Glucose metabolism in children during the first day after burn injury

C. CHILDS*, D. F. HEATH*, R. A. LITTLE* & M. BROTHERSTON†

* NWIRC (MRC Trauma Group), University of Manchester, Stopford Building, Manchester and † Birmingham Accident Hospital, Bath Row Birmingham

SUMMARY

Plasma and blood metabolites were measured in 31 children over the first day after burn injury. In 14 of them blood glucose peaked, rising within 1–4 h to 10–20 mmol/l and then falling, by 4–8 h, to 5–10 mmol/l. Usually the peak value preceded treatment and the fall occurred during infusion of dextrose-saline. Peak incidence was independent of burn severity. There was no evidence of similar peaks in children or adults with other injuries, or in 8 adults with burn injuries; though high glucose levels have been reported in children with head injuries.

Lactate, non-esterified fatty acids, insulin, cortisol, epinephrine and norepinephrine were also measured. Values in the first 4 h were similar to those reported in adults with other injuries, except for lactate, which rose less in the children.

Unexpectedly, the hyperglycemia in the children with burns was poorly related to epinephrine concentration at all times to 24 h. Insulin resistance probably developed within the first hour or two; but from 8 h did not seem to depend on synergism between epinephrine and cortisol.

INTRODUCTION

There appeared to be no information on the acute metabolic response to burn injury in children. Since one of us (C.C.) was working in a children's hospital where it was customary to take a number of blood specimens to monitor resuscitation after burn injury, the opportunity was taken to measure metabolites and hormones in such samples. The first few measurements of glucose concentration revealed a pattern that has not been reported before, namely, a rapid rise to very high values, followed by a fall within about 8 h to values similar to those found in adults shortly after other injuries. Therefore, a more detailed study was undertaken.

What could be done was limited by amount of blood available; but useful numbers

---

Correspondence: Dr Charmaine Childs, North Western Injury Research Centre, University of Manchester, Stopford Road, Manchester M13 9PT, U.K.

of glucose, lactate, NEFA (non-esterified fatty acid), insulin, cortisol, and catecholamine concentrations were obtained.

Ideally, comparisons should have been made with children with other injuries and adults with burns. This was only possible to a limited extent. For children with other injuries there were some published data (Parish & Webb, 1988), and more in our database. An attempt was made to obtain data on adults with burns, and these are reported. It proved, however, difficult to match severities, the adults tending to have either more severe burns (over 65% of body surface) or much less severe ones (under 15%). Consequently most comparisons with adults are made with those with non-burn injuries. This may not matter. The acute effects on glucose metabolism of burn and other injuries are very similar in animals (Heath & Corney, 1973; Heath, 1986), and, as far as can be judged from the sparse data, in humans also.

SUBJECTS AND METHODS

Ethical permission

The study was carried out with the prior approval of the Salford (U.K.) Area Ethical Committee.

Subjects

The children were aged 7 months to 12 years and the adults 17 to 65 years. Children with burn injury were patients at Booth Hall Children's Hospital, Manchester, U.K., as were child controls, from whom blood specimens were taken 3−4 h after food and before pre-medication for minor elective surgery. Adults with burn injury were patients at The Accident Hospital, Birmingham, UK; Hope Hospital, Salford, UK; or The Yorkshire Regional Burns Unit, Wakefield, UK. The data for adults and children with other, non-burn, injuries were taken from the database of the MRC Trauma Groups (Hope Hospital), with the exclusion of those likely to have additional disturbances of glucose metabolism, i.e., those with diabetes, or who died within a day, or with blood ethanol above 5 mmol/l. Control adults were healthy individuals of both sexes, from whom blood specimens had been taken 2−10 h after food as part of other studies over the period 1977−1988.

Injury severity was graded by the Injury Severity Score, ISS (Baker *et al.*, 1974), calculated from the Abbreviated Injury Scale (AIS). Burns were graded by the 1985 version of the AIS, other injuries by the 1980 version. However, the two scales are very similar for the blunt injuries suffered by nearly all the patients without burns (Copes *et al.*, 1988a). Since children with burns had no other injuries, their ISS values were the squares of the AIS values, namely 1, 4, 9, 16 and 25. Those with minor burns (ISS = 1) were excluded, and those with scores of 16 and 25 were combined into a single group. For comparison with the three resulting groups, patients with non-burn injuries were grouped initially by ISS values in the bands 4−8, 9−15 and > = 16, in accordance with the suggestions made by Copes *et al*. (1988b).

