROP, 11 of whom received cryotherapy. The median gestational age at which maximum retinopathy severity occurred was 34.5 weeks (range 31 - 40 weeks). Of the 16 controls, 10 did not develop ROP, 3 developed grade 1 and 3 developed grade 2 ROP.

A comparison of seven factors of illness severity showed no significant difference between the cases and controls (table 16), though there was a trend for less severe illness in the controls.

Table 16 Illness severity factors in infants with ROP compared with controls

	Cases n = 12	Controls n = 16	p
	Median (iqr)		
Ventilation (days)	47 (34-58)	36 (17-49)	*p = 0.27
Oxygen requirement (days)	80 (65-135)	76 (49-100)	*p = 0.91
tcpO2 monitoring (days)	51 (37-61)	30 (17-45)	*p = 0.10
Average number of blood gases in first 7 days	6.5 (5.6-7.7)	5.3 (4.6-6.4)	*p = 0.11
Average volume colloid/kg given in first 7 days (mls)	8.7 (6.7 - 12.0)	5.4 (1.5-9.5)	*p = 0.10
Dexamethasone (number of infants)	9	8	†p > 0.2
Age at starting dexamethasone (days)	26 (16 - 37)	35 (24 - 46)	*p = 0.20

* Wilcoxon signed rank

† Chi squared with Yates' correction

The number of minutes each day that the tcpO2 was greater than 12 kPa is summarised in table 17. The data in the table excludes artifact, and contains the following 3 groups of values: (1) Total time spent with tcpO2 > 12kPa (p=0.814) (2) time with tcpO2 >12 kPa in supplemental oxygen (p = 0.583), (3) time spent with tcpO2 > 12kPa in air (p=0.657).

Table 17 Time spent (minutes per day) with tcpO2 greater than 12 kPa.

		Cases		Controls	
	*p =	Median	*iqr*	Median	*iqr*
Total time >12 kPa	0.814	17.7	*12.0 - 35.8*	19.1	*14.8 - 24.4*
Time >12 kPa in air	0.657	0.6	*0 - 5.3*	1.4	*0.1 - 8.7*
Time >12 kPa in added oxygen	0.583	15.6	*10.0 - 32.8*	16.3	*7.1 - 19.1*

*Wilcoxon signed rank test

The amount of data excluded as artifact was not specifically determined in this study. However the amount of tcpO2 data removed as artifact in the '3 observers study' (Chapter 6), was an average of 2.4 hours per day (sd 29 minutes). This is equivalent to the time taken to calibrate the tcpO2 probe, i.e. 20 minutes every 3 - 4 hours (2.0 - 2.7 hours per day). In our experience, inspired oxygen remains unchanged during probe calibration, unless there is a clinical deterioration in the infant. The minute averaging of our data could mask short rises in tcpO2 > 12 kPa, however this should have minimal effect as tcpO2 is usually kept well below 12 kPa.

To assess whether there was any change in the control of transcutaneous oxygen during the analysed period, we calculated the regression coefficient for the number of minutes each day that the tcpO2 was > 12 kPa, against the age (in days) of each infant (i.e. were staff less

strict about tcpO2 control as time went by). The mean regression coefficient for all index cases was + 0.21, reducing to a mean of +0.18, when regression coefficients for index cases and controls were combined. We would not therefore expect a longer study of tcpO2 to reveal any new association of a high paO2 with ROP.

We were concerned that the matching procedure employed during this study had failed to find suitable controls; the birthweight controlled group had significantly higher gestations than the index cases and the gestation matched controls had a trend towards higher birthweight. It was apparent that discrepancies in the matching procedure, might account for the detected differences in tcpO2, as much as the development of ROP. A multiple logistic regression was therefore performed, to adjust for the differences in birthweight and gestation between index cases and controls. The presence or absence of ROP, adjusted for birthweight and gestation, was tested against the seven factors of illness severity and the time spent with a tcpO2 >12 kPa: as before (1) total time > 12kPa (2) time >12 kPa in supplemental oxygen (3) time >12 kPa in air. All factors included in the multiple logistic regression either had no change or became less significant than previously noted in the Wilcoxon rank sum. The one exception was the significance value for the time spent with a tcpO2 >12 kPa in supplemental oxygen; this fell from p=0.58 (Wilcoxon rank sum) to p=0.11 (Multiple logistic regression).

8.4 Discussion

Historically oxygen has been accepted as a causative factor in the development of ROP, but the strength of this association in infants receiving modern neonatal intensive care has not been well assessed. The introduction of computers, has enabled an assessment of tcpO2 and other physiological parameters measured over long periods of time. A randomised controlled trial would be ethically inappropriate, as it would not accurately reflect current practice. We therefore chose a retrospective analysis of computer trend data with matched controls. Flynn and colleagues have recently reported a significant association between tcpO2 and ROP [Flynn *et al.*, 1992]. Their data was almost 10 years old when published, pre-dating the rapid advances in neonatal and ophthalmological care that have occurred in this past decade. Our minute by minute CPTM system has enabled closer inspection of actual tcpO2 values than Flynn's group. An earlier report by Flynn's group on the same cohort of unmatched infants, demonstrated that random allocation to either continuous tcpO2 monitoring or standard care (tcpO2 monitoring when in >40% oxygen), was unable to prevent ROP in infants with birthweight less than 1100g [Bancalari *et al.*, 1987].

The incidence of grade 1 and grade 2 retinopathy in babies of birth weight <1000g is very high, approximately 50-80% [Palmer *et al.*, 1991] [Ng *et al.*, 1988]. Grades 1 and 2 retinopathy do not lead to visual loss and usually resolve without treatment. These grades might therefore be considered a 'normal' transient feature. Grade 3 retinopathy however, is sight threatening and so represents a qualitatively different pathological process, with the growth of extraretinal new vessels [CRYO-ROP study,

1990]. The incidence of grade 3 ROP during the 12 months investigated was 21.4% of infants <1251g birthweight, surviving to more than 28 days of age. This is comparable to the incidence of 18.3%, in infants <1251g (4099 infants) reported in the CRYO-ROP study [CRYO-ROP study, 1990].

Controlled matching is an important, though difficult procedure in infants at the lower extremes of weight and gestation, where survival without ROP is uncommon. We were the first group to attempt controlled matching of extremely low birth weight infants with ROP. This was partially successful, in that control infants were found for all index cases within the initially agreed limits of (a) +/- 10% of birthweight (b) same gestation. However the matching procedure failed, as the surviving infants recruited as controls were often heavier and more mature, creating a statistically significant difference between the cases and controls. The statistical assessment of the paired data, revealed a strong lack of association between grade 3 ROP and a tcpO2 >12 kPa. However, when adjustments were made for poor matching, this significance value was reduced to the limits of acceptability and too close for any firm conclusions to be drawn.

In 1986, a health authority was successfully sued for negligence when ROP developed after administration of excess oxygen. The evidence relied heavily on data from the early studies. In considering the Appeal, Judge Mustill was caused much 'anxiety' by the fact that two expert neonatologists felt that excess oxygen had caused the ROP whilst another two did not [Wilsher vs Essex, 1986]. CPTM has enabled a detailed investigation of this association, unfortunately without providing a definite answer. We now intend to extend the study in the near future, to include a greater number of index infants and controls. This will hopefully produce a more

conclusive result as to the association between oxygen and ROP in modern neonatal ICU.

Chapter 9

CHAPTER 9

Cyclical variation of blood pressure and heart rate

9.1 Introduction

The presentation of physiological vital signs as trends, provides a new perspective on the temporal relation of individually monitored values. Through the use of CPTM in our neonatal unit, we have revealed a patho-physiological cyclical variation of blood pressure that has been previously unreported in intensive care neonates.

The blood pressure 'waves' were first noted in a severely asphyxiated infant who died at 3 days of age (figure 21). They were 25 mmHg in amplitude with a wavelength of 25 minutes, and occurred at 17 hours of age lasting for 23 hours. As in many subsequent cases, there were associated synchronous waves in heart rate and transcutaneous oxygen.

Over the next 15 months we identified a further 18 infants with the same cyclical disturbance of blood pressure.

Blood pressure instability is perceived as detrimental to intensive care neonates. The maintenance of blood pressure within a 'normal' range, is important to optimise the perfusion of vital organs, reduce the risk of hypoxic ischaemic damage and to decrease the incidence of intraventricular haemorrhage [Miall-Allen *et al.*, 1987]. The physiological adjustment of blood pressure is complex, involving neural, cardiovascular and endocrine components. The opposing actions of the sympathetic and parasympathetic

nervous systems are the dominant blood pressure controls. Sympathetic activity from spinal nerve centres increases heart rate, ventricular contractility and peripheral vascular resistance. It is far more powerful in altering blood pressure than parasympathetic control mediated by carotid baroreceptors [Gebber, 1977]. In normal physiological states, respiration may minimally affect blood pressure, but more significant alterations of blood pressure can be caused by certain pathological states, including cerebral asphyxia, hypovolaemia and increased cerebrospinal fluid pressure.

The development of blood pressure control mechanisms in the human fetus and neonate remains poorly understood, as ethical and moral issues restrict invasive cardiovascular research and so such data is primarily derived from animal models. Blood pressure waves might therefore represent a window of opportunity to non invasively investigate these control mechanisms, in infants where these mechanisms were exposed or damaged, possibly because of their illness or prematurity. Indeed the prematurity of some of the infants involved might help to reveal the fetal development of cardiovascular control.

The characteristics of the blood pressure waves were investigated in 19 infants. Details from each of these infants were compared to two controls, matched for weight and gestation. This chapter discusses these investigations, the other methods we have used involving CPTM to determine the cause of blood pressure waves and the possible significance of blood pressure waves to cardiovascular control and to the well being of the infant.

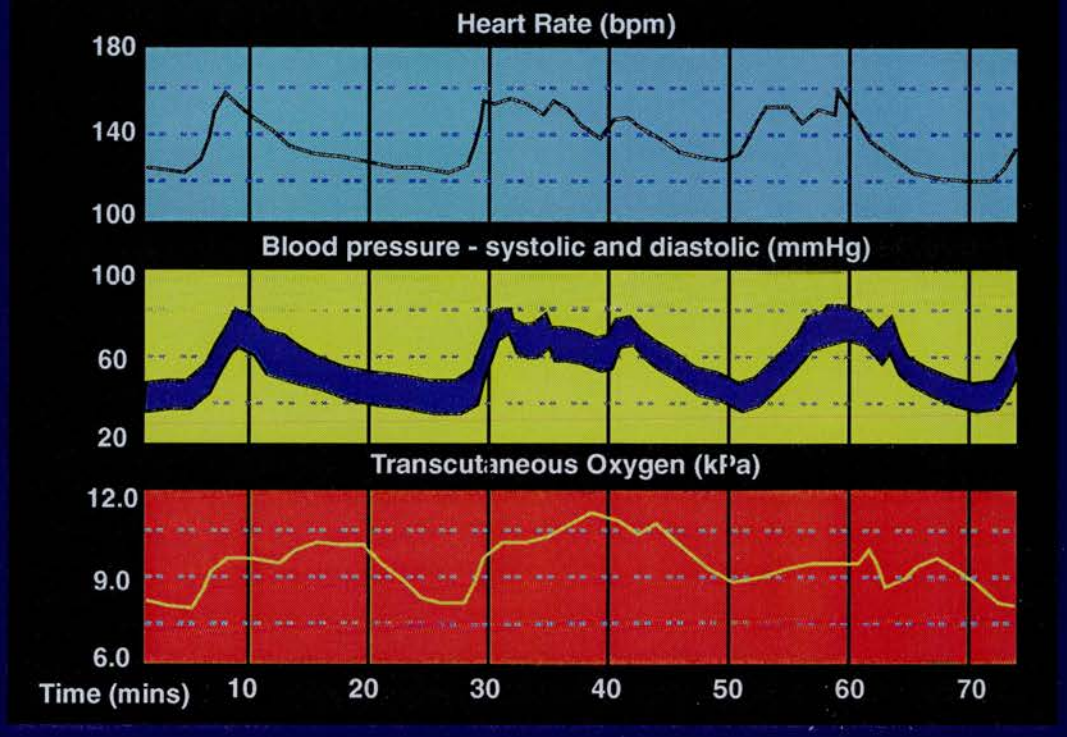


Figure 21 Cyclical variation of blood pressure, heart rate and tcpO2

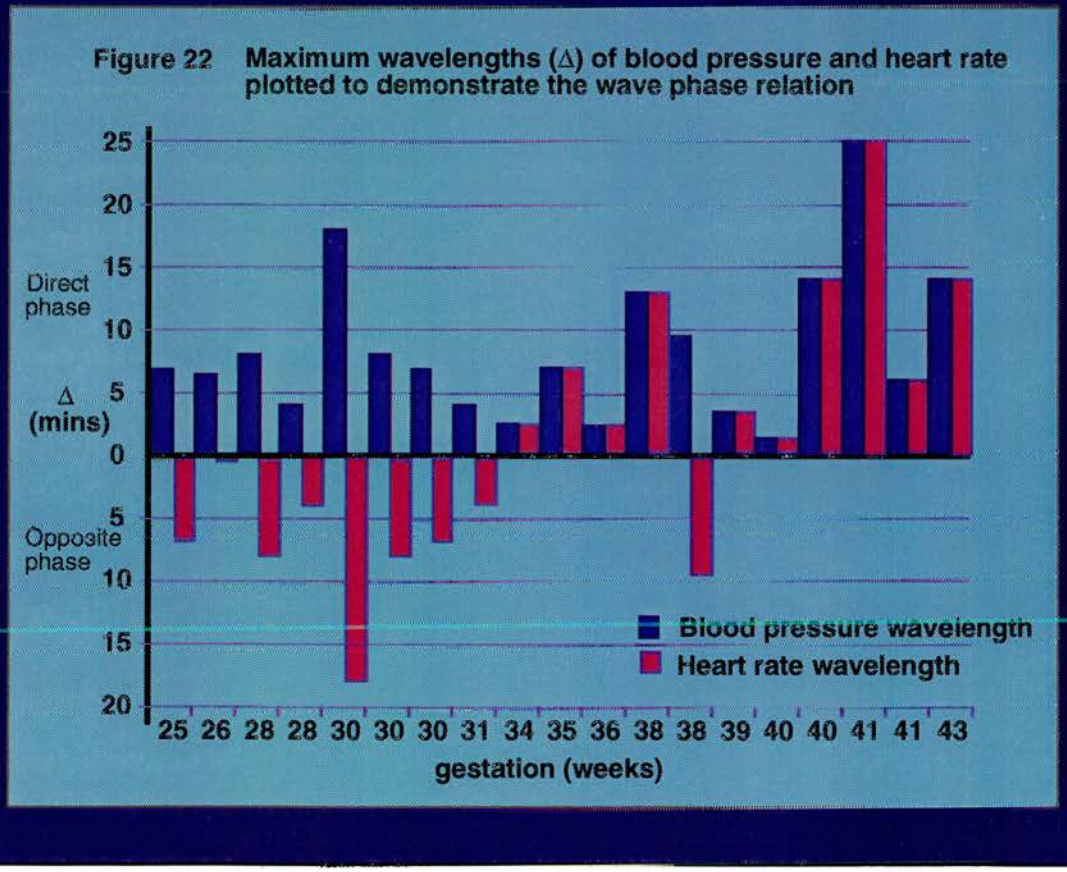


Figure 22 Maximum wavelengths (Δ) of blood pressure and heart rate plotted to demonstrate the wave phase relation

9.2 Description of blood pressure waves in 19 infants.

The 19 infants were of a median gestation of 35 weeks (iqr 30-40 weeks) and a median birthweight of 1900g (iqr 1186-2930g). A total of 37 wave episodes were seen in the 19 infants. 13 infants had 1 episode, 3 infants had 2 episodes, 1 infant had 4 episodes and 2 infants had 7 episodes. The wave episodes began at a median age of 76 hours (iqr 35-226) and lasted for a median of 5 hours (iqr 2-8).

Each episode was analysed over at least 10 cycles to obtain a median value for the amplitude and wavelength of systolic and diastolic blood pressures (values quoted later in the text during this description, are a mean of these two values), heart rate and transcutaneous oxygen. Details of wave amplitude and wavelength are contained in table 18. The phase relation of the blood pressure and heart rate waves was also noted.

Table 18 Comparison of blood pressure wave amplitude and wavelength in 19 infants.

	n=	Amplitude		Wavelength (minutes)	
		median (iqr)			
Blood pressure (mmHg)	37	10	(7 - 12.5)	7	(4 - 10)
Heart rate (bpm)	34	8	(5 - 14)	7	(4 - 10)
Transcutaneous oxygen (kPa)	22	1.0	(0 - 1.8)	7	(4 - 10)

Heart rate waves were an associated finding in 92% of blood pressure wave episodes and transcutaneous oxygen waves associated in 60% of episodes.

The phase relation of the blood pressure and heart rate waves is shown in figure 22, where the maximum blood pressure and heart rate wavelengths for each of the 19 infants are used to demonstrate the relation. Heart rate waves occurred only either directly in phase or directly in opposite phase to blood pressure waves. In figure 21, the blood pressure and heart rate waves are directly in phase and therefore peaks correspond to peaks and troughs to troughs, whereas if they were in opposite phase blood pressure peaks would correspond to heart rate troughs and vice versa. In figure 22, heart rate wavelength is plotted above the midline if it occurred in phase with the blood pressure waves or below the midline if in opposite phase. The figure demonstrates that infants less than 32 weeks gestation had an inverse phase relation between heart rate and blood pressure waves, i.e. when blood pressure increased the heart rate decreased and vice versa. Neonates greater than 34 weeks gestation had a direct phase relation between heart rate and blood pressure waves, i.e. heart rate increased as blood pressure increased. Only one infant of 38 weeks gestation did not correspond to this precept, this infant had a congenital cardiac abnormality and subsequently died.

