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(Accepted 24 April 1980)

Value of repeated blood pressure measurements in children—the Brompton study

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Summary and conclusions

Systolic blood pressures were measured in 1797 infants aged 4 days and then repeated at 6 weeks, 6 months, 1 year, and then yearly until 4 years of age. The mean pressure rose from 76 mm Hg at 4 days to 96 mm Hg at 6 weeks but did not vary appreciably between subsequent measurements. Serial correlation coefficients of blood pressure adjusted for weight and degree of consciousness were calculated, comparing measurements at each age. At ages under 1 year the correlation coefficients were relatively weak, though most were significant ($r < 0.2$). As the children grew older these serial correlations became stronger, so that the correlation coefficient in blood pressure between ages 3 and 4 years was 0.47.

Introduction

Casual measurements showing raised blood pressures in adults, a potent risk factor for cardiovascular disease, are of considerable importance. Values usually continue to be raised when the blood pressure is measured subsequently. The correlation coefficient of repeated blood pressure measurements in adults is between 0.6 and 0.7.¹ Zinner *et al.*,² comparing blood pressure measurements 4-8 years apart, have shown that such a correlation coefficient is achieved by about 18 years of age. Though we found significant correlations in blood pressure in a group of infants aged between 4 days and 6 weeks,³ the correlation coefficient was weak ($r = 0.17$). We have therefore continued to measure blood pressure in infants initially aged 4 days to determine at what age the correlations become stronger.

TABLE 1—Numbers of children and blood pressure measurements, and causes and numbers of exclusions at ages 4 days to 4 years

	4 Days	6 Weeks	6 Months	1 Year	2 Years	3 Years*	4 Years*
Initial No of children	1895†	1797	1777	1738	1681	122	11
No moved from area or withdrawn	88	20	34	57	77	1	1
Deaths	10	0	5	0	2		
Total remaining	1797	1777	1738	1681	1602	1050	346
Failed to contact or too uncooperative	39	32	27	47	146	120	20
Ill at time of measurement	16	104	153	188	153	108	34
No of measurements analysed	1742	1641	865‡	1341‡	1303	822	292

*Data incomplete.

†Excluding 105 born prematurely.

‡Excluding measurements with 5 cm cuff (693 at 6 months and 105 at 1 year).

These observations suggest that "tracking" for blood pressure starts at about 1 year and is much stronger by 4 years. Taken in conjunction with the findings of other long-term follow-up studies in older children, this suggests that children develop blood pressures indicative of their adult values between 1 and 4 years.

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Subjects and methods

POPULATION

The parents of 2000 eligible infants born consecutively at Farnborough Hospital, Kent, were approached for permission to enter their children to the study. The criteria for entry were that the parents were residents of the London borough of Bromley and did not expect to leave the area within six months. We excluded 105 infants born before 38 weeks' gestation (table 1) but will report our findings on these separately. The parents of 88 infants refused to co-operate, and 10 infants born at or after 38 weeks' gestation died in the neonatal period. Thus 1797 infants, including 32 born after twin pregnancy and recruited between 1 May 1975 and 21 June 1977, were available for study. Of the 1797 infants, 1734 (96.5%) were white.

Some children subsequently moved from the area or were with-

drawn by their parents; table I shows the number remaining in the study at each measurement age up to 2 years. Children entering the study towards the end of the recruitment period had not attained 3 years of age, but we give the data on the first 1050 3-year-olds and the first 346 4-year-olds.

BLOOD PRESSURE MEASUREMENTS

Systolic blood pressure was measured as described^{4,5} at the ages of 4 days, 6 weeks, 6 months, and yearly from 1 to 4 years by one of four research nurses using the Parks Doppler ultrasound system⁶ and random-zero sphygmomanometer.⁷ This equipment is not suitable for measuring diastolic blood pressure. Most measurements at 4 days, and all subsequent measurements, were made in the children's homes; on each occasion the children were weighed, usually on bathroom scales, as described.⁴ Individual families were visited at about the same time of day.

