SEQUENTIAL MEASUREMENT OF THE MEDIAN NERVE SOMATOSENSORY EVOKED POTENTIAL DURING ISOFLURANE ANAESTHESIA IN CHILDREN

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SUMMARY
We have used sequential measurements of median nerve somatosensory evoked potentials (mnSSEP) in 10 children to estimate the equilibration time of an inhalation anaesthetic agent between alveolar gas, arterial blood and brain. MnSSEP were obtained sequentially every 90–180 s. After control measurements in the absence of isoflurane, the end-tidal concentration was increased stepwise (0.25, 0.5 and 0.75 MAC). Each isoflurane concentration was maintained for 15 min. The point at which the N20 latency reached stability was determined; the mean time between reaching a stable end-tidal isoflurane concentration and this point varied between 5 min 16 s and 7 min 37 s. This technique may be useful in circumstances in which a "steady state" of anaesthesia is important, such as in the determination of MAC or during intraoperative monitoring of evoked potentials. (Br. J. Anaesth. 1992; 69: 567-569)

KEY WORDS
Anaesthesia: paediatric. Monitoring, median nerve somatosensory evoked potentials.

Graded changes in latency and amplitude of the median nerve somatosensory evoked potential (mnSSEP) with changing end-tidal concentrations of inhalation anaesthetic agents have been demonstrated in adults [1-3]. Similar graded changes occur in children with increasing concentrations of isoflurane [4]. In the investigation of this relationship, it is important to ensure that equilibration between alveolar gas, arterial blood and brain concentrations of the volatile agent has occurred before measuring evoked potentials (EP). This is to ensure that a steady state has been achieved before taking measurements. In the majority of such investigations in adults, a period of 10–15 min has been allowed between reaching the desired end-tidal concentration and measuring the EP [1,2]. In the definition of the minimum alveolar concentration (MAC), 15 min should be allowed for this equilibration [5]. This equilibration period is determined mainly by the blood/brain partition coefficient of anaesthetic agents and known values of cerebral blood flow in adults. However, no technique has been devised which can determine this equilibration period for individual patients during administration of a volatile anaesthetic agent. Sequential mnSSEP measurements are used in this study, in an attempt to determine this equilibration period in children.

PATIENTS AND METHODS
We studied 10 children of ASA grade I without neurological deficit. Informed consent was given by their parents or guardians and the project was approved by the Ethics Committee of the Hospitals for Sick Children. A standard anaesthetic technique was used as described previously: in summary, this consisted of oral premedication with trimetazine 4 mg kg⁻¹ and atropine 0.04 mg kg⁻¹ 90 min before induction of anaesthesia with 3 % halothane in nitrous oxide and oxygen [4]. This was followed by atracurium 0.5 mg kg⁻¹ to facilitate oral tracheal intubation. Maintenance of anaesthesia comprised 70 % nitrous oxide in oxygen and caudal extradural anaesthesia using 0.25 % bupivacaine 0.5 ml kg⁻¹. The lungs were ventilated using a Siemens 900B ventilator to produce an end-tidal carbon dioxide concentration of 5% at a rate of 12 b.p.m. Heart rate, ECG, SPO₂, FIO₂ and FİNO₂ and nasopharyngeal temperature were recorded together with the end-tidal concentration of carbon dioxide and isoflurane using a Datex Capnomac. Mean arterial pressure was recorded non-invasively every 3 min using a Dinamap 1846 Vital Signs Monitor. MnSSEP were measured as described previously [4]. After non-stimulus controls, EP were measured 20 min after the induction of anaesthesia, before introduction of isoflurane and at start of surgery. EP were recorded thereafter every 90–180 s in a sequential manner. The end-tidal concentration of isoflurane was noted.
at the end of each sequence. After six control EP in the presence of 70\% nitrous oxide in oxygen, isoflurane was introduced stepwise to reach an end-tidal concentration equivalent to 0.25, 0.5 and 0.75 MAC (corrected for the age of each child, but not for the presence of nitrous oxide [5]). The required end-tidal concentrations of isoflurane were produced using over pressure and held constant for a 15-min period at each value. As in the previous investigation, EEG was recorded continuously [4]. All data were recorded onto magnetic disk and analysed off-line. The end-tidal isoflurane concentrations and N20 latencies for each child were plotted against time. Data were analysed to determine the point of N20 latency stability by inspection, and confirmed using a technique of analysis of the ratio of the variance. For each MAC value, we used measurements of the ratio of the variance of successive groups of N20 latencies from end-tidal stability to the end of the 15-min period. The point at which the smallest ratio occurred was considered the point of N20 latency stability. The time from reaching a stable end-tidal isoflurane concentration to this point could then be determined at each MAC value and for each child.