The wavelength, amplitude and time of onset of the waves were compared to the gestation, birthweight and apgar scores of the 19 infants using the Pearson correlation co-efficient. None of the comparisons had a correlation of $\geq +/- 0.5$.

9.3 Comparison of 'wave' infants to matched controls

9.3.1 Wave comparison methods

To identify aetiological factors that might predispose infants to exhibit blood pressure waves, we matched these infants to controls. Each of the 19 index cases was matched with two controls; the first within 10% of birthweight and the second of the same gestation. Forty maternal and neonatal details were then compared in the index cases and their two controls (table 19). Demographic details were analysed only once (factor n=19). Details under the heading 'wave episodes' (factor n=37) were analysed for each of the wave episodes (or in controls at the time from birth corresponding to the index wave episode). Exceptions to this were IVH, convulsions and postnatal hypoxia, which once present continued to be counted for subsequent wave episodes. Statistical analysis was by a two tailed paired t test or McNemar's test.

9.3.2 Wave comparison results

A paired t test comparing index cases and their controls showed no significant differences in either birthweight (Control 1 $p=0.913$, Control 2 $p=0.680$) or gestation (Control 1 $p=0.713$, Control 2 $p=0.845$).

12 of the 40 details examined were statistically significant at the $p<0.05$ level in both controls (table 19). Index cases had lower Apgar scores at 1 and 5 minutes, and a ventilatory requirement at the time of the wave episodes. They also had a greater incidence of IVH (of any grade), postnatal asphyxia[1], convulsions and a significantly higher requirement for blood volume support both at the time of the waves and in the 48 hours before

[1]Postnatal asphyxia defined as; blood gas arterial oxygen of < 5 kPa, with a base deficit of more than 10 for more than 10 minutes.

and 6 hours after the waves.

Four medications were also more commonly used in the treatment of index cases; benzylpenicillin, morphine, phenobarbitone and dopamine. Four other factors were significant compared with just one control; increased birth asphyxia[1], total number of days of intubation, and a lower haemoglobin and calcium at the time of the waves.

[1]Birth Asphyxia defined as; initial pH < 7.10, 5 min apgar <5 or signs of hypoxic ischaemic encephalopathy

Table 19 Neonatal variables associated with blood pressure waves

factor (n=19)	*	C	C1	C2	factor (n=37)	*	C	C1	C2
Infant					**wave episodes**				
Sex (m:f)	x^2	11:8	8:11	11:8	Ventilation	x^2	37	1†	6†
Gestation	t	*34.4*	*33.7*	*34.0*	IVH (any grade)	x^2	10	2†	2†
Birthweight (g)	t	*2146*	*2110*	*2291*	$Hypoxia_{postnatal}$	x^2	11	0†	1†
Apgar 1	t	*3.4*	*6.0†*	*5.6†*	Convulsions	x^2	10	1†	0†
Apgar 5	t	*5.7*	*8.1†*	*7.6†*	**Drugs**				
Birth Asphyxia	x^2	8	1†	4	Gentamicin	x^2	19	10	7
Intubation (days)	t	*11.7*	*2.1†*	*3.5*	Benzylpenicillin	x^2	25	11†	11†
Neonatal Death	x^2	6	1	1	Morphine	x^2	20	2†	3†
Race (non cauc)	x^2	1	1	1	Pancuronium	x^2	11	0	3
Maternal					Tolazoline	x^2	3	0	0
Age	t	*27.4*	*26.5*	*27.6*	Phenobarbitone	x^2	11	1†	0†
PET	x^2	2	2	3	Dopamine	x^2	11	0†	0†
Diabetes	x^2	1	0	0	Dobutamine	x^2	4	0	0
IUGR	x^2	5	5	1	Curosurf	x^2	7	1	3
Multiple birth	x^2	2	1	1	Volume support	x^2	10	1†	1†
APH	x^2	5	4	4	Support -48/+6	x^2	29	3†	4†
Induced birth	x^2	2	5	2	**Haem/Biochem**				
Urgent LSCS	x^2	12	5	5	Haemoglobin	t	*14.7*	*16.0*	*16.4†*
Drugs at resus	x^2	6	1	2	Sodium	t	*140.1*	*139.2*	*137.3*
					Potassium	t	*4.1*	*4.6*	*4.4*
					Calcium	t	*2.0*	*2.0*	*2.3†*
					Creatinine	t	*135.7*	*88.4*	*91.6*

Figures in *italics* represent the mean of all values for infants in that category, other numbers are the total from (n)
* statistical test used for analysis comparing C with C1 and C with C2: t = paired t test (data presented as mean of all cases) and x^2 = McNemar's chi squared test (data presented as number of cases).
† $p < 0.05$

9.4 Blood pressure waves induced by stress

Seven infants have demonstrated transitory blood pressure waves which have been induced by stress (figure 23). Six infants had only one episode, whilst the seventh had 4 episodes (only the first was analysed). Seven stress induced blood pressure wave episodes were analysed, one from each of the seven infants (table 20). All these episodes were associated with physiologically stressful events: 5 episodes were induced by bradycardia, 3 resulted from a blocked endotracheal tube and 2 occurred during transient hypoxic episodes. None of the episodes were associated with similar waves in heart rate or transcutaneous oxygen.

Table 20 Details from seven infants demonstrating stress induced waves.

	Median	Interquartile range
Birthweight (g)	1302	1194 - 2647
Gestation (weeks)	29	27.5 - 35.5
Amplitude (mmHg)	5	5 - 10
Wavelength (minutes)	1.0	0.6 - 7.8
Episode duration (minutes)	8	6.5 - 32.5
Age of occurrence (hours)	117	73 - 342

9.5 Further investigation of blood pressure waves

Real time computer trends have enabled us to further investigate the origin of blood pressure waves and their effects on the cerebral circulation. Although blood pressure waves tend to occur in infants with more severe neonatal illness, the inability to accurately predict the timing of onset of the blood pressure waves, has limited the opportunities for investigation. Neonatal unit staff have taken an active interest in blood pressure waves and have kindly informed me when they have occurred in a monitored infant.

9.5.1 Serum noradrenaline and blood pressure waves

Blood pressure is controlled in part by vasoactive catecholamines e.g. noradrenaline, adrenaline and dopamine. To determine whether catecholamines were associated with the blood pressure waves, two blood samples were taken corresponding to the peak and trough of a single blood pressure wave noted in the real time trend data of 5 infants. In two infants we were able to collect two sets of consecutive peak and trough samples. Samples were always taken from indwelling arterial catheters. One ml blood samples in EDTA tubes were placed into ice and separated within 12 hours. Catecholamines were measured using High Performance Liquid Chromatography with dual electrode coulochem detection[1].

The results of the consecutive peak and trough samples are shown in table 21. The five infants had a median birthweight of 2620g (iqr 956 - 3001) and median gestation 33 weeks (iqr 27 - 38). The median wavelength

[1]Samples analysed by Rhona Smith, Child Life and Health Laboratories, University of Edinburgh.

of 14.3 minutes (iqr 7.3 - 16.2) and amplitude 13.2 mmHg (iqr 8.3 - 19.4) were larger than the values quoted for the initial 19 infants assessed. Mean blood pressure recorded by CPTM at the time of sampling was compared to plasma noradrenaline and dopamine levels using the Wilcoxon signed rank test. Mean blood pressure and noradrenaline were significantly associated (p=0.021), whereas dopamine was not (p=0.487). Adrenaline was mainly undetectable.

Table 21 Relationship of plasma catecholamines to blood pressure waves.

Infant	Wave Δ (mins)	Wave amp (mmHg)	age (hours)	peak or trough	mbp mmHg	NA pmol/ml	DA pmol/ml	Adr pmol/ml
1	16.2	31.4	31	p	69	118.0	279.6	<0.1
				t	*42*	*71.2*	*146.3*	*<0.1*
1	16.2	31.4	31	p	70	43.12	82.6	<0.1
				t	*38*	*21.52*	*50.6*	*<0.1*
2	8.9	8.3	93	p	49	10.5	<0.16	<0.1
				t	*41*	*3.87*	*0.48*	*<0.1*
2	8.9	8.3	93	p	49	2.71	<0.16	<0.1
				t	*40*	*1.82*	*<0.16*	*<0.1*
3	14.3	8.3	60	p	42	3.97	257	<0.1
				t	*36*	*2.42*	*269*	*<0.1*
4	16.2	13.2	192	p	43	6.3	1.4	<0.1
				t	*34*	*5.7*	*0.7*	*<0.1*
5	2.9	15.4	40	p	62	33.5	19.0	1.0
				t	*48*	*30.0*	*21.1*	*0.8*

Infants 1 and 5 both had high detected dopamine levels due to dopamine infusions at the time of sampling. It is unclear whether the associated increased noradrenaline levels result from the breakdown of dopamine, or a dopamine induced release of noradrenaline from neuroterminals; the latter is more probable [Stopfkuchen *et al.*, 1991]. Neither is it clear whether the release and effect of noradrenaline would be diminished, in the face of raised plasma levels induced by dopamine. Despite the dopamine infusions there continued to be a strong association between serum noradrenaline and mean blood pressure during wave peak and troughs, that did not exist with serum dopamine levels. Of the 37 wave episodes initially reported only 11 episodes occurred during dopamine infusions.

Both infants with 2 sets of peak and trough samples showed a reduction of noradrenaline over time in the 4 assays. The samples were taken at approximately 8 and 4 minute intervals in infants 1 and 2 respectively. These time intervals were in excess of the two to three minute half life of plasma noradrenaline [Esler *et al.*, 1984]. It appears therefore that blood pressure waves may either be induced by a large initial surge in noradrenaline and the half life quoted is incorrect for neonates, or that there are repeated surges of noradrenaline, the degree of which is not linearly related to the mean blood pressure achieved.

9.5.2 Cranial doppler ultrasound and blood pressure waves

Using real time trend monitoring we have correlated mean blood pressure to doppler ultrasound recordings of the Internal Carotid artery blood flow velocity during wave episodes. Again our inability to predict the waves and technical errors with the doppler recording equipment have limited the number of cases we have been able to collect. The possibility of this association however is important to establish, as the immature or hypoxic neonatal brain often loses cerebral autoregulation and is poorly able to protect itself against surges in systemic blood pressure [Cowan *et al.*, 1989]. Hypertensive blood pressure waves therefore, if transmitted to the cerebral circulation, may have serious detrimental effects on the brain [Perlman *et al.*, 1985] [Milligan, 1980].

The doppler recordings were made using a 5 MHz probe on a Toshiba colour doppler ultrasound machine (Sonolayer SSH 140A). The optimal internal carotid artery doppler signal was located using both waveform shape and acoustic volume. The probe was held in place by a supported hand using colour doppler guidance. Recordings were made for approximately eight to ten minutes onto standard videotape. The ultrasonographer (myself) was unable to see the computer trend screen at the time of the recording. Resistance indices were calculated as the average of 8 consecutive waveforms sampled every 20 seconds. These values were then compared to the synchronised mean blood pressure values on CPTM. Figure 24 shows the relationship between mean blood pressure and resistance index[1]. Changes in cerebral blood flow velocities correlate well with cerebral blood flow [Hanson *et al.*, 1983], and a change in resistance

[1](systolic cerebral blood flow velocity - diastolic cerebral blood flow velocity + systolic cerebral blood flow velocity)

index indicates an alteration of blood flow impedance [Raju, 1991]. Alteration of heart rate and blood pressure can also produce a change in resistance index [Thompson, 1987] [Raju and Sim, 1989] and so it may be that blood pressure waves are directly responsible for the changes and are independent of the vasoparalysis caused by asphyxia or prematurity. Each of the five cases were recorded during a wave episode, and although numbers are very small a definite trend can be seen.

Figure 23 Stress induced blood pressure waves

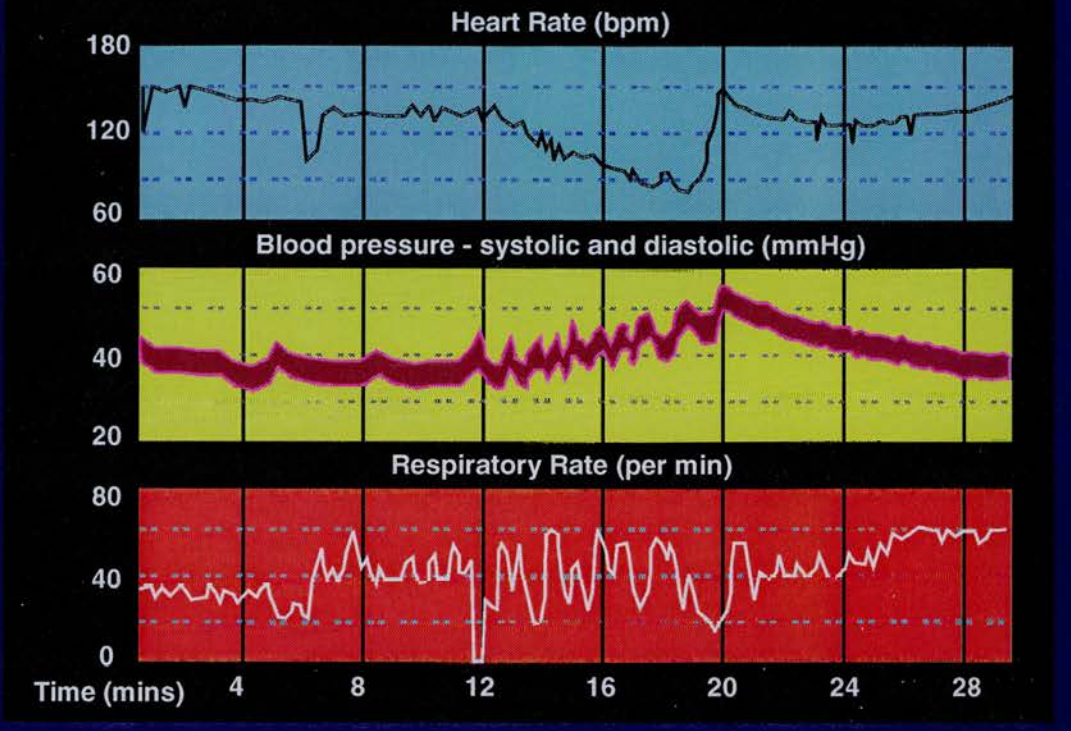
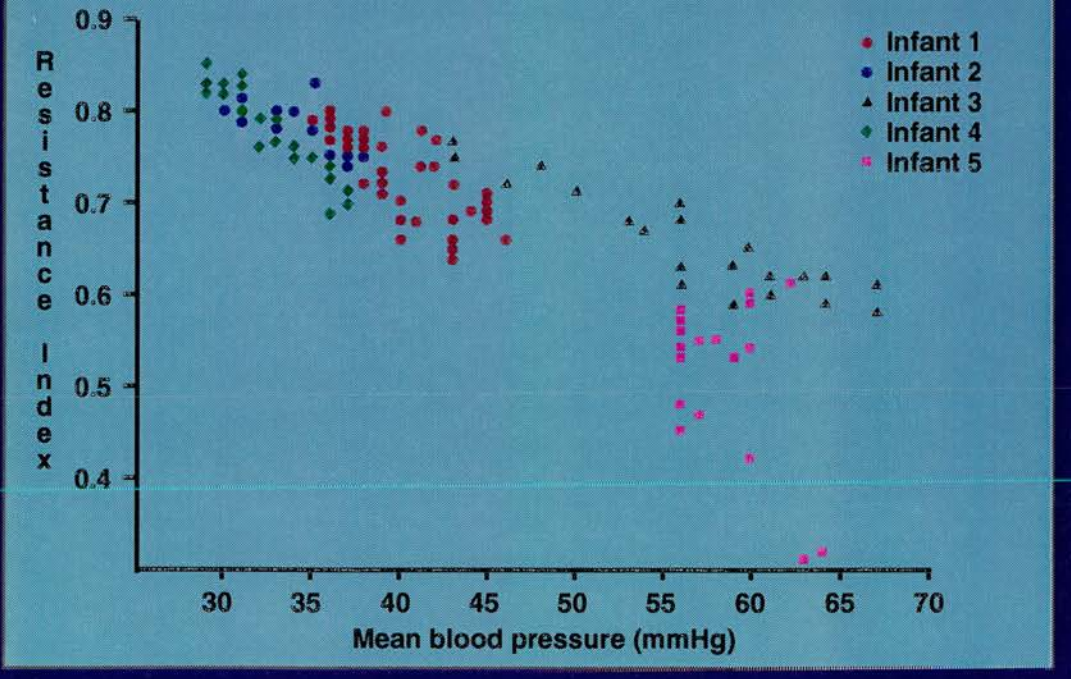


Figure 24 Relationship between mean blood pressure and internal carotid artery resistance index during five wave episodes



9.6 Discussion

Blood pressure waves are are widely described; indeed one of the first continuous physiological monitoring systems to be developed, was a smoke covered drum that in 1847 measured respiratory induced blood pressure waves in horses [Ludwig, 1847]. The blood pressure waves we describe however, are the first description in neonates and are predominantly of a different order from those blood pressure waves previously described.