ANALYSIS OF DATA

Table I shows the population studied and the number of measurements made at each age up to 4 years. At 6 months and 1 year, 693 and 105 measurements respectively were excluded because they were made with a 5 cm cuff, which gave artificially high values.^{4,5} At the time of each measurement a child was categorised as ill if taking

Table III shows the correlation matrix of adjusted blood pressures for all ages. Although there were significant correlations between blood pressures measured at ages under 1 year and later measurements, none of the correlation coefficients for these results was greater than 0.2. Blood pressures at 1 year, however, were correlated with all subsequent measurements with coefficients greater than 0.2, and the strongest correlation coefficient (0.47) was between blood pressures measured at 3 and 4 years.

Discussion

We present these data even though they are incomplete for children aged 3 and 4 years because of their importance and because the numbers at these ages are still substantial (822 and 292 respectively). Thus the conclusions will probably not change when the remaining observations on the 3-year-olds and 4-year-olds are available.

The tendency of subjects to maintain their relative position within the distribution of blood pressure as a function of age has been defined as tracking. We suggest that children start tracking for blood pressure at the age of about 1 year and that the tracking is stronger by 4 years. Rosner *et al* showed tracking from the age of 5 years.¹ They also showed that the correlation coefficient of blood pressure measurements repeated at four-year intervals

TABLE II—Mean ($\pm$ SD) systolic blood pressures (mm Hg) of children awake at ages 4 days to 4 years

	4 Days	6 Weeks	6 Months	1 Year	2 Years	3 Years	4 Years
Blood pressure ..	76 $\pm$ 9	96 $\pm$ 11	93 $\pm$ 13	94 $\pm$ 11	96 $\pm$ 11	97 $\pm$ 9	98 $\pm$ 9
No of children ..	171*	1135†	865	1341	1303	822	292

*Only 10% of infants were awake at 4 days.

†A total of 69% of infants were awake at 6 weeks.

TABLE III—Serial correlations in children's blood pressure, corrected for weight and degree of consciousness, between ages of 4 days and 4 years. Numbers in parentheses are numbers of paired observations compared at each age

	6 Weeks	6 Months	1 Year	2 Years	3 Years	4 Years
4 Days ..	0.17*** (1594)	0.09** (845)	-0.01 (1303)	-0.05 (1265)	-0.04 (797)	0.10* (287)
6 Weeks ..		0.04 (807)	0.05 (1244)	0.02 (1212)	0.10** (765)	0.18*** (280)
6 Months ..			0.12 (704)	0.12* (652)	0.18*** (766)	-0.03 (274)
1 Year ..				0.26*** (1056)	0.27*** (679)	0.23*** (223)
2 Years ..					0.35*** (710)	0.32*** (250)
3 Years ..						0.47*** (259)

*p<0.05; **p<0.01; ***p<0.001.

medicine prescribed by a doctor and the measurement excluded, since illness might have affected the blood pressure. In the 1050 3-year-olds and 346 4-year-olds 108 and 34 measurements respectively were excluded because of illness.

In children aged 4 days, blood pressure is on average 4.4 mm Hg higher in those awake (eyes open at the start of the measurement) than in those asleep (eyes closed).^{4,8} At 6 weeks of age the average difference is 7.0 mm Hg.⁴ The results in the 90% of the children who were asleep at 4 days and those in the 31% who were asleep at 6 weeks were adjusted accordingly to correct their blood pressures to those of the awake state so that comparisons of values measured at different ages could be made. Blood pressure is also related to weight in children.⁴ We therefore adjusted blood pressure measurements at all ages accordingly.

Results

Table II gives the mean systolic blood pressures from ages 4 days to 4 years. The largest change in blood pressure (from 76 to 96 mm Hg) occurred between 4 days and 6 weeks.

between the ages of 5 and 75 years rises with age from 0.25 to about 0.65. Clarke *et al*, in the Muscatine study, reported a two-year correlation in repeated blood pressure measurements of 0.27 to 0.35 (for boys and girls) from 5 to 7 years of age.⁹ Our two-year correlations at 1 and 2 years are similar (0.23 and 0.32 respectively) and we, therefore, believe that tracking can be shown in children aged under 5 years.

We originally reported the correlation in blood pressures between 4 days and 6 weeks as evidence of tracking,³ but this has not been confirmed as the children have grown older. Blood pressures at 4 days were not correlated with subsequent blood pressure measurements. Levine *et al* reported significant tracking in the first year of life with a correlation coefficient of 0.34 between the ages of 6 months and 1 year.¹⁰ Their report, however, did not include measurements in children older than 1 year.