RESULTS
Satisfactory mSSEP were obtained from all children. Several sequences of EP contained electrical interference from diathermy and were not included in the data. It was not possible to obtain the time to N20 latency stability at 0.25 MAC isoflurane for patient No. 5 because of diathermy interference. The mean arterial pressure did not change by more than 15\% of the control value in any patient and the nasopharyngeal temperature was within 0.5 °C of control values in all children.

The N20 latencies and the end-tidal isoflurane concentrations were plotted against time for each child. A curve and plateau was obtained at each MAC value for both the end-tidal isoflurane concentrations and N20 latencies. A delay between reaching a stable end-tidal MAC and achieving N20 latency stability was observed. Figure 1 shows such a plot for patient nine. The duration from reaching each stable fractional MAC of isoflurane to each stable N20 latency for each patient is shown in table I (related to age) and displayed graphically in figure 2.

DISCUSSION
Anaesthetic agents alter neurophysiological function and it seems reasonable to assume that there is a constant relationship between changes in evoked potential measurements and changes in concentration of anaesthetic agents in the brain [1]. The N20 latency is a convenient neurophysiological reference point for measuring the effects of anaesthetics on the brain in children, although it may not represent the primary site of action. With any inhalation anaesthetic agent, it takes a finite time for equilibration to occur between alveolar gas, arterial blood and the brain. The time taken for the N20 to stabilize after changes in end-tidal anaesthetic concentration is therefore likely to estimate this equilibration period.

The equilibration period is determined mainly by the solubility of the anaesthetic agent and the
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800
700-
600-
500-
400-
300-
200-
100-
0.25 0.50 0.75
MAC isoflurane (%)

Fig. 2. Time to N20 latency stability after achieving each stable MAC isoflurane concentration. Each symbol represents results from a different patient; X = patient No. 9, for whom data were also presented in figure 1.

metabolic rate, which in turn is related to cardiac output and cerebral blood flow. In the determination of MAC, a 15-min period is allowed for this equilibration. This was derived from known values of cerebral blood flow and the blood brain coefficient of anaesthetic agents in adults. Quasha, Eger and Tinker noted that global cerebral blood flow values were used in the determination of this period [5]. However, anaesthetic agents have a major effect in specific regions of the brain which may have a greater blood flow, and therefore it is likely that 15 min is an overestimate of the equilibration period. In children, who have a greater metabolic rate than adults, one would expect equilibration to occur even more rapidly. In most of the patients investigated, the time to equilibration was less than 10 min, which would support this hypothesis.

Knowledge of the equilibration period between alveolar gas, arterial blood and brain of inhalation anaesthetics, and hence the effects of anaesthesia on neurophysiological function, has important practical applications. When investigating effects of anaesthesia on EP, it is essential that measurements are made during a steady state. One solution to this problem is to specify a fixed minimum interval between achieving a desired anaesthetic concentration and taking EP measurements. However, in previous studies, this interval has varied, which makes comparisons of the results less valid. For example, Samara and co-workers [1], Thornton and co-workers [6] and Nogueira and co-workers [7] allowed an equilibration period of 10 min, while Sebel and co-workers [2] allowed 15 min. Moreover, the present study showed considerable variation in the equilibration period, not only between individual children, but also between each fractional MAC of isoflurane; indeed, taking the whole group, the range was between 175 s and 736 s. If this same degree of variability is found in adults, a fixed period of 15 min may not be universally applicable. This would have implications for the determination of MAC of new volatile anaesthetic agents.

When using EP to monitor the integrity of neural pathways during surgery, it is important to be able to differentiate between changes caused by surgery and the effects of changes in anaesthesia and other non-surgical factors. More certain knowledge of the time taken to reach anaesthetic equilibration may therefore improve accuracy and confidence when EP changes are interpreted, particularly during critical periods of an operation.

The technique of sequential measurement of mNSEEP to determine the equilibration period described here could be applied to EP measurement in various situations in the operating theatre. Incorporating this technique into an on-line information system would enhance intraoperative EP monitoring and neurophysiological studies of the effects of anaesthetic agents.

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REFERENCES