9.6.1 Classification of blood pressure waves

First order blood pressure waves are due to the ejection of stroke volume with each heart beat. Second order blood pressure waves are caused by the changes in venous return with each respiratory cycle. Third order waves include both (1) Traube-Herring waves due to autonomic variation during the respiratory cycle and occur at a rate equal to the respiratory cycle; approximately 6 Hz (though not mechanically induced), and (2) Mayer waves which are caused by a rhythmic variation of the vasomotor centre and occur at a slower frequency than respiration, as slow as one per minute [Polosa, 1984]. Other types of blood pressure waves have been described both in vivo and induced experimentally. Classification of these waves is poor and there is no consistent description for blood pressure waves with a wavelength greater than one per minute [Miyakawa *et al.*, 1984].

9.6.2 Physiological control of blood pressure

Blood pressure is modulated by several major physiological controls, including the autonomic nervous system, the endocrine system and the cardiovascular system. These combine to produce a blood pressure that varies little from its physiological norm, providing a stability of perfusion essential for the function of major organs. Blood pressure deviates from this norm when this balance is pathologically interrupted, such that other contributing controls cannot compensate. The blood pressure waves we describe fluctuate around the mean blood pressure of the infant. I have found only one previous report of blood pressure waves similar to those we describe occurring in humans. In that report an adult intensive care patient had blood pressure waves with a 30 minute wavelength that lasted for 18 hours; no cause was found [Carroll, 1990].

The embryological development of human gross cardiovascular anatomy is well described, from the initial pumping of a single chambered heart at 23 days gestation to the final transition from the fetal to newborn circulation at birth. The embryological development of the control of the cardiovascular system remains poorly understood [Versmold, 1991]. Preterm neonates are now being cared for at almost half their intended gestation. It is possibly unreasonable to assume that cardiovascular control is complete at these early gestations, when the fine control of all other major organs is not. Despite this we often assume adult blood pressure control mechanisms when managing a 4 month premature infant.

9.7 Cyclical Nature of Blood Pressure Waves

The synchronous relationship between the blood pressure and heart rate wavelengths (table 18), would indicate that these waves share the same origin. Numerous postulates could account for this exact chronicity. The cardiovascular system is controlled by a number of neural and endocrine sites, many of which have an intrinsic rhythm which underlies their control. These rhythms may be exaggerated or have their frequency altered by hypoxia [Kocsis *et al.*, 1989]. A sinusoidal pattern of heart rate in the fetus has been demonstrated on cardiotocograph [Baskett and Koh, 1974] in association with hypoxia and severe anaemia, with a subsequent poor prognosis. A similar sinusoidal pattern in heart rate was reported post-natally in eight neonates suffering from perinatal or postnatal asphyxia [McC Reid *et al.*, 1979], only two of the eight survived, but with severe handicap, it is not stated whether blood pressure measurements were taken and no conclusions were made as to the origin of the heart rate waves. In comparison with matched controls, our infants with blood pressure waves were relatively hypoxic, demonstrating significantly lower apgar scores at 1 and 5 minutes and an increased incidence of postnatal hypoxia. One group of controls also showed a significantly lower incidence of birth asphyxia.

9.7.1 Autonomic disturbances

Baroreceptors provide an important blood pressure control. Oscillations in blood pressure very similar to those we describe, have been induced by sectioning the afferent nerve supply from arterial and cardiopulmonary baroreceptors in non anaesthetised dogs [Persson *et al.*, 1990]. The blood pressure waves produced in the dogs had a wavelength of

approximately 20 minutes and an amplitude up to 80 mmHg. Hypoxia of these same pathways in the human fetus might reduce their feedback function revealing an underlying intrinsic rhythm [Waldmann *et al.*, 1979]. Removal of 20% of the blood volume from a pig foetus induces 4 per minute waves in blood pressure and heart rate [MacDonald, 1983]. Severe antepartum haemorrhage in the human neonate has also produced the cardiotocograph cyclical heart rate rhythm described above. A requirement for blood volume support during and around the time of the wave episodes was significantly greater in neonates with blood pressure waves. Index cases also demonstrated a lower haemoglobin than controls during wave episodes (significant only for group C2).

9.7.2 Endocrine disturbances

Endocrine feedback often shows cyclical variability e.g. glucagon, insulin and thyrotrophin release [Lang *et al.*, 1982]. Arginine vasopressin has been demonstrated to induce blood pressure waves [Murata *et al.*, 1985]. Longitudinal data on neonatal endocrine function is scanty because of the difficulties (technical and ethical), of repetitive blood sampling in neonates. New micro assays enable a better appreciation of the temporal relationships of humoral control of blood pressure in neonates. Adrenaline, noradrenaline and dopamine are vasoactive catecholamines that may be detected in the circulation. Using microassays we were able to measure these substances in five infants demonstrating blood pressure waves. The 3 assays although performed on a small number of infants and complicated by dopamine infusions in two cases, demonstrated a strong correlation between mean blood pressure during the waves and serum noradrenaline levels (table 21). Blood pressure waves might be mediated by surges in

noradrenaline. It is probably less likely that blood pressure waves induce surges in noradrenaline. Noradrenaline is released as a stress hormone and we have shown a small number of infants in whom blood pressure waves were induced by a stressful event. Infants demonstrating stress induced blood pressure waves were of lower birthweight and gestation, and had waves that were both smaller in amplitude and wavelength than the infants originally described. Heart rate is predominantly effected by catecholamines from the adrenal medulla in mid gestation, in later gestations neural components are more predominant [Hanson, 1993]. Stress induced blood pressure waves therefore, may be physiologically different and arise due to a different mechanism. A larger study would be necessary before firm conclusions could be drawn regarding the role of noradrenaline in blood pressure waves.

9.7.3 CSF pressure waves

Cerebrospinal fluid (CSF) pressure waves are well described [Lundberg, 1960]. Of the three types of pressure wave, 'a' and 'b' waves, with a wavelength of 5-20 minutes and 2-4 minutes respectively, are pathological and episodic, resulting from a temporary reduction in intra-cerebral compliance. 'c' waves are physiological and are thought to occur secondary to the well described 6 per minute Traub Herring blood pressure waves ('second' order blood pressure waves). Short term changes in intracranial pressure noted during CSF pressure 'a' waves are sometimes conveyed to the systemic blood pressure [Lundberg, 1960], others have been unable to confirm this [Hayashi *et al,*. 1985]. CSF 'a' waves have been described in asphyxiated neonates [Raju *et al.*, 1981]. These waves were also

episodic, in one case occurring on 5 of the 10 days of life and lasting for periods of up to 7 hours with an amplitude of up to 60 mmHg. The CSF pressure waves in these infants occurred both spontaneously and in response to external stimuli (e.g. suction). No reference is made to continuous blood pressure recordings in these neonates, but if the CSF pressure waves were conveyed to the systemic blood pressure, waves such as those we have described would be produced. The hypertensive CSF pressure waves act by inducing the central nervous system ischaemic reflex oscillation [Guyton and Satterfield, 1952]. Although monitoring of intracranial pressure by subarachnoid catheters has been performed in some neonatal units, the lack of benefits to the care of the infant resulting from this form of monitoring does not justify its use in the investigation of blood pressure waves. Non-invasive intracranial pressure monitoring devices could be used if infants could be more easily identified and if the equipment could be attached, without the disturbance to the infant eradicating the waves. Intraventricular haemorrhage was significantly increased in infants demonstrating blood pressure waves. Even relatively small IVH's can cause fluctuations in intracranial pressure due to obstruction to the flow of CSF caused by the blood clot [Bada *et al.*, 1982]. Whether IVH's can induce CSF pressure waves is unknown.

9.7.4 Seizure activity

Cerebral epileptic activity is often associated with variability of blood pressure and heart rate [Lou and Friis-Hanson, 1979]. Infants with blood pressure waves had a significantly higher incidence of convulsions and the use of phenobarbitone. I can find no reports of epilepsy in neonates leading to a cyclical variation of blood pressure. 24 hour EEG in one infant during a

prolonged episode of blood pressure waves, revealed no seizure activity.

Sleep patterns might explain the periodic nature of blood pressure waves, as neonates spend most of each 24 hours asleep, a large proportion of which is REM sleep. However, it would seem unlikely that only single episodes of the blood pressure waves would be manifest if they were sleep induced.

9.7.5 Biochemical / Medication induced changes

Changes in serum biochemistry and medication can clearly alter cardiovascular responsiveness [Guyton, 1991], and might therefore have induced temporary alteration in cardiovascular function producing a release of an intrinsic rhythm. Benzylpenicillin is a commonly used drug in intensive care neonates and its strong association is of doubtful significance. Morphine is also commonly used and has effects on both the central nervous system and blood pressure. Morphine produces hypotension and therefore might induce blood pressure waves by effects on either the carotid baroreceptors or the central nervous system. In our series, morphine was only being infused in 54% of the wave episodes. Dopamine as a vasoactive substance was also strongly associated with blood pressure waves, though it was being infused in only 30% of the wave episodes.

9.7.6 Peripheral vasoconstriction

The cyclical variation of transcutaneous oxygen that is associated with blood pressure and heart rate waves is most likely a secondary phenomena. It may occur as a result of peripheral vasoconstriction and dilatation caused by the same autonomic process that induces blood pressure waves, or may represent an increase blood flow to the skin caused

by the hypertensive blood pressure waves. Thermoregulatory vasomotor cycling may produce fluctuations in blood volume and so could possibly cause blood pressure waves, though there is little evidence to support this [Kitney, 1975].

9.7.7 Electromechanical artifact

Electromechanical artifact might produce a regular variation in blood pressure. However, the blood pressure waves described have occurred over a 15 month period, on a variety of computers, monitors and infusion pumps and we can determine no artifact that could cause such regular variation, especially one that can be altered just by lightly touching the baby.

9.8 Phase Relation of Blood Pressure Waves

The phase relation of blood pressure and heart rate waves undergoes a transition at 32-34 weeks. Figure 22 demonstrates both the maximum wavelength for blood pressure and heart rate in each of the 19 infants and uses this to illustrate the phase relation that exists. Mammalian models show a consistent asynchrony in the development of the autonomic control of the cardiovascular system. The sympathetic system is the principle control of the cardiovascular system by 0.5 term gestation and keeps control until near term. At this stage the parasympathetic nervous system, until now relatively dormant, markedly increases its contribution. The change in phase relation that we have demonstrated, may herald a distinct period of change in the control mechanisms of blood pressure in

the human neonate. Frequent bradycardias in preterm infants may be due to a parasympathetic system attempting to increase its share of control before it is physiologically mature [Lagercrantz *et al.*, 1990], especially as bradycardia of the preterm may be eradicated by atropine [Kattwinkel *et al.*, 1976]. Both respiratory sinus arrhthymia [Thompson *et al.*, 1993] and heart rate variability [Siassi *et al.*, 1979] mediated by the vagal nerve, have significant alterations in activity at 32-34 weeks gestation.

As baroreceptors mature, their sensitivity to surges in blood pressure decreases with a correspondingly poorer parasympathetic output [Hanson, 1993]. Further work has demonstrated that surgical vagotomy is associated with a simultaneous increase in blood pressure and heart rate, whereas a (possibly incomplete) medical baroreceptor vagal block, caused by atropine, produces an increase in blood pressure with a decrease heart rate [Murata *et al.*, 1985]. Thus, whereas a rise in blood pressure at an early gestation may be associated with a fall in heart rate, at later gestations loss of baroreceptor sensitivity and a more predominant sympathetic activity might even reverse the bradycardia.

The sympathetic and parasympathetic nervous systems work in unison. An increase in sympathetic activity increases both cardiac contractility and heart rate, simultaneous parasympathetic activity reduces heart rate, thus allowing an increase blood pressure without a profound tachycardia. This relationship however may be disrupted. Mild hypoxia affects the parasympathetic system before the sympathetic, causing a slightly delayed, but greater parasympathetic impulse of a longer duration. Consequently an increase in blood pressure due to sympathetic activity is accompanied by a fall in heart rate [Koizumi *et al.*, 1984]. This data is taken from experiments in adult dogs. If this effect were seen in the human fetus,

but disappeared with increasing maturation of the parasympathetic system, then a phase relation might appear similar to that we have described.

Immature infants lack the cardiac reserve of term neonates; myocardial contractility and sympathetic tone are already at near maximum. Thus, a paradoxical fall in stroke volume and cardiac output might result from an increase in heart rate in an immature cardiovascular system, whereas a mature infant with a slower heart rate and increased cardiac reserve would be able to increase blood pressure by an increase in heart rate. This might account for the change in phase relation of heart rate and blood pressure between the term and preterm infants [Winberg and Ergander, 1992] [Agata *et al.*, 1991].

9.9 Conclusions

As with many other investigators, the blood pressure waves we describe cannot be fully explained. They appear to be distinct from other descriptions (except for the one case in an adult) and yet as their wavelength may vary from one to twenty five minutes the group may not be discrete, containing blood pressure waves induced by several pathological processes. 'Stress' waves with a shorter wavelength than other waves and may result from catecholamine surges, what induces the other waves is not clear.

The phase relation of blood pressure waves has only previously been clearly demonstrated in experimental animals and had not been previously observed in the human. Although no firm conclusions are yet possible, the extrapolation of data from animal work offers further areas for investigation.

Whilst blood pressure waves in animals and adults represent an interesting physiological phenomena, blood pressure waves in the preterm and asphyxiated term human neonate may possibly have important pathological effects on the frail physiological systems in these infants. We have demonstrated a possible transmission of blood pressure waves to the cerebral circulation. The blood pressure waves may have an amplitude equivalent to 50% of resting blood pressure and so may represent a significant tension on the frail blood vessels of the germinal matrix in the preterm. At later gestations, asphyxial loss of cerebral autoregulation and ongoing vasogenic and cytotoxic oedema may be compounded by damage from hypertensive blood pressure waves. For these reasons further investigation of these blood pressure waves is warranted, to determine both how they are induced and what pathological effects, if any, they produce.

Chapter 10

CHAPTER 10

Discussion

10.1 Introduction

Computers have been emphatically promoted within the medical profession by a few 'computer eccentrics', who believe virtually anything is possible, whilst the majority of 'hands on' medical staff remain indifferent about such developments. The latter group have to be convinced of the value of computers in medicine [Young, 1993], against a background of popular cynicism and computer phobia. This success can only be achieved if computers are easy to use and productive to the people they serve [Weaver, 1987] [Lissauer *et al.*, 1991]. Advocates of computerisation cannot afford to forge ahead, leaving behind those for the whom the system is intended, frustrated at the limitations of the computer system to cope with them.

It was my absolute intention at the start of this research not to become a computer eccentric. I wished to avoid becoming embroiled in computer jargon and the art of computer programming. To all intents and purposes I wished just to use (and be seen just to use) standard computer software and help others to use it, thereby creating a link between the two extremes. System faults were discussed in proportion to their nuisance value, without bias. Equally system benefits were promoted when due. Inevitably, the research team have been seen as 'experts', however we

have always maintained that the system is not our system, but belongs to the clinical staff on the unit (as with the advent of the end of the computer study it will do). We have never coerced any one into using the system that did not want to use it and no checks were made as to who used the system or when. This managed to quell many early murmurings of 'Big Brother'.

10.2 Delayed familiarity

The system has been a gradual success, but in my opinion a definite success. Both medical and nursing staff were initially wary. After 6 months the majority of nursing staff were regularly using trend monitoring and became familiar with the possible functions. There was then a lag until about 18 months post introduction before a large number of nurses began using the trend monitoring in a better and more informed capacity; changing time scales, graph scales and graphs displayed to demonstrate the optimal trends for their infant's illness. Medical staff were equally slow. Initially one or two interested doctors gained clinical information from trends graphs, now they are frequently used by most doctors, and form a valid contribution to active decision making in emergencies and on ward rounds. The long lag time that occurred with the majority of nurses, between learning how to use the software (6 months) and developing the skills to intelligently interpret trends (18 months) was unexpected. The lag still exists, though familiarity with trends by regular staff has decreased this learning time for newcomers.

Although visual data trends can be more easily assimilated [Cole, 1990], the highly variable and detailed data presentation in Mary CPTM

requires new learning. Other CPTMs with less detailed trends have not had this problem [Ross *et al.*, 1990]. The flexibility of Mary CPTM data hallmarks its advantage, providing a greater influence over infant physiology. One of the most exciting benefits of the introduction of CPTM into our unit, has been the increased awareness by both medical and nursing staff of neonatal physiology and the physiological effects of our interventions. In hindsight the lag time in familiarity had the advantage of an eventual improved trend utilisation, better than expected in many cases. The disadvantages were the poor initial use and the effects this may have had on the moral of the unit. The nursing questionnaire demonstrated that after 6 months use, many nurses felt that they were under utilising the computer system. Others have also found that computer systems can take a long time to be properly utilised [East *et al.*, 1992 (2)]. An appreciation of delayed familiarity would be of benefit to those introducing CPTM into ITU, as some manufacturers claim just a 20 minute learning time (Emtek 2000)!