We believe that tracking starts between the ages of 1 and 5 years, and that by 4 years the correlation coefficient in repeated blood pressure measurements of 0.47 is approaching the adult value of 0.65. Further studies may show to what degree of

confidence these data can be used to predict adult blood pressures, and therefore those at risk from hypertension as adults, when tracking starts between 1 and 5 years.

M de Swiet and the nurses helping in this study were supported by the Medical Research Council. We are grateful to Susan Cowley for help in preparing the manuscript.

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(Accepted 28 April 1980)

Adverse effect of plasma exchange on anti-D production in rhesus immunisation owing to removal of inhibitory factors

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Summary and conclusions

Intensive plasma exchange was used to reduce the maternal anti-D concentration in a case of severe rhesus haemolytic disease. Initially the concentration fell from 30 to 4 IU/ml, but after six exchanges it increased to 490 IU/ml despite continued exchanges, and intrauterine fetal death eventually ensued. The increase in the rate of maternal anti-D production coincided with, and may have resulted from, removal of plasma immunoregulatory factors that inhibited in-vitro lymphocyte functions.

These results suggest that the role of plasma exchange in haemolytic disease of the newborn is more complex than simply removing the antibody and that further investigations are needed.

Introduction

Plasmapheresis and plasma exchange have been used to reduce maternal anti-D concentrations in severe haemolytic disease of the newborn with differing degrees of clinical success.^{1,2} Plasma exchange may be more desirable than plasmapheresis alone, since plasmapheresis merely removes plasma while plasma exchange replaces the patient's plasma with normal plasma, replenishing plasma components and diluting maternal IgG anti-D relative to total plasma immunoglobulin.^{3,4} Pregnancy-associated plasma factors, however, will not be replaced when normal plasma is used for exchanges. Such factors might be important—for example, in maintaining maternal immunological tolerance of the "fetal allograft." We report here our observations of the effects of plasma exchange on maternal anti-D

and serum lymphocyte-regulating activity in a case of severe haemolytic disease of the newborn.

Methods

Plasma exchanges were carried out with a continuous-flow cell separator (Aminco Celltrifuge). During each exchange an average of 4 l of maternal plasma was exchanged for an equal volume of normal donor fresh-frozen plasma. Maternal serum was obtained from clotted blood samples taken before and after each exchange: the serum anti-D concentration was measured by routine autoanalyser techniques,⁵ and serum for lymphocyte studies was decomplexed (56°C for 30 minutes) and stored at -40°C for retrospective investigations.

Antibody-dependent cell-mediated cytotoxicity was determined by using column-purified peripheral blood lymphocytes as effectors (K-cell activity) and Rh(D)-positive human red cells as targets (ratio of effector to target 10:1) in the presence of test anti-D sera as described.⁶

The effects of sera on lymphocyte proliferative responses to mitogens were determined by modifications of previously described culture techniques.⁷ Lymphocytes were cultured at 0.2×10^6 /l in 150 μ l volumes on round-bottom microculture plates (24-ARTL, Flow Labs) and stimulated by concanavalin A ($\times 3$ recrystallised in ammonium sulphate, Miles Labs) at 16 mg/l. Cultures were supplemented with 20% decomplexed human serum: control cultures contained pooled normal human serum alone, while test cultures contained a one to one mixture of pooled normal human serum to test serum (that is, 10% v/v respectively of final cultures). Responses were measured by the amount of tritiated thymidine incorporated into lymphocytes and results expressed as a percentage of the lymphocytes' response in the control culture (pooled normal human serum alone). The results shown were obtained by using maternal lymphocytes (from a sample obtained two months after intrauterine death) for the studies of antibody-dependent cell-mediated cytotoxicity and proliferation.

Case report—A 36-year-old group O, Rh-negative (cde/cde) woman presented in the 27th week of gestation of her third pregnancy with detectable serum concentrations of anti-C+D. Her husband's blood group was B, R₁R₂ (CDe/cDE). She had developed anti-C+D during her second pregnancy, when the baby was Coombs positive and mildly jaundiced but required no postnatal treatment. At presentation her antibody concentrations were: antiglobulin titre

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