10.3 Clinical advantages of CPTM

The questionnaires (chapter 3) demonstrated the willingness of nurses to use the computers and the minimal effect that use had on parents. However, apart from answers to questionnaires we can provide little but anecdotal evidence of the clinical benefits of CPTM to neonatal ICU. The computer study (chapter 2) showed no important significant benefits (though importantly no detrimental effects either) to having CPTM. Whilst early learning problems and broad outcome measures may account for part of this, it may be that the clinical benefits of CPTM are too

subtle for such a trial. Others looking at specific events have found an advantage to CPTM over nursing observations [Aukburg *et al.*, 1989] [Kari *et al.*, 1990]. We have demonstrated the improved accuracy of vital sign recording by CPTM (chapter 5). Had the study been a resounding success, we could have heralded a new age of monitoring, had it been a disaster we could have dismissed CPTM as a waste of money. As it is we have convinced ourselves of its value, and therefore other computer eccentrics, but have equally fuelled the computer cynics who will quite gladly use these results to disregard computers as an expensive clinical excess. The computer cynics are not wrong, though neither are the computer eccentrics.

10.4 Research advantages of CPTM

Neonatology is firmly based on anecdote and folklore. Our concepts of what constitutes 'normality' and appropriate treatment for these infants needs to be challenged. CPTM provides unequalled benefits to do this; both work presented within this thesis and other papers, have shown the undoubted advantage of CPTM in neonatal physiological research [McIntosh *et al.*, 1993] [Deere *et al.*, 1991] [Powell *et al.*, 1992]. The studies contained in this thesis have explored three areas. We have used CPTM to challenge the long held belief that oxygen is an important cause of ROP, though as yet we have been unable to draw any firm conclusions. In addition, we have been able to advance neonatal medicine with the production of reference blood pressure values for vlbw infants, using more infants and more detailed information than has previously been possible. Finally, CPTM enabled us to discover a new phenomenon in

newborn infants. Blood pressure waves are an exciting development, that will need further investigation as to their origin and effects on the infant. As a clinically based physiological research tool I have found no equal.

10.5 Cost and appropriateness

There is a market demand for CPTM. In a survey of hospitals in the USA, 4.8% had computerised vital signs [Summers *et al.*, 1989] and in our U.K. survey, 26% of neonatal units wished to have physiological monitoring for clinical management and 31% research purposes. The clinical value of CPTM lies in the active management of the acutely sick infant and subsequent physiological reassurance of the 'convalescing' vlbw infant. It may also benefit these infants through active research. CPTM is not inexpensive (appendix 7). Cost will deny most neonatal units the opportunity of CPTM. It is unlikely that local health authorities will provide funds and CPTM may therefore cause a considerable drain on the sources from which it is purchased. With current restraints on finances this may well be a luxury, but if we are to provide quality advanced healthcare with an ability to improve through research, then CPTM will prove cost efficient: One day of intensive care for a vlbw infant costs approximately £1000, the cost of a cheap 486 PC.

CPTM is not appropriate for all neonatal units. It requires commitment from a large number of neonatal unit staff and an identified person available to answer questions and sort out problems. The majority of problems, though simple, can disable a cot station and diminish staff confidence if not quickly corrected. Costs can be minimised by nominating

a permanent member of staff (perhaps the neonatal technician) as the identified computer contact person. Formal initial and continued teaching is imperative (chapter 3) and smaller units might find this difficult to provide both in terms of staff and resources. Software designers could increase their potential market by providing better teaching aids for their systems. As CPTM is of greatest value in the management of acutely sick infants, learning how to use trend monitoring optimally requires exposure to large numbers of such infants. CPTM is therefore most applicable to larger neonatal units, with a commitment and interest in using the data for routine care and research [Sivek *et al.*, 1989]. Typically these will be teaching hospital neonatal units, however many large district general hospitals could equally benefit.

10.6 Improvements that could be made in hardware

Whilst computer hardware is now relatively cheap, machines at the lower end of the price range though affordable, are bulky and lack the durability needed to work continuously at temperatures exceeding 25°C. To prevent cluttering ICU workspaces, monitors have to be mounted on shelves. Keyboards placed on workspaces may have their access limited by other equipment e.g. infusion pumps and are prone to many forms of damage. The distance between monitor and keyboard may make data entry difficult. Cabling is often tangled with other cables and can easily be damaged.

10.6.1 Possible solutions

An improvement in the ergonomics of ICU computers could be gained with limited financial output. Wall mounted suspended monitors and keyboards would enable staff to position monitors at a suitable height to be seen from a distance and yet be brought down to an easier height for data entry and review. Robust network links and cable are an essential but often overlooked component of the network; network downtime has a profound effect on staff confidence. Radio linked networks are now available, though beyond the cost of most hospital local area networks. Smaller or remote computers (at present limited by the possible length of the patient monitor link), would help reduce the clutter in ICU caused by CPTM. Laptop or hand held computers have been used as databases [Stoeckeler and Ellis, 1989] or fluid/drug calculators [Large, 1988]. They are limited however in their application to network CPTM, as they are easily mislaid and have a small screen size. Laptop computers will have a role

for CPTM during patient transport.

10.6.2 Problems experienced with hardware

The computers for the computer study (Dell 80386SX) required maintenance approximately once every 18 months, with an operational lifetime of approximately 3-4 years (at which stage they become too slow and unreliable for software updates). Monitors have had a lifetime of approximately 15 months (permanent 24 hours use). Problems with network cables have occurred five times in 2.5 years, causing a temporary network crash (<1 hour), except for one 36 hour 'down time' requiring the assistance of the medical physics department.

10.7 General problems with software design

There are many small details of 'Mary' software that I would alter, but they are small details. Potential purchasers of CPTM systems should be aware that excess demands for individualised software, create a poorer overall software design and increase the price for everybody. Commercial pressures on vendors often cause them to agree for fear of losing the sale. Software developments must occur in the context of what is useful for many units. Current software is too expensive. Health care software should be available in a similar fashion to e.g. a word processing package; efficient accurate software with an accompanying literature that is appropriate for both the system manager and for teaching the computer phobic student nurse on her first day (optimally by on-line tutorials).

Creating 'in-house' designs may solve a local problem but usually

constitutes little general progress in the field, as the vast majority do not flourish beyond that unit [Gardner and Shabot, 1990]. 'Mary' is successfully used as a network in five other UK regional neonatal units. Whilst small databases are a relatively easy tasks for in-house design teams, CPTM requires complex programming that is not within the capabilities of most 'in-house' programmers. The 'in-house' CPTM designs that I have seen, generally had poor graphics with minimal flexibility [Ross *et al.*, 1990] [Stoodley *et al.*, 1992]. It is the flexibility of 'Mary' in the manipulation of the graphed data that delineates its success in neonatal care over other possible systems [Kari *et al.*, 1990] [van der Weil, 1987].

10.7.1 Software complexity

It is a mistake to assume that computer systems have to be complex to be good [Bash and Thorp, 1987] [Osborn, 1982]. We may now create complex multiple channel trend images with an accompanying database, blood gas charts, fluid charts, ventilation charts, drugs packages, nursing notes, patient reminders etc. A system that is so complex, it can interplay all these factors for the purposes of being an 'expert' system. It has the danger however of needing to be an expert, because the data held within it is now no longer readily accessible to the clinical staff on the ground. A more complex system will result in a reduction in the number of clinical staff able to use it appropriately and this may cause resentment of the computer system [Spencer, 1991] [Stoodley *et al.*, 1992]. Undoubtedly, it is easier to pick up a sheet of observations at the end of the cot, rather than find your way through multiple computer screens to the same information [Lowe *et al.*, 1992]. With current technology we should be more reflective in choosing the correct applications for the job, and more

critical of the effects of the introduction of computers [Spencer, 1991]. Simplicity of presentation and data access, without paucity of information, is very important.

In the past, restricted computational power limited software designs to providing maximum functional capability, with only secondary consideration given to ease of use. We now have the ability to develop fast, friendly and flexible software, without the on screen complexity that has earned computers their warranted unfriendly reputation. Apple Macintosh have contributed greatly to ridding computers of this image and wisely other manufacturers now follow suit [Shultz and Brown, 1989]. Unsatisfactory graphical presentation of data has been criticised in several CPTM systems [Gilhooly *et al.*, 1991] [Stoodley *et al.*, 1992]. Software designers will hopefully use these improved visual capabilities to entice the occasional phobic user to feel at ease with data entry and manipulation [Cole, 1990] [Cole and Davidson, 1989].

As most clinical staff possess minimal keyboard skills, limiting the role of the 'QWERTY' keyboard in health care systems is important [Colvin and Kenny, 1986]. The use of a mouse, tracker ball or light pen, especially in a windows environment can only enhance the ability of the basic user to feel at ease with data entry and graph manipulation. Carevue currently uses a trackerball with great success.

Experienced users quickly lose tolerance with 'slow' on screen speed and become frustrated if the software does not live up to their expectations [Gardner and Shabot, 1990] [Nolan-Avila and Shabot, 1987] [Gardner *et al.*, 1982]. Cheaper, faster hardware and developing software should keep up with this expectation, despite increasingly complex network functions (expert systems/on line artifact removal).

Though theoretical trend detection expert systems have been described [Horio *et al.*, 1989], to my knowledge no expert clinical physiological system is yet routinely in use, even for adults. It forms an exciting prospect, but it will not be available for many years. Many complex inter-relations between neonatal physiological parameters are poorly understood. Expert systems will inevitably contribute to this understanding. Many neonatal collapses occur with little warning and whilst CPTM enables us to detect these collapses earlier, expert systems would hope to predict the collapse.

10.7.2 Validation of software

The purchase of CPTM software is fraught with problems. Within the U.K. there are four multinational neonatal CPTM vendors and one small commercial vendor (chapter 1). Competition enables bargaining, however the systems are very different in style and function, and the price tag shouldn't hide this. Several papers have been published on the practicalities of purchasing software, in particular that by Bland [Bland, 1987], and others [Sivek *et al.*, 1989] [Blum, 1986(2)] [Paganelli, 1989]; information which should be more widely available as it is otherwise only discovered by expensive trial and error. It is not within the remit of this thesis to discuss purchase at length except to note that 'purchase' should also include software maintenance (10-15% per year of standard [NOT cost] price), hardware maintenance (one quarter of purchase price for 5 year warranty), teaching, wear and tear, consumables (eg optical/floppy discs).

In the USA, a 'Which' style magazine is produced which critically assesses health care computer products [Health Devices, 1992]. This expensive journal serves a very useful purpose and its cost is minute in

comparison to the wasted software money in most health authorities in the U.K.. The health sector is currently being swamped by computer software, often produced at minimal cost, with minimal software and clinical testing [Benson, 1993]. The expense of NHS computer failures are well publicised [Kelsy, 1993] [Porter, 1993]. Inadequately designed or tested software may antagonise staff, alienate patients and may render the physician legally liable for software errors [Miller *et al.*, 1985]. Although validation of software takes time and money, the practice must be encouraged [Beier, 1988]. If the control of NHS computer purchasing was not as fragmented, appropriate software could be specifically implemented into identified units for full scientific assessment. These results together with advice about the purchase of computers and systems (perhaps even NHS computer deals) could be published [Sockolow, 1989]. The government have recently set up an expert group, to advise the NHS on information technology [BMJ News, 1993]; it remains to be seen how well this advice sinks down to 'grass roots'.

10.8 Confidentiality

Both nurses [Fenny and Donovan, 1989] and patients [Rethans *et al.*, 1988] are concerned about the confidentiality of computer held records. There is little evidence to support these concerns, though of course they must be addressed. Security is at risk either by inadvertent access by un-authorised staff/members of the public to ward terminals, or by illegal entry to the system via telephone modems. The information contained on CPTM is generally of a low sensitivity and most non-authorised users would have little use for the data, as they would be poorly able to interpret it or use it for improper means [Birz, 1987]. A closed network i.e. no external communications, has minimal security risk. External CPTM links via modems would enable 'hackers' to enter the system, remove and possibly manipulate data. Data manipulation, if undetected, could have serious detrimental effects on infant care via CPTM. The price of greater access would paradoxically be greater security. Security access in an ICU with large numbers of permanent and temporary staff, poses a difficult problem and will require the development of simple yet effective access procedures e.g. passwords, hospital identification cards, 'PIN' numbers, computerised finger print or signature identification, etc [Miller *et al.*, 1985].

10.9 The threat of CPTM to nursing levels

CPTM as a patient monitoring system has the ability to perform routine physiological monitoring, a task which up until now has been a nursing duty [Clochesy and Henker, 1986]. This will lead to increased accuracy [Reekie *et al.*, 1975] and greater flexibility of this data (chapter 5). Concern has been raised that this may lead to loss of a guaranteed period of patient observation [Hendrickson and Kovner, 1989]. The effects on patient care of this form of data collection will need full assessment prior to and following implementation. Computers may paradoxically increase the amount of time required in direct patient care, to ensure that the human elements of care are not lost [Clifford, 1986]. With current pressure on staffing levels, the ability of computers to perform nursing tasks may be seen as an opportunity to reduce the nurse:patient ratio even further. Siemens EMTEK 2000 is marketed on the premise that it can help reduce nurse staffing levels (this system combines a CPTM with nursing reports and fluid charts). The attempts of computer systems to categorise nursing duties however will fail to appreciate their role as 'care co-ordinator' [Hendrickson and Kovner, 1989], orchestrating all aspects of a patient's care, including; trained clinical observations, patient care provider, medical information integrator, psychological care of the patient and family [Lancet (Ed), 1974]. Computers can at best augment nursing care [Osborn, 1982], they cannot provide appropriate clinical judgement and cannot reduce responsibility [Clochesy and Henker, 1986]. In the USA non-medical monitor watchers, are hired to watch ICU computer monitors for alarms and to inform nursing staff of 'important' alarms. This is a reckless policy aimed at reducing nursing staff levels and should be condemned

[Health Devices, 1992]. Computer monitoring is an extension to informed clinical decision making not a substitute [Osborn, 1982].

10.10 Possible adverse effects of CPTM

Whilst a new method of monitoring may unveil trends in data that have previously been unappreciated e.g. blood pressure waves, concern may be raised over the possibility that newly observed harmless trends might result in detrimental intervention. The computer study assessed whether there was any change in the number of blood gases or colloid support given in response to trend observation; no change was seen. Legally, the issue of liability for clinical errors resulting from the use of computers is far from clear [Miller *et al.*, 1985] [Gruendling and MacKay, 1988] [Brahams and Wyatt, 1989]. Though no test case has been performed in the U.K., it is likely that clinicians will be responsible for the interpretation of computerised data and deciding whether that data is clinically correct. Responsibility for errors in programming may rest with either the software company or the clinician. Paradoxically, in certain hospitals in the USA it may now be illegal not to have computer monitoring, as this would indicate a lack of 'reasonable prudence' in the care of a patient [Watson and Bernstein, 1988].

CPTM has increased the interest of medical staff in neonatal physiology and far from diminishing clinical acumen, has in my opinion greatly contributed to the neonatal education of all levels of staff [Eberhart, 1982]. Whilst staff have been happy to observe trends, they have continued to do so in the context of the infant's physical illness and examination.

CPTM and in particular Mary monitoring, provide the user with a clinical tool to assist with care when needed, with minimal immediate contribution required. The reduction in patient time reported by other groups caused by PDMS is principally because of the time spent in computer charting [Pryor, 1989]. As this is not part of our system, the computers do not detract from the time available for patient care.

The use of CPTM in small peripheral hospitals is limited, as staff will not gain sufficient experience to become familiar with trend graphs. The concept of 'remote' assistance (i.e. advice from a tertiary referral unit) by CPTM modem if introduced, should cautiously assessed. We are still unable to interpret many trends that we see in sick neonates and it would appear unwise to attempt to interpret these trends without the ability to examine the infant and all relevant equipment. Sick infants should be transferred to specialised tertiary neonatal units by tertiary staff as quickly as possible. CPTM should not prevent this.

Neither staff or parents had an adverse reaction to the introduction of the computer system (chapter 3). Indeed their comments and criticisms have constructively enabled us to improve both the system and our teaching methods.

10.11 Final Comments

There is a definite potential for CPTM, limited by finance and commitment. Financial restraints may limit the ability of the market to reach its potential and may ultimately cause its collapse; especially in those systems that do not provide CPTM within a neonatal patient monitor (Carevue 9000, Mary).

The advantage CPTM confers to the development of neonatal care, guarantees those enthusiastically adopting the method a wealth of opportunity for improving patient care, staff awareness and research studies. Finance will always be restricted, it would be to the detriment of neonatal services however if this restriction limited the further development of neonatal CPTM.

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Appendices

APPENDIX 1

Mary Neonatal Monitoring

Description of functions

Mary uses a fixed window presentation to display information. The large main window may be split into two, so that menus and patient details can be reviewed, while the most recent real time data is displayed in a smaller window. Functions are performed using menus, PC 'function' keys and other keys e.g. Alt, Ctrl, arrow keys etc. 'Hot' keys (quick access function keys), by-pass menus and allow the user a faster access to functions.

The following changes may be made to graphs;

Displayed choice of channels

A maximum of seven channels can be viewed as five trend graphs, in any combination of those currently monitored; heart rate (Hewlett Packard), respiratory rate, transcutaneous oxygen, transcutaneous carbon dioxide, central temperature, peripheral temperature, combined central and peripheral temperature, mean blood pressure, systolic blood pressure, diastolic blood pressure, combined systolic and diastolic blood pressure, central venous blood pressure, heart rate (oxygen saturation monitor), oxygen saturation, inspired oxygen.

Time scale

The real time full screen window displays 11 hours of one minute graphs. To expand the time scale this window is split into two. The smaller window continues to display 2 hours of the latest real time one minute graphs. The larger window may have its time scale expanded or contracted. When displaying one minute data the time scale may be expanded from 7 hours to 3 days, with 10 intervening time scales. One second graphs may be expanded from 7 to 78 minutes with 10 intervening time scales.

Graph scale

The scale of a graph may be individually chosen or alternatively all displayed graphs may have a scale automatically determined by the computer to best display the data present on screen.

Graph size

An individual graph size may be changed relative to others.

Artifact levels

Artifact levels are preset for each channel. Data outside these levels are not displayed or used in statistical calculations (appendix 2).

Join/Separate data points

Graphs default to joined data points.

Display of mean /standard deviation

The mean and standard deviation of data points within each hour (one minute graphs) or each minute (one second graphs) may be displayed instead of individual data point trend graphs.

Colours

There is a selection of eight colour choices for each graph.

Comments

Comments of up to 40 characters can be entered in real time or retrospectively when identified by a cursor in the recorded trend data (such retrospective comments are marked by an asterisk). Comments are automatically date and timed when entered. It is not possible to remove comments, however they may later be questioned by use of a ' ? ' function. This records the comment in grey rather than white, indicating that there is a question about its veracity. Comment identification is voluntary, usually by an individual entering their initials. Individual comments may be viewed along the base of the screen with the appropriate graphs appearing above (see figure 3). Alternatively a list of all comments can be viewed.

Mary Software Specifications

(provided by Meadowbank Medical Systems)

Mary 3 is written in Borland Turbo Pascal V5-7. A few small screen handling routines are written in Assembly language to gain extra speed.

The source code totals approximately 75,000 line of pascal

The combined program MARY.EXE is approximately 800Kb with many sections of the program overlayed. It is an MS-DOS based program.

When running, Mary 3 makes good use of RamDrive and EMS memory for overlay swapping.

Mary 3 runs well on any IBM PC compatible with an 80386 (or later) processor running at 16 MHz or better.

The printer support for Mary 3 is a HP Laser Jet III (or IV), as the HPGL2 printer plotting language is required for high quality detailed trend graph prints.

Analogue to digital conversion is done using the Blue Chip AIP-24 A/D board. Though the A/D conversion is done to twelve bit precision, Mary stored trend values to only eight bit precision.

RS232 interfaces are written in Pascal when required for new monitoring devices.

APPENDIX 2

Mary preset artifact limits

heart rate	(< 5 or > 250 bpm)
respiratory rate	(< 3 or > 125 breaths per minute)
transcutaneous oxygen	(< 0.7 or > 20.0 kPa)
transcutaneous carbon dioxide	(< 0.3 or > 16.7 kPa)
mean blood pressure	(< 5 or > 250 mmHg)
diastolic blood pressure	(< 5 or > 250 mmHg)
systolic blood pressure	(< 5 or > 250 mmHg)
central venous blood pressure	(< 0 or > 250 mmHg)
temperature 1 (core)	(< 22.5 or > 45.0 °C)
temperature 2 (peripheral)	(< 22.5 or > 45.0 °C)
oxygen saturation	(< 5 or > 100 %)
heart rate oxygen saturation	(< 5 or > 250 bpm)
inspired oxygen	(< 5 or > 100 %)

APPENDIX 3

COMPUTERISED COT MONITORING TRIAL

	FORM 1: BASELINE INFORMATION	[1]	1
HOSPITAL NUMBER		[ ][ ][ ][ ][ ][ ][ ][ ][ ]	2-10
TREATMENT GROUP	*(A=1, B=2, C1=3, C2=4)*	[ ]	11
DATE AND TIME OF BIRTH		[ ][ ][ ][ ][ ][ ] [ ][ ][ ][ ]	12-21
DATE AND TIME OF ENTRY TO TRIAL		[ ][ ][ ][ ][ ][ ] [ ][ ][ ][ ]	22-31
MOTHER:	Age	[ ][ ]	32-33
	Parity	[ ]	34-35
	Race *(caucasian=1, other=2)*	[ ]	36
	PMH *(unremarkable=1, problem=2)*	[ ]	37
PREGNANCY:	PET *(yes=1, no=2)*	[ ]	38
	IUGR *(yes=1, no=2)*	[ ]	39
	Multiple preg *(yes=1, no=2)*	[ ]	40
	Other sig problem *(yes=1, no=2)*	[ ]	41
	State.....		
LABOUR:	Onset *(spontaneous=1, induced=2, LSCS before labour=3)*	[ ]	42
	Duration of MR *(hours)*	[ ][ ][ ]	43-45
	Fetal distress *(yes=1, no=2)*	[ ]	46
	State.....		
	Mode of delivery *(see code list)*	[ ]	47
BABY:	Sex *(male=1, female=2)*	[ ]	48
	Birth weight *(grammes)*	[ ][ ][ ][ ]	49-52
	Gestation *(completed weeks)*	[ ][ ]	53-54
	Congenital abnormality *(yes=1, no=2)*	[ ]	55
	Place of booking *(SMMP=1, other=2)*	[ ]	56
	Age at transfer *(in utero=-1, < 12 hr=0, 12-24 hr=1, > 24 hr: state in days)*	[ ][ ]	57-58
	Apgar at 1 minute	[ ][ ]	59-60
	Apgar at 5 minutes	[ ][ ]	61-62
	Age at intubation *(mins)*	[ ][ ][ ]	63-65
	Duration of intubation *(mins)*	[ ][ ][ ]	66-68
	Drugs at resuscitation *(yes=1, no=2)*	[ ]	69

APPENDIX 4

COMPUTERISED COT MONITORING TRIAL

FORM 3: OUTCOME [3] 1

HOSPITAL NUMBER [ ][ ][ ][ ][ ][ ][ ][ ][ ] 2-10

SHORT TERM OUTCOME

INTRACRANIAL HAEMORRHAGE

Code grade as 0 = None, 1 = Germinal layer haemorrhage,
2 = Haemorrhage to ventricle, 3 = > 50% of ventricle filled
4 = Parenchymal extension

Code flare and cyst as 1 = Yes, 2 = No; Enter ventricle size in millimetres

	Grade R	Grade L	Flare R	Flare L	Cyst R	Cyst L	Ventricle size R	Ventricle size L	ICA Doppler RI	
Day 1									•	11-25
Day 2									•	26-40
Day 3									•	41-55
Day 4									•	56-70
Day 5									•	71-85
Day 6									•	86-100
Day 7									•	101-115

VOLUME OF COLLOID SUPPORT (mls)

Day 1	[ ][ ]	116-117
Day 2	[ ][ ]	118-119
Day 3	[ ][ ]	120-121
Day 4	[ ][ ]	122-123
Day 5	[ ][ ]	124-125
Day 6	[ ][ ]	126-127
Day 7	[ ][ ]	128-129

NUMBER OF BLOOD GASES

Day 1	[ ][ ]	130-131
Day 2	[ ][ ]	132-133
Day 3	[ ][ ]	134-135
Day 4	[ ][ ]	136-137
Day 5	[ ][ ]	138-139
Day 6	[ ][ ]	140-141
Day 7	[ ][ ]	142-143

LONG TERM OUTCOME

SURVIVAL (Yes=1, No=2)	[ ]	144
TIME TO DEATH/DISCHARGE (Days)	[ ][ ][ ]	145-147
TIME VENTILATED (Days)	[ ][ ][ ]	148-150
TIME IN OXYGEN (Days)	[ ][ ][ ]	151-153
ULTRASOUND AT DISCHARGE (Normal=1, Abnormal=2)	[ ]	154

APPENDIX 5

Parent Questionnaire

shown as a percentage (%)

1 Are you the parents mother or father?

Mother 71.7 Father 25.4 Unstated 2.9

2 Do you have a computer or wordprocessor at home?

Yes 25.4 No 74.6

3 Do you have a computer or wordprocessor at work?

Yes 52.0 No 48.0

4 What previous use/contact have you had with a computer?

never touched one	12.3
have only played games on one	24.2
use one occasionally	25.0
use one regularly	16.4
use one frequently	21.3
(no reply	0.8)

5 Did you know that the progress of some of the babies in the unit were being monitored by computer?

Yes 80.3 No 19.7

6 Was your baby being monitored by a computer?

Yes 80.7 No 19.3

(if no you can stop the questionnaire here)

Answers from this point shown as a percentage of those parents who said their baby was being monitored by computer (197)

7 Could you differentiate your baby's computer from the rest of the monitoring equipment?

Yes 83.2 No 14.2 (no reply/don't know 2.5%)

8 Was the purpose of the equipment explained to you?

Yes 69.0% No 28.9 (no reply/don't know 6.1%)

9 Who explained the equipment and computer?

Consultant	2.5	Research doctor	2.5
Junior doctor	0.5	Research nurse	3.6
Nurse	47.7	(no reply 31.5	don't know 1.5)

10 What was it for?
(verbatim response)

23.4% had reasonable correct response

11 Would you have liked further explanation?

Yes 45.7 No 44.7 (no reply/don't know 9.6%)

12 How did the computer make you feel?

A lot more anxious	2.0
more anxious	8.6
no difference	43.1
less anxious	24.4
a lot less anxious	18.3
(no reply/don't know	3.5)

13 Why do you believe the computer was there?

mainly for baby's benefit	43.1
mainly for the advancement of science	5.1
a bit of both	48.7
no reply/don't know	3.0

14 On balance, how do you feel now about knowing that your baby was being monitored by computer?

very pleased	27.4
pleased	17.8
no worries if it helps	53.8
a bit worried	1.0
I don't like it	0.0

15 Were the doctors keen about the use of computers?

all of them	29.9	some of them	7.6	a few of them	3.6
none	0.5	no reply	1.0	don't know	57.4

16 Did the doctors understand the computers?

all of them	38.1	some of them	4.6	a few of them	2.0
none	0	no reply	1.5	don't know	53.8

17 Did the doctors seem to think the computers were important?

all of them	34.0	some of them	8.1	a few of them	2.0
none	0	no reply	1.5	don't know	54.3

18 Were the doctors confident with the computers?

all of them	32.5	some of them	8.6	a few of them	3.0
none	0.5	no reply	1.5	don't know	53.8

19 Were the nurses keen about the use of computers?

all of them	36.0	some of them	18.3	a few of them	3.0
none	0.5	no reply	1.0	don't know	41.1

20 Did the nurses understand the computers?

all of them	42.6	some of them	18.8	a few of them	1.0
none	0	no reply	1.0	don't know	36.5

21 Did the nurses seem to think the computers were important?

all of them	38.1	some of them	17.3	a few of them	0.5
none	0	no reply	1.0	don't know	43.1

22 Were the nurses confident with the computers?

all of them	42.1	some of them	21.3	a few of them	1.0
none	0.5	no reply	1.5	don't know	33.5

23 Write any further comments you would like to make regarding the computers here

Further analyses

Chi-squared and Wilcoxon rank sum tests used as appropriate.

Parental experience of computers and telling whether or not being monitored by computer (question 6).
Significant association p=0.0124

	None	Games only	Occasional user	Regular user	Frequent user	**Total**
Yes	12	31	48	32	41	**164**
No	5	11	6	3	2	**27**
Total	**17**	**42**	**54**	**35**	**43**	**191**

i.e. Parents with greater experience of computers were better able to distinguish the computer equipment.

Confidence of parents in the presence of computers in relation to previous experience (question 12).
(p = 0.5796)

	more anxious	no difference	less anxious	**total**
None	3	6	9	**18**
Marginal user*	12	40	42	**94**
Experienced user†	6	39	33	**78**
Total	**21**	**85**	**84**	**190**

i.e. previous computer experience did not necessarily improve parental confidence in the computers.
*combines games and occasional users.
†combines regular and frequent users.

Parental computer experience and attitudes towards scientific benefit (question 13).
significant association (p=0.011)

	None	Games only	Occasional user	Regular user	Frequent user	**Total**
Mainly baby's benefit	12	24	21	13	14	**84**
Science only and both science and baby	5	16	33	22	30	**106**
Total	**17**	**40**	**54**	**35**	**44**	**190**

i.e. parents with greater computer experience tended to feel that science would benefit as much as baby from the computers.

Parental computer experience and attitude to computerised monitoring (question 14)
Significant association (p=0.0257)

	None	Games only	Occasional user	Regular user	Frequent user	**Total**
Pleased	6	14	24	15	29	**88**
No difference /worried	14	28	30	20	16	**106**
Total	**20**	**42**	**54**	**35**	**45**	**196**

i.e. parents with increased computer experience tended to be more pleased about the computer monitoring. Those parents with less computer experience tended to be more indifferent.

APPENDIX 6

Staff questionnaires

Shown as a percentage (%)

Questions 1-6 not analysed

1. Age
2. Grade of staff
3. Mainly day shift y/n
4. Permanent night shift y/n
5. Date you first started in the neonatal unit

7. Have you had any previous exposure to a computer or word processor?

never touched one	29
only played games on one	16
use one occasionally	47
use one regularly	4
use one frequently	2
no reply	2

8. How thorough was the initial teaching session that you had about the computer?

(a)	extremely thorough	1			
	quite thorough	53			
	not what I needed at all	6			
	no reply	23			
	didn't have one	15			
	(Written in)	*not very thorough*	*1*	*very basic*	*1*

(b)	easy to understand	37
	reasonable	31
	difficult to understand	3
	no reply	14
	didn't have one	15

9. Did you have a talk/tutorial on the use of computers generally?

yes	25
no	73
no reply	2

10. Did you have a talk/tutorial on their use in the NNU?

yes	55
no	44
no reply	1

11. Did you have a talk/tutorial on how to use the computer?

yes	63
no	36
no reply	1

12. Did you have personal instruction on how to use the computer?

yes	73
no	23
no reply	4

13. Did you want to know more about the computer system after the teaching session?

yes	65
no	21
no reply	14

14. Where did you get further help with the computer when you needed it?

(more than one can be answered)

consultant	2
SR	1
Registrar	9
research fellow	31
research nurse	59
sister	67
staff nurse	58
no reply	0

15. How often did you seek further advice after your teaching session on the computer?

frequently	27
occasionally	57
hardly at all	12
no reply	4

16. Did you find the explanatory booklet about MARY helpful?

yes	53
no	8
did not see one	30
no reply	9

17. Did you find that the written instructions about how to use the computer were understandable?

yes	86
no	1
did not see any	6
no reply	7

18. What aspects of the computer have you used?

(a) connected computer to patient

yes	46
no	50
no reply	4

(b) admitted patient to computer

yes	71
no	28
no reply	1

(c) looked at the current monitoring values

yes	89
no	9
no reply	2

(d) changed the screen colours

yes	71
no	28
no reply	1

(e) used the screen scroll facility

yes	67
no	32
no reply	1

(f) used the 48 hour screen recall

yes	51
no	48
no reply	1

(g) used the statistical manipulations

yes	6
no	92
no reply	2

(h) printed data out

yes	20
no	78
no reply	2

19. Did you always use the computer when it was on a baby that you were looking after?

yes	66
no	31
no reply	3

19 (b) If no, in about what percentage of 'computerised babies' that you were looking after did you use it?

30 / 40 / 50 / 50 / 60 / 70 / 70 / 70 / 75 / 75 / 75 / 75 / 75 / 75 / 80 / 80 / 80 / 80 / 80 / 80 / 85 / 90 / 90 / 90 / 90 / 90 / 95 / 98

no reply 3

20. How did you find setting up the computers?

(a) simplicity;

very easy	15
moderately easy	38
moderately difficult	25
very difficult	0
no reply	22

(b) time;

very lengthy	1
moderately lengthy	34
fairly quick	29
very quick	3
no reply	36

(c) value;

waste of time	0
some value	21
moderate value	26
much value	19
no reply	34

21. How many months was it before you felt familiar with the computers on the baby?

<1 month	2
1	11
2	17
3	21
4	5
5	1
6	6
still not familiar	11
no reply	26

22. Do you feel unreasonably pressed into using the computer?

yes	11
no	86
no reply	3

23. Do you feel threatened by having to use the computer?

yes	5
no	93
no reply	2

24. Would you like to do without the computer?

yes	8
no	84
no reply	7
(written in) sometimes	*1*

25. The computer is (mark along the line)

(no reply 7)

one machine too many	X	2
	X	4
	X	13
	X	21
	X	28
a valuable addition	X	25

26. For managing a baby, the computer is

no help	6
little help	15
moderate help	48
very helpful	30
no reply	1

27. For record keeping, the computer information is

no help	1
little help	9
moderate help	31
very helpful	56
no reply	3

28. The computers

help me do my job	46
little effect on how I do the job	46
get in the way of the job	4
no reply	4

29. Do you find any aspects of the computer daunting?

yes	28
no	66
no reply	6

30. Does the computer come up to your expectations?

yes	73
no	8
no reply	19

If no, in what way do you expect it to do differently? (written answers)

31. How has the computer affected your understanding of neonatal physiology?

considerable help	5
some gain	52
no change	40
it has confused me	0
no reply	3

32. As a result of the computers (mark along the line)

(a) the unit is easier to work in	X	7
	X	16
	X	59
	X	10
more daunting	X	4
no reply 4		

(b) I am when on duty

more anxious	X	1
	X	6
	X	76
	X	10
less anxious	X	6
no reply 2		

(c) parents in the unit are

more anxious	X	6
	X	27
	X	47
	X	7
less anxious	X	3
no reply 10		
(written in) sometimes more anxious 1		

33. What effect do you think the computers have on the confidence of the parents with regard to our care for the babies?

very reassuring	7
quite reassuring	32
no change	26
adds a little to their worries	22
very worrying	0
don't know	4
no reply	7
(written in) depends on parents' knowledge	*2*

34. What effect do the computers have on parents' confidence?

very reassuring	3
quite reassuring	26
no change	28
makes them a little more worried	28
makes them a lot more worried	2
don't know	4
no reply	6
(written in) depends on parents' knowledge	*3*

35. Are there any changes in the way you manage neonates that you believe were due to insight that you gained from the computers?

Please describe them.

36. Can you list some of the ways that you feel that the computer may benefit the baby?

37.(a) Do you think the computer system is working well?

yes	71
no	19
no reply	7
don't know	3

If no,

(b) is this because the teaching about the system has been poor?

yes	13
no	6

(c) and/or because the system itself breaks down too often?

yes	3
no	12

(d) and/or the staff are too anxious about the system (i.e. the system is not friendly enough)

yes	6
no	9

APPENDIX 7

Costs

incurred for the purchase, installation and 3 year maintainance of the 12 cot Mary CPTM network.

Hardware	£
10 Cotside computers (80386sx)	30,400
1 Doctors computer (80386sx)	2,600
1 Network server	5,500
1 Optical disc drive (+2 discs)	5,000
Software and licences	
For above + 2 additional cots	34,737
Installation	2,000
Software maintainance for years 2 and 3	14,600
Total	£ 93,037

In addition hardware maintainance (on-site parts and labour) costs were approximately £100 per computer per year in years 2 and 3.

APPENDIX 8

Examples of Mary graphs used as basis for illustrations contained in this thesis.

Figure 3 General Mary screen with comment -

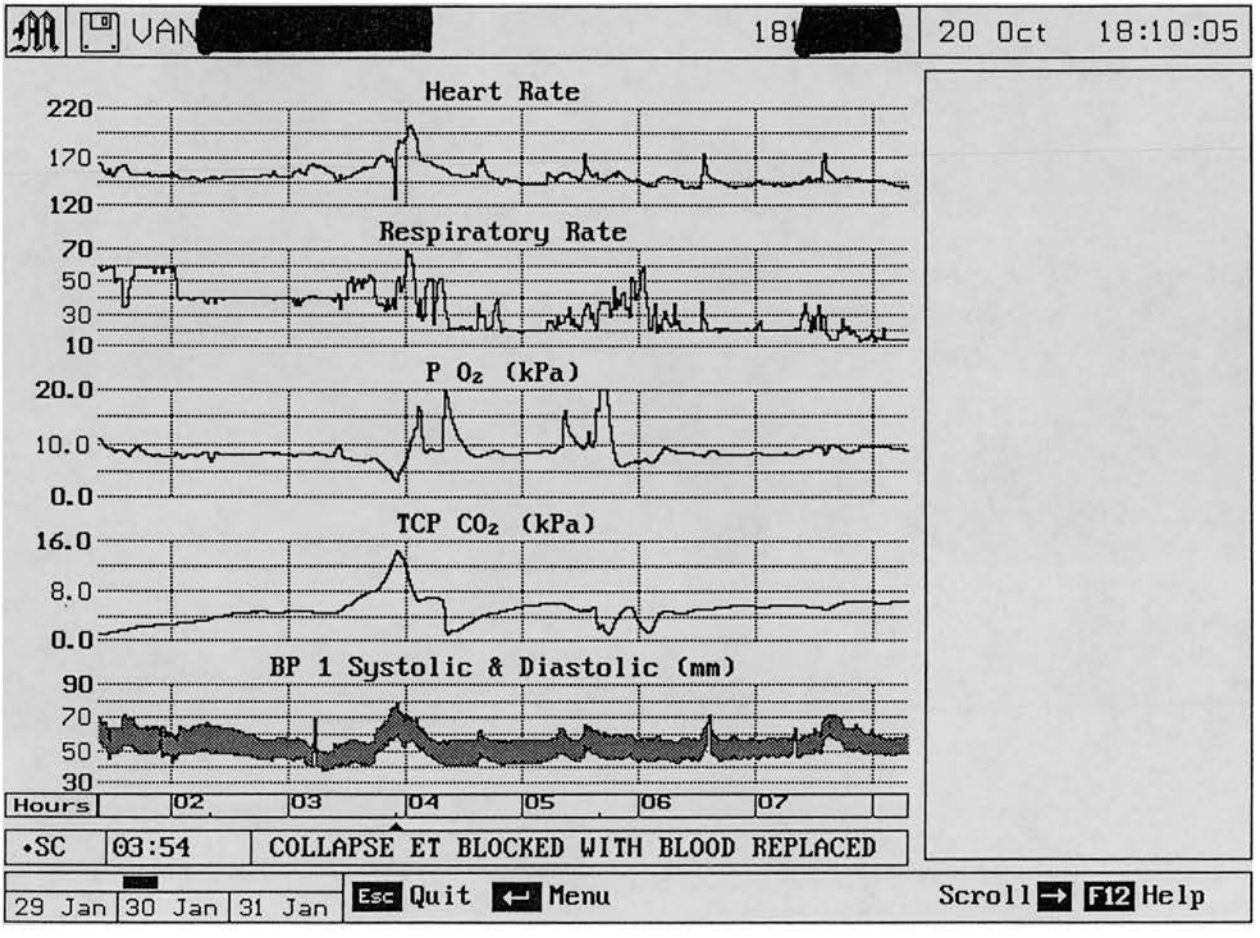


Figure 13 Artifact due to calibration of a transcutaneous gas probe

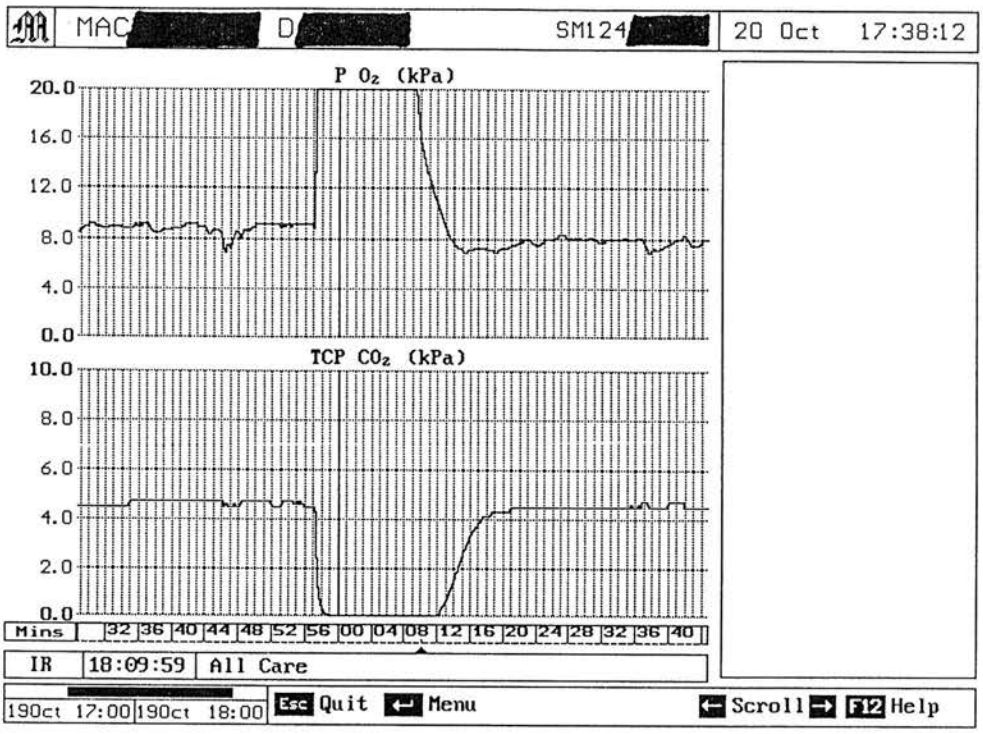


Figure 14 Artifact due arterial line sampling

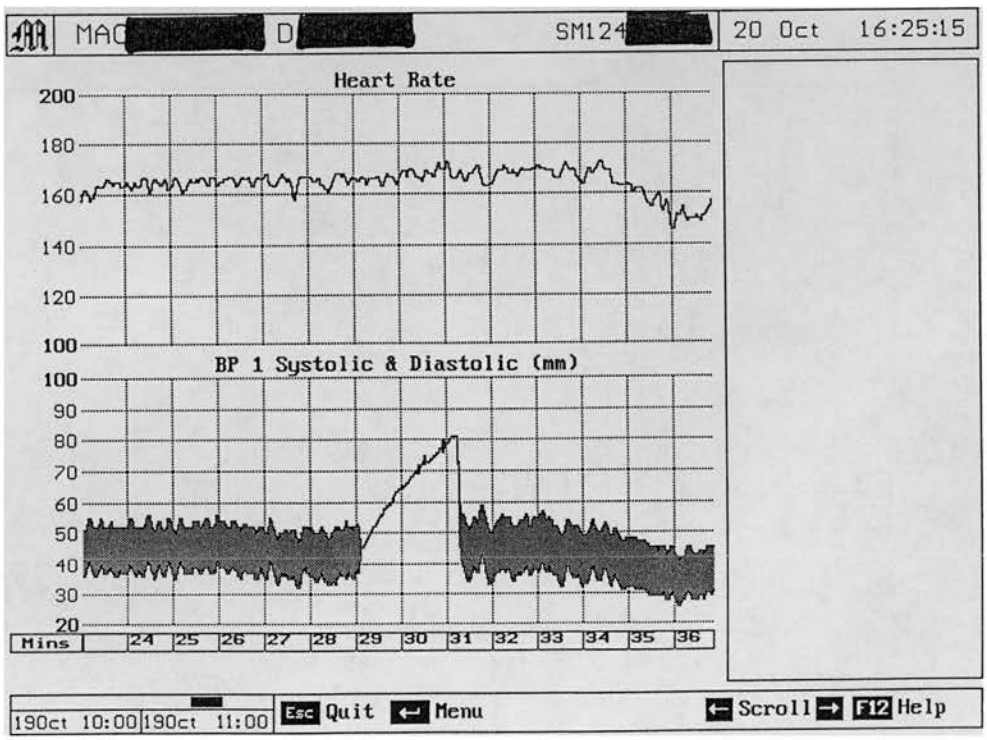


Figure 23 Stress induced blood pressure waves

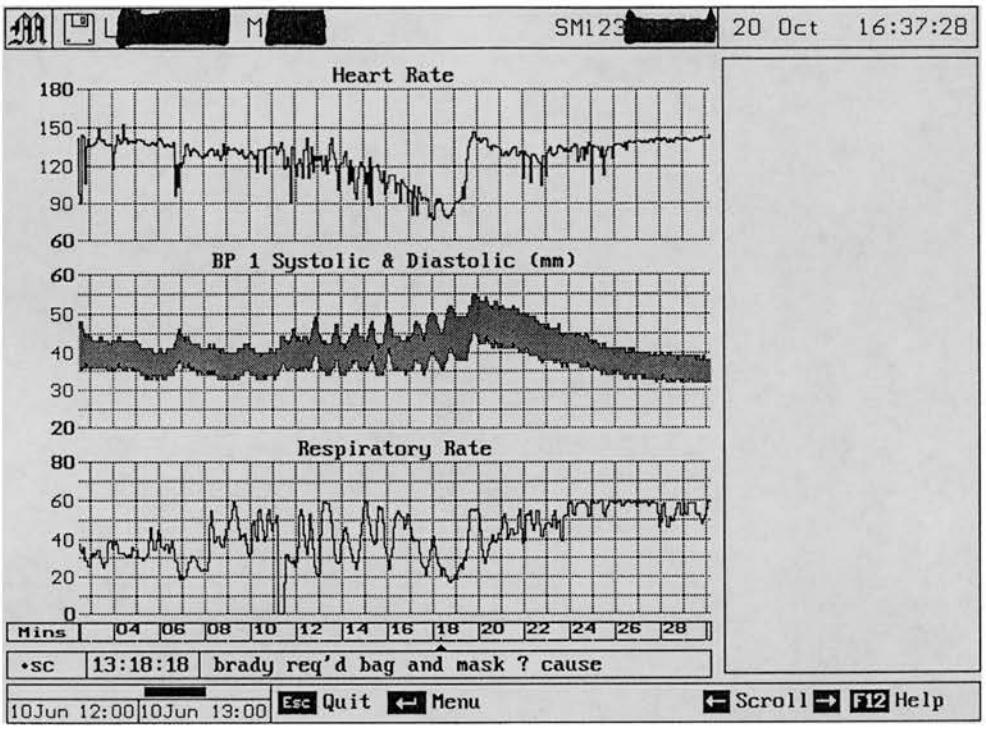
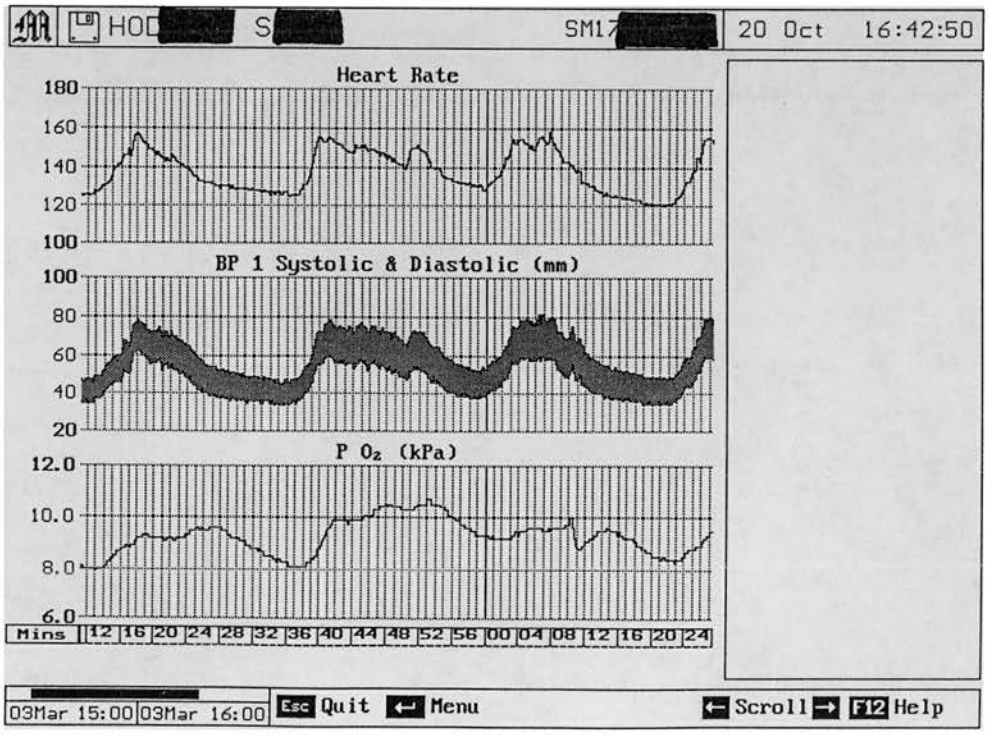
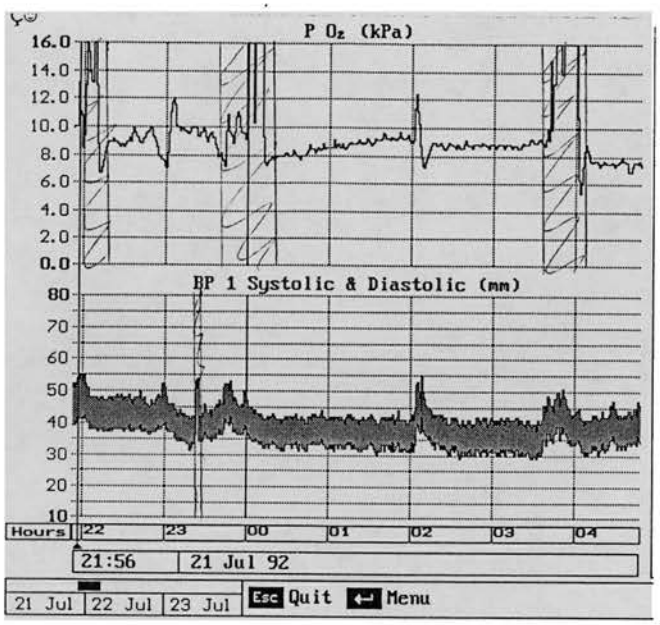


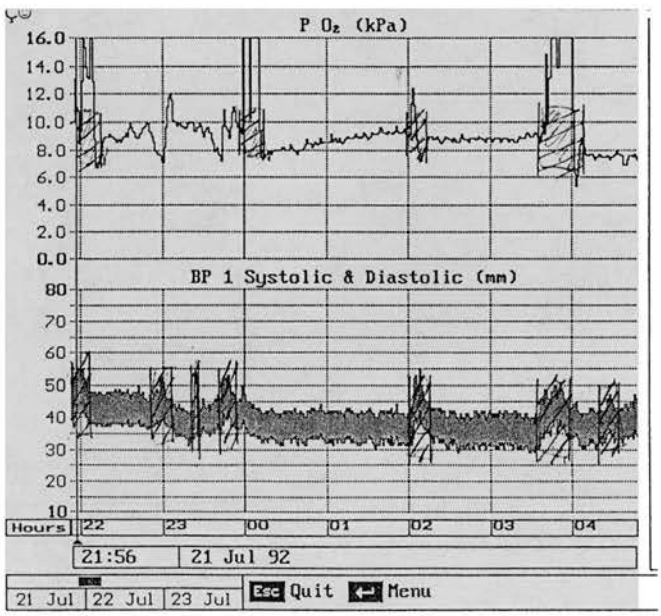
Figure 21 Cyclical variation of blood pressure, heart rate and tcpO2



Observer 1



Observer 2



Observer 3

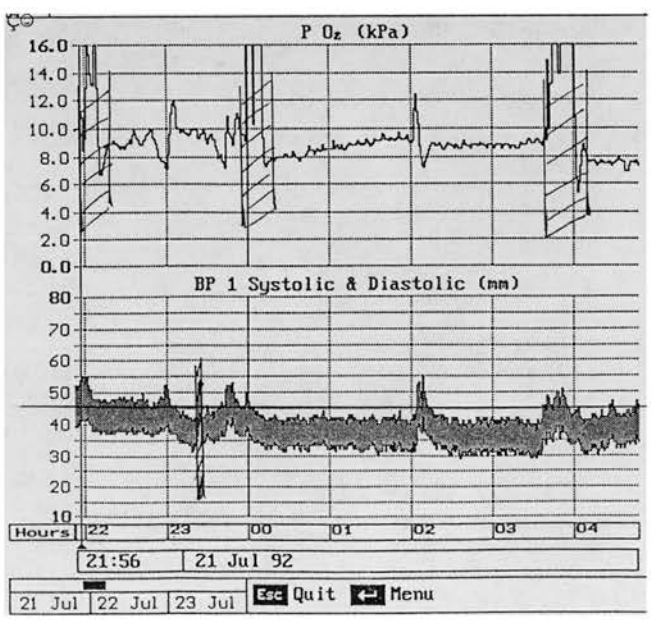


Figure 15/16 Artifact removal by 3 observers from tcpO2 and blood pressure

Published Papers

Archives of Disease in Childhood 1993; **69**: 64–67

Cyclical variation of blood pressure and heart rate in neonates

S Cunningham, S Deere, N McIntosh

Abstract

Using a computerised physiological monitoring system a cyclical variation in blood pressure (waves), with associated changes in heart rate and transcutaneous oxygen, was observed. Twenty five episodes were seen in 10 neonates, with a median gestation of 33 weeks (range 28–42 weeks). Eight neonates had an asphyxial injury.

Blood pressure waves had a mean (SD) amplitude of 11·6 (5·6) mm Hg with a mean wavelength of 9·0 (5·2) minutes. Both amplitude and frequency were independent of gestation. In neonates of less than 34 weeks an inverse phase relation existed between heart rate and blood pressure waves (blood pressure rose as heart rate fell); in infants with a gestation greater than 34 weeks a direct phase relationship occurred (blood pressure and heart rate rose together).

It is postulated that hypertensive blood pressure waves may cause or exacerbate cerebral pathology in neonates with a pressure passive cerebral circulation.

(*Arch Dis Child* 1993; **69**: 64–67)

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Accepted 12 February 1993

We have noted cyclical variation in blood pressure and heart rate in neonates in intensive care and attempted to identify aetiological or predisposing factors.

The maintenance of normal blood pressure in neonates in intensive care is important to optimise the perfusion of vital organs. Blood pressure maintained within the 'normal' range reduces the risk of hypoxic ischaemic damage and may decrease the incidence of intraventricular haemorrhage.[1]

The normal adjustment of blood pressure is complex, involving neural, cardiovascular, and endocrine components. The opposing actions of the sympathetic and parasympathetic nervous systems are the dominant blood pressure controls. Sympathetic activity from spinal nerve centres increases heart rate, ventricular contractility, and peripheral vascular resistance. It is far more powerful in altering blood pressure than parasympathetic control mediated by carotid baroreceptors.[2] In normal physiological states respiration may minimally alter blood pressure, but significant alterations of blood pressure can occur in certain pathological states, including cerebral asphyxia, hypovolaemia, and increases in cerebrospinal fluid pressure.

The blood pressure waves we describe may give some insight into cardiovascular control mechanisms in the neonate, and because of the prematurity of some of the infants, the fetal development of this system.

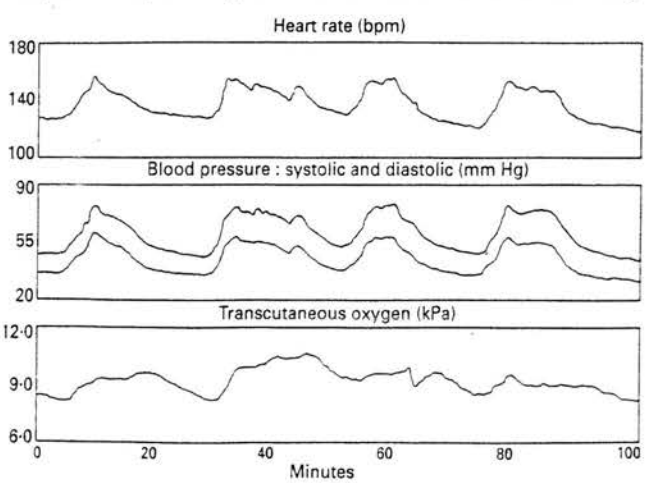

Figure 1 Cyclical variation of heart rate, blood pressure, and transcutaneous oxygen.

Patients and methods

All infants who required neonatal intensive care at the Simpson Memorial Maternity Pavilion since January 1991 were monitored using a computerised physiological cot monitoring system.[3] Each infant in intensive care was monitored by a Hewlett Packard 78834A multichannel monitor that was connected to a standard industry 316 SX computer by means of an analogue to digit board. Data was sampled each second by the computer and up to 32 channels of physiological data could be accessed. The information was stored and could be shown as trend graphs over variable time periods from seven minutes to three days.

Cyclical oscillations ('waves') in blood pressure were first observed in the trend recorded data displayed on the computer of a severely asphyxiated neonate. The same oscillations were also present in the heart rate and transcutaneous oxygen. A sample of the data is shown in fig 1. Four distinct waves can be seen in the heart rate, blood pressure, and transcutaneous oxygen. This episode occurred at 17 hours of age and continued for 23 hours.

Over the next five months, March to July 1991, we observed similar blood pressure waves in nine other neonates. To identify possible causes we considered the neonatal course of these 10 neonates (table 1). Daily intracranial ultrasound was performed including measurement of internal carotid artery

Table 1 Patient details

Gestation (weeks)	*Birth weight (g)*	*Asphyxia*	*Apgar score*		*Grade of intraventicular haemorrhage**	*Resistance index†*	*Neonatal death*	*No of episodes*
			1 min	*5 min*				
28	1129	Postnatal	6	9	3	0·55	No	1
30	1755	No	7	5	0	0·69	No	1
30	1770	No	6	7	0	0·89	No	1
30	948	Postnatal	4	7	2	0·63	No	7
31	1358	Postnatal	7	9	0	–	No	1
35	1900	Birth	0	5	0	0·56	No	1
38	2735	Postnatal	9	9	0	0·55	No	7
41	3886	Birth	0	0	0	0·35	Yes	1
41	2430	Postnatal	2	6	0	–	Yes	1
42	3125	Birth	2	4	4	0·30	Yes	4

*Based on Papille *et al* grades 1 to 4.[18]
†Internal carotid artery resistance index ≤0·55 is considered abnormal.[19]

Table 2 Comparison of amplitude (mm Hg) and wavelength (min) during the wave episodes

	Mean (SD)
Blood pressure (n=25):	
Amplitude	11·6 (5·6)
Wavelength	9·0 (5·2)
Heart rate (n=23):	
Amplitude	9·4 (6·3)
Wavelength	9·2 (5·4)
Transcutaneous oxygen (n=17):	
Amplitude	0·8 (0·7)
Wavelength	7·4 (6·1)

resistance index. Eighteen other variables of neonatal intensive care were considered retrospectively from casenotes.

Electromechanical artefact might produce a regular variation in blood pressure. However, the blood pressure waves described have occurred over a five month period on a variety of computers, monitors, and infusion pumps and we can determine no artefact that could cause such regular variation, especially one that can be altered just by touching the baby.

Each episode of waves was analysed to obtain the mean systolic and mean diastolic blood pressure (values quoted in later text are a mean of these two values), heart rate, and transcutaneous oxygen over at least 15 cycles. The phase relation between each of the three indices was also noted.

Ethical permission for the use of computer monitoring was obtained from the Lothian Health Board medical ethics committee.

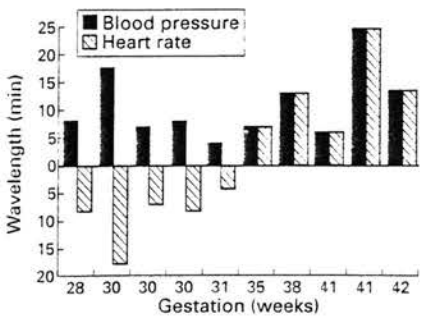

Figure 2 Maximum wavelength and phase relation of both blood pressure and heart rate in the 10 neonates. Heart rate is plotted above the zero line when the heart rate and blood pressure are in phase (peak for peak and trough for trough). When the blood pressure peak coincides with a heart rate trough (that is the opposite phase) the heart rate is shown below the zero line.

Results

A total of 25 episodes were seen in 10 ventilated neonates over the five month period. Seven neonates had just one episode, one had four episodes, and two neonates had seven episodes. The episodes had a median duration of five hours with a range from one to 38 hours. These 25 episodes occurred at a median of 101 hours of age with a range from 17–315 hours. The 10 neonates (table 1) had a median gestational age of 33 weeks (range 28–42 weeks) and birth weight median of 1835 g (range of 986–3886 g). Apgars scores were low, reflecting the presence of three severely birth asphyxiated neonates in the cohort. Five other neonates had postnatal asphyxia; this was defined by blood gases as an arterial oxygen tension of less than 5 kPa in conjunction with a base deficit more severe than 10 mmol/l for more than 10 minutes.

The mean and SD of the amplitude and wavelength of the blood pressure, heart rate, and transcutaneous oxygen are shown in table 2. The largest mean amplitude and wavelength recorded in blood pressure waves were 25 mm Hg and 25 minutes respectively. Heart rate and transcutaneous oxygen waves were not always associated with waves in blood pressure. Heart rate waves were associated in 92% of blood pressure waves and transcutaneous oxygen waves associated in 68% of blood pressure waves.

The wavelength, amplitude, and time of onset of the waves were unrelated to the gestation, birth weight, or Apgar scores. Benzylpenicillin, gentamicin, and morphine were commonly associated with the episodes. Hypocalcaemia (serum calcium concentration <1·8 mmol/l) was the only biochemical factor of those we analysed to be commonly associated (seven out of 10 neonates). Blood volume support was needed by five infants during their wave episodes; this increased to nine neonates when the period of 48 hours before and up to six hours after the wave episodes were included.

The phase relation of the blood pressure and heart rate waves is demonstrated in fig 2, where the maximum blood pressure wavelength is plotted with the maximum heart rate wavelength for each of the 10 infants. Heart rate waves occurred only either directly in phase or directly in opposite phase to blood pressure waves. In fig 1, the blood pressure and heart rate waves are directly in phase, that is peaks correspond to peaks and troughs to troughs, whereas if they were in opposite phase blood pressure peaks would correspond to heart rate troughs and vice versa. In fig 2 heart rate wavelength is plotted above the midline if they occurred in phase with blood pressure waves or below the midline if in opposite phase. This figure demonstrates that infants less than 32 weeks' gestation have an inverse phase relation between heart rate and blood pressure waves, that is when the blood pressure increases the heart rate decreases and vice versa. Neonates greater than 34 weeks' gestation have a direct phase relation between heart rate and blood pressure waves, that

is heart rate increases as blood pressure increases.

Discussion

Blood pressure is modulated by several major physiological controls, including the autonomic nervous system, the endocrine system, and the cardiovascular system. These combine to produce a blood pressure that varies little from its physiological norm, providing stability of perfusion essential for the function of major organs. Blood pressure deviates from this norm when this balance is pathologically interrupted such that other contributing controls cannot compensate.

The embryological development of human gross cardiovascular anatomy is well described, from the initial pumping of a single chambered heart at 23 days' gestation to the final transition from the fetal to newborn circulation at birth. The embryological development of the control of the cardiovascular system remains less well understood.[4] Preterm neonates are now being cared for at little more than half their intended gestation. It is possibly unreasonable to assume that cardiovascular control is complete at these early gestations, when the fine control of all other major organs is not. Despite this we often assume adult blood pressure control mechanisms when managing a 4 month premature infant.

CYCLICAL NATURE OF BLOOD PRESSURE WAVES

The synchronous relationship between the blood pressure and heart rate wavelengths (table 2), would indicate that these waves both share the same origin. Numerous postulates could account for this exact chronicity: the cardiovascular system is controlled by a number of neural and endocrine sites, many of which have an intrinsic rhythm that underlies their control. These rhythms may be exaggerated or have their frequency altered by hypoxia.[5] A sinusoidal pattern of heart rate in the fetus has been demonstrated on cardiotocography[6] in association with hypoxia and severe anaemia with a subsequent poor prognosis. A similar sinusoidal pattern in heart rate was reported postnatally in eight neonates suffering from perinatal or postnatal asphyxia.[7] Only two of the eight survived, but with severe handicap. It is not stated whether blood pressure measurements were taken and no conclusions were made as to the origin of the heart rate waves.

Baroreceptors provide an important blood pressure control. Oscillations in blood pressure very similar to those we describe have been induced by sectioning the afferent nerve supply from arterial and cardiopulmonary baroreceptors in non-anaesthetised dogs.[8] The blood pressure waves produced in the dogs had a wavelength of approximately 20 minutes and an amplitude up to 80 mm Hg. Hypoxia of the same pathways in the human neonate might reduce their feedback function revealing an underlying intrinsic rhythm.[9] Removal of 20% of the blood volume from a pig fetus induces 4 per minute waves in blood pressure and heart rate.[10] Severe antepartum haemorrhage in the human neonate has also produced the cardiotocography cyclical heart rate rhythm described above. Blood volume support was needed in five of the neonates in this study during their wave episodes.

Endocrine feedback often shows cyclical variability – for example glucagon, insulin, and thyrotrophin release.[11] Longitudinal data on neonatal endocrine function is scanty because of the difficulties (technical and ethical) of repetitive blood sampling in neonates. New microassays may enable a better appreciation of the temporal relationships of humoral control of blood pressure in neonates.

Cerebrospinal fluid (CSF) pressure waves are well described.[12] Of the three types of pressure wave, 'a' and 'b' waves, with a wavelength of 5–20 minutes and 2–4 minutes respectively, are pathological and episodic, resulting from a temporary reduction in intracerebral compliance, whereas 'c' waves are physiological and are thought to occur secondary to the well described 6 per minute Traub Herring and Mayer blood pressure waves. Short term changes in intracranial pressure noted during CSF pressure 'a' waves are sometimes conveyed to the systemic blood pressure,[12] others have been unable to confirm this.[13] CSF 'a' waves have been described in asphyxiated neonates.[14] These waves occurred only at intervals, in one case occurring on five of the 10 days of life and lasting for periods of up to seven hours with an amplitude of up to 60 mm Hg. The CSF pressure waves in these infants occurred both spontaneously and in response to external stimuli (for example suction). No reference is made to continuous blood pressure recordings in these neonates, but if the CSF pressure waves were conveyed to the systemic blood pressure, waves such as those we have described would be produced. Cerebral epileptic activity s often associated with variability of blood pressure and heart rate. We can find no reports of epilepsy in neonates leading to cyclical blood pressure waves. Sleep patterns might explain the periodic nature of the blood pressure waves. However, as neonates spend most of each 24 hours asleep, a large proportion of which is rapid eye movement sleep, it would seem unlikely that only single episodes of the blood pressure waves would be manifest if they are sleep induced.

From this study we have been unable to identify any factors that might have convincingly induced the waves or cause them to disappear. Changes in serum biochemistry and medication can clearly alter cardiovascular responsiveness and might therefore have induced temporary alteration in cardiovascular function producing a release of an intrinsic rhythm.

PHASE RELATION OF BLOOD PRESSURE WAVES

The phase relation of blood pressure and heart rate waves undergoes a transition at 32–34

weeks. Figure 2 demonstrates both the maximum wavelength of each of the 10 neonates and uses this to illustrate the phase relation that exists between blood pressure and heart rate. Mammalian models show a consistent asynchrony in the development of the autonomic control of the cardiovascular system; the sympathetic system is the principle control of the cardiovascular system by 0·5 term gestation and keeps control until near term. At this stage the parasympathetic nervous system, until now relatively dormant, markedly increases its contribution. The change in phase relation that we have demonstrated may herald a distinct period of change in the control mechanisms of blood pressure in the human neonate. Frequent bradycardias in preterm infants may be due to a parasympathetic system attempting to increase its share of control before it is physiologically mature.[15]

Immature infants lack the cardiac reserve of term neonates; myocardial contractility and sympathetic tone are already at near maximum. It is likely therefore that in the very immature cardiovascular system an increase in heart rate may reduce stroke volume and thus cardiac output. This might account for the change in phase relation of heart rate and blood pressure between the term and preterm infants.[16 17]

CONCLUSIONS

Our main concern in gestations less than 32 weeks is that instability of blood pressure may predispose to intraventricular haemorrhage. The blood pressure waves may have an amplitude equivalent to 50% of resting blood pressure and so may represent a significant tension on the frail blood vessels of the germinal matrix. At later gestations the waves are frequently associated with birth asphyxia or a significant degree of postnatal asphyxia. Asphyxial loss of cerebral autoregulation and ongoing vasogenic and cytotoxic oedema may be compounded by damage from hypertensive blood pressure waves. A hypertensive encephalopathy could exacerbate the cerebral pathology.

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Neonatal physiological trend monitoring by computer

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Abstract

A premature baby born up to four months early is a fragile patient dependent on intensive care. The body systems are physiologically immature and so tolerate stress badly. The tendency of these infants to rapidly deteriorate, has led us to use a cotside computer monitoring system which displays physiological trends. Information from standard neonatal monitors is accessed by individual cotside PC's linked to a central network server and Doctors terminal. Trend graphs can be easily manipulated, displaying from 7 minutes to 3 days of physiological information on a single screen. Pathology may be observed in real time as it occurs. The system has 3 main areas of use, (1) as a real time clinical aid to patient management, e.g. apnoea of the newborn; (b) as a research tool, demonstrating the effects of procedures on physiology; (c) for educating members of staff about how physiological events develop. Data is saved for the whole of each neonates intensive care stay. Assessment of staff and parent attitudes by questionnaire have been favourable.

Introduction

Routine critical care management has been assisted by the development of computers. This involves not only the routine charting of physiological parameters and biochemical results but also the development of expert systems to detect and warn of patient instability. Whilst it is recognised that Intensive Care areas lend themselves to computer involvement [1], it is essential that computers are not used simply because they are advanced technology and imperative that they do not interfere with direct patient care [2]. It is equally important that the life span of the computer system is not limited to that of the motivating figure within the unit [3]. Medically orientated computer programmes should be simple in presentation with easy access [4]. If these criteria are not matched, computers will compound the considerable stress recognised in such units and increase the rate of staff turnover.

Neonatal intensive care could benefit greatly from computer assisted care. As yet however, there has been very limited development in comparison with adult intensive care areas. It is now possible for neonates born as early as 24 weeks gestation and weighing as little as 500 grams to survive. The risks associated with promoting such survival are potentially very significant and include; sepsis, cerebral intraventricular haemorrhage, acute and chronic pulmonary problems eg. blocked ET tube, pneumothorax, bronchopulmonary dysplasia and spontaneous apnoea. Such events may be frequent in small, immunologically and physiologically immature infants. There is often little warning of deterioration and without immediate resuscitation death or serious handicap may result.

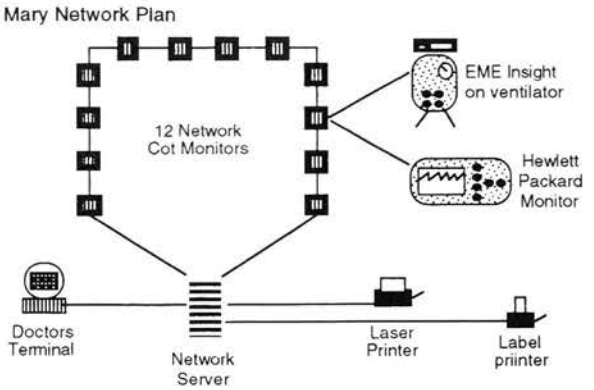

Fig. 1. Mary Network Plan.

Computer monitors for Neonatal Units must differ from their adult counterparts for several important reasons:

(a) the sick neonate is relatively invisible, often hidden by bubble plastic, enclosed within an incubator and discoloured by blue phototherapy units
(b) the fragile infant requires as little handling as possible to ensure thermal and fluid stability [5] and to allow adequate rest between potentially frequent handling procedures [6].
(c) neonatal units often have a 1 : 2 or 1 : 3 nurse/patient ratio, whereas adult ITU has a ratio of least a 1 : 1
(d) deteriorations in sick neonates are often acute over seconds or minutes. They occur with apparent suddenness partly at least because of the inability of the neonatal patient to verbally indicate deterioration but also because of the immaturity of neonatal homeostatic mechanisms.

In essence, because a neonatal patient is poorly visible and unable to communicate deterioration, clinical information may frequently be limited to the physiological parameters measured on monitors. For nurses who have to cope with more than one poorly visible intensive care patient at one time, computers could assist by providing continuous informative trends of the monitored values over variable time periods chosen because of each specific neonates degree of instability. Physiological trend screens can be viewed across crowded units for doctors and nurses to assess an unstable baby whilst at the same time performing a procedure on another baby.

Mary monitoring

Many intensive care computer applications have a bias towards the collection and presentation of laboratory and numerical physiological data [7, 8]. In Edinburgh, U.K. we use a computer system (called 'Mary') [9] which emphasises the presentation of multi channel physiological data as trend graphs. Trend graphs have been chosen because of the ease with which data can be assessed. This helps when rapid decisions have to be made [10]. Assessment of an ICU monitoring system in Aberdeen U.K. demonstrated that although doctors found the system of value, they expected better graphically presented data [11]. We have attempted to ensure easy cotside access to the trend graphs for staff previously untrained in computer use. Simple graph manipulation helps to identify developing pathology as it occurs. We believe this enables faster response times to emergency situations.

The system is based in a 16 cot supraregional neonatal intensive care unit. Each individual cot has a standard industry 16 MHz 316SX PC with screen and keyboard, connected in a circuit to a Nexos network server and then to a remote doctors terminal and printer. See Fig. 1.

Mary is a menu based system (with alternative 'hot' keys), which allows real time and previously recorded trend display of physiological data. Physiological data is taken from Hewlett Packard multichannel recorder (78834A) and Nellcor oxygen saturation monitors. Respiratory information is taken from EME Insight and Critikon Oxycheck monitors. Input to the computers is either via an A to D board or by RS232 output from the monitors.

Up to 32 channels of physiological information can be monitored. A maximum of five channels, in any combination of those currently monitored can be viewed. Paramount in the system design is ease of manipulation of the displayed physiological information. Each channel of physiological informa-

tion can be changed with regard to its value scale, time scale and its relative size and position to the other displayed graphs. Thus the components of physiological events can be viewed together in a highly flexible fashion. All these functions require the use of only two keys. An autoscaling function chooses the most appropriate scale for the displayed graphs. A cursor can identify the exact values at any chosen time.

Data can be viewed in real time either as one second information (denoted by a red time bar) where each one second value is plotted, or as one minute information (denoted by a blue time bar) where sixty one second values are averaged to produce a one minute point value. One second graphs can be viewed over a period ranging from 7 minutes to 78 minutes with 10 intervening time scales. One minute data can be viewed over a range of 7 hours up to 3 days, with 10 intervening time scales. This manipulation requires the use of only two keys. One second data is automatically stored for 72 hours during which time a request can be made to permanently save the one second data points. When monitoring in real time all other Mary functions can be performed and viewed by use of a large window whilst the last two hours of real time physiological data are displayed in a smaller window on the right of the screen. Data from any part of the infants monitored stay in the neonatal unit can be recalled. Scrolling of this recorded trend data allows an appreciation of the natural progression of events as they would appear in real time.

A popular 'user friendly' function is the ability to change the colours of the displayed graphs. Staff often change the colours of the graphs to their favourites at the beginning of their shift. Trend data may be viewed as the mean and standard deviation of the data points over each minute in one second data, or each hour in one minute data.

Data and timed comments of up to 40 characters can be entered in real time or when identified by a cursor in the recorded trend data (retrospective comments are marked by an asterisk). It is not possible to remove comments, however they may later be questioned by use of a '?' function. This records the comment in grey rather than white

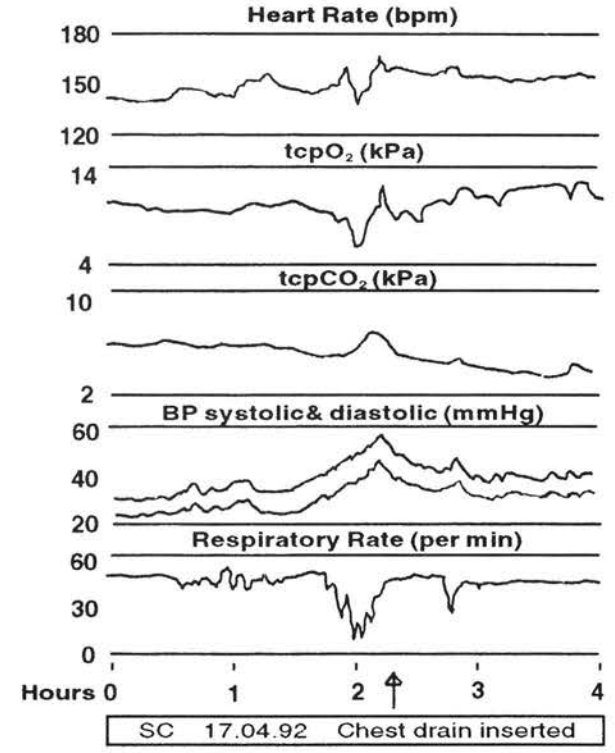

Fig. 2. Pneumothorax with comment.

indicating there is a question about the veracity of that comment. Comment identification is by voluntary entering of initials by the clinical staff. Individual comments may be viewed along the base of the screen with the appropriate graphs appearing above (see fig. 2). Alternatively a list of all comments made can be viewed.

Nurses receive initial instruction on the computer system on arrival to the unit by the computer research staff. Patient information is entered onto a patient registration form, which forms part of a comprehensive neonatal database. A statistics programme allows the analysis of collected data. Statistical results may be printed or transferred to an ASCII file for further analysis on a commercial statistical software package.

Ventilator data can be viewed as a table with automatic storage of each significant change timed and displayed. Blood gas results can be manually entered into a flow sheet and also appear on the comments page. Help screens are available to assist

at any stage. Patient recorded data can be archived to and from the hard disc of the server at any time.

Assessment of the system

New equipment should always be carefully assessed prior to its acceptance within an intensive care area. Over three years we hope to assess; (a) The short term and long term outcome of the neonates comparing randomised monitored and non monitored groups, (b) the perceived value by members of staff, (c) the perceived value by parents and (d) the accuracy of the computer record. Consideration will also be given to the reliability of the system hardware and software.

Analysis of first 98 babies, showed that neonates spend a range of 1 to 89 days (median 7) being monitored on computer. An assessment of computer usage can be inferred by the number of comments entered. An average of 22 comments per day (SD 4.84) were entered in the first seven days. Comment numbers remain consistent throughout the seven day period.

We are assessing staff and parental responses to the introduction of this new system by anonymous questionnaire, Table 1 and 2.

Discussion

Computers have common applications in both adult and neonatal intensive care areas. The nature of the neonatal patient however demands special consideration when the design requirements of a neonatal computer monitoring system are being chosen. We have attempted to address these considerations in Edinburgh with the development of a system with three particular areas of use, (1) a real time clinical tool to assist care, (2) a system to continually evaluate neonatal physiology and aid neonatal research, (3) a system that can educate staff.

Clinical real time use

We have begun to noticeably alter patient management in response to physiological trends by using one second trend data:

Apnoea and bradycardia; Staff are now able to detect developing apnoeas and bradycardias, a common neonatal problem, and using real time graphs differentiate between central and obstructive apnoea. Central apnoea is quickly followed by a bradycardia (Fig. 3), whereas obstructive apnoea will be associated with initial tachycardia followed later by hypoxic bradycardia (Fig. 4). This has lead to the correct replacement of partially blocked ET tubes.

Pneumothorax; Pneumothorax has always been regarded as causing an immediate deterioration in a neonate. The computer trend data shows identifiable trends of deterioration often one to two hours prior to the pneumothorax being clinically obvious; increasing heart rate (initially), blood

Table 1. Parent Questionnaire.

Given to all parents whose babies have been monitored by computer in the neonatal unit, 71 analysed (%).

Q1	Have you previously used a computer		Yes	87	No	13	
Q2	Was your baby being monitored by computer		Yes	85	No	15	
Q3	Could you differentiate your baby's computer from the rest of the equipment		Yes	87	No	13	
Q4	How did the computers make you feel						
	more anxious	5	no difference	43	less anxious	52	
Q5	Why do you believe the computer was there						
	for baby's benefit	40	for research	7	for both	53	
Q6	How do you feel about your baby being monitored by computer						
	pleased	43	not worried if it helps	57	worried	0	

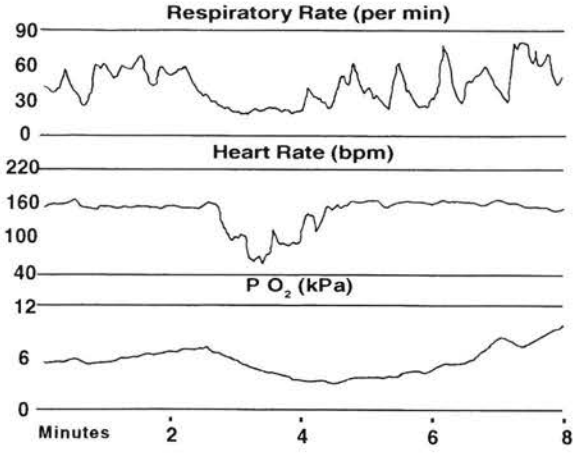

Fig. 3. Central Apnoea.

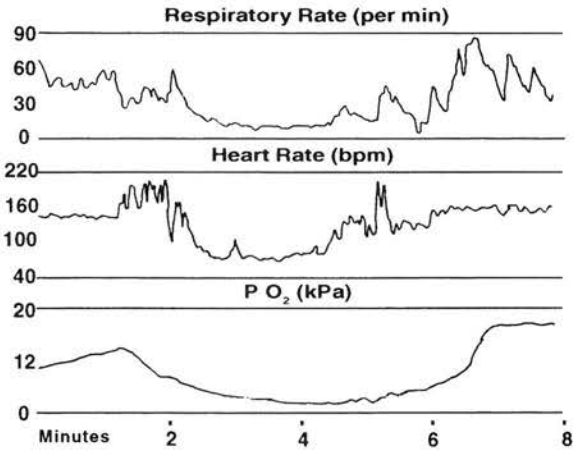

Fig. 4. Obstructive Apnoea.

pressure and tcpCO2 with falling tcpO2 and an erratic respiratory rate (Fig. 2). As pneumothorax is probably a major precipitant of intraventricular haemorrhage in early neonatal life, early identification may have significant effects on the long term outcome of these neonates.

Neonatal distress; A distressed infant has an increased variability of heart rate, respiratory rate and transcutaneous oxygen [12]. Real time trend display of the standard deviation of heart rate and respiratory rate gives a valuable indication of the distress associated with procedures e.g. extubation, and therefore how well the infant is coping.

Neonatal physiological research

Computer monitoring is an invaluable aid in the assessment of the effects of treatments and procedures on the neonate. The effects of handling procedures on transcutaneous carbon dioxide have been demonstrated [13]. TcpCO2 changed more significantly during ET suction than with four other procedures. We are currently assessing different methods of ET suction to minimise the effect of this procedure on the neonate.

Previously undescribed cyclical variation of blood pressure in severely ill neonates have been demonstrated using this network [14]. The effects of these hypertensive blood pressure waves on the pressure passive neonatal cerebral circulation are being investigated.

Trend recorded data as a teaching aid

Recorded data print outs are used to teach both medical and nursing staff the physiological basis of

Table 2. Staff questionnaire.

Given to all members of staff after 6 months computer usage. 62 questionnaires assessed, following replies received (%).								
Q1	Have you previously used a computer				Yes	65	No	35
Q2	For managing the baby, is the computer							
	No help	8	Little help	20	Moderate help	50	Very helpful	22
Q3	How many months was it before you felt familiar with the computers							
	1–2 months	30	3–4 months	30	5–6 months	5	still unfamiliar	25
Q4	Do you feel hassled into using the computer				Yes	10	No	90
Q5	How much has the computer affected your understanding of neonatal physiology							
	Increased it	51	No change	49	Confused me	0		
Q6	Does the computer come up to your expectations				Yes	92	No	8

neonatal intensive care and the patterns of physiology associated with frequent deteriorations. We are increasing staff awareness of the stress of handling on the neonate. The discussion of neonatal deteriorations can be aided by re-appraisal of the physiological changes that occurred both acutely at the time and in the periods prior to the event.

Staff acceptance of the computer system assessed by responses to an anonymous questionnaire have been favourable (Table 2); as in other centres acceptance by doctors has been slower than nurses, but we are beginning to see developing interest. The ability to change graph colours is appealing and this simple introduction to the computer software increases awareness of the system and reduces apprehension. Fear that the system will detract from patient care does not seem to be born out by our initial observations. The ability of the nurses to scroll back through the data and place retrospective comments enables them to use the data in real time to anticipate problems and if busy go back later to describe their actions at that time.

Although our patients can express no opinion on their care, it is important that their parents accept and acknowledge the value of the computer system for the care of their baby. Parent questionnaires show a satisfactory response (Table 1). The consequences of neonatal care on the developing relationship between parents and their child can be quite damaging in the long term [15] and it is important that we are aware of this when increasing the 'intensity' of that care.

Neonatal intensive care can benefit from computer assisted data presentation. We believe it is the flexibility of this system in the manipulation of the graphed data that delineates its success in acute care situations. Other systems have not easily been applied to neonatal care as they have not had the same degree of flexibility [16, 17]. Whilst it is true that most intensive care computer programmes only gain acceptability in the unit in which they are developed [18], 'Mary' has already superseded this by successfully being used as a network in four other UK regional neonatal units.

Neonatal computer systems may well be less developed than adult counterparts, but we believe they are beginning to catch up.

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