Resuscitation of children with burns

The first blood specimens were taken just before or very shortly after the start of resuscitation.

Later specimens were taken during infusion of fresh frozen plasma (FFP), in amounts given according to the 'Mount Vernon' formula (Muir & Barclay, 1962), with 5% dextrose in 0·45% NaCl. The treatments varied somewhat from patient to patient, but in general terms all children received dextrose-saline at about 4 ml/kg.h from the time the first blood specimen was taken until 12 h after injury. In addition, those with ISS scores of 4 and 9 also received FFP at 1−2 ml/kg.h and those with ISS scores of 16 and 25 FFP at 4−9 ml/kg.h. Rates were often halved at 12 h.

Analytical methods

Blood glucose was measured in specimens from children and some adults with burns using a glucose oxidase method (YSI Glucose Analyzer, Clarendon Scientific, Yellow Springs Instrument Co., Ohio, U.S.A.). Other measurements of glucose (using hexokinase) and all measurements of other metabolites were made on perchloric acid extracts of plasma. Lactate was measured enzymatically using a Cobas Bio (Roche Instruments, Welwyn Garden City, U.K.) insulin (Morgan & Lazarow, 1963) and catecholamines (Frayn & Maycock, 1983) by published methods; and cortisol by a radioimmunoassay kit (Immunodiagnostics Ltd., UK). A few of the very high glucose concentrations found in blood were confirmed by measurements on stored plasma. Glucose concentrations measured in plasma were divided by 1·10 (the ratio of the water contents of plasma and blood) to convert them to 'blood' values.

Statistics

Since several sets of data were neither normally nor log-normally distributed, all data, except in Figure 1, are shown as medians with the ranges that included the central two thirds of the values. This 2−5 sextile range corresponds roughly to the standard deviation range for data with a normal distribution. When the sample size was less than 6 the total range is shown. Inter-group comparisons were carried out using the Wilcoxon rank sum test, and simple correlation using Kendall's rank correlation test (Bradley, 1968). Multiple regression analysis was carried out using SPSS (Statistics Package for the Social Sciences). Since data were not normally distributed, estimates of probability from this procedure must be treated with caution.

RESULTS

Concentrations in controls

Median values were not significantly different in control children and normal
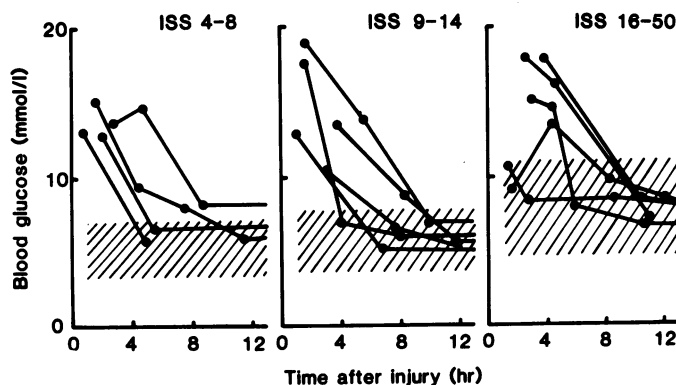
Fig. 1. Blood glucose concentrations in individual children after burn injury compared with those in adults with other injuries.
The time course is shown up to 12 h after burn injury for those children in whom one value exceeded 10 mmol/l. In some children values were obtained after 12 h. In these cases the lines are extended beyond 12 h. The values for adults with other injuries are shown as bands containing 90% of the measured values up to 24 h, as shown in Table 3. Values in adults were not significantly variable with time.

adults except for glucose and cortisol (Table 1). For glucose the differences in medians and ranges were very small, and seem unlikely to account for the differences in the response to injury. Cortisol was measured in specimens taken at similar times of day in children and adults — 11 55 hr (10 30−17 05 hr) and 11 50 hr (9 45−16 10 hr) (medians and ranges) respectively — and differences in timing could not account for the differences in values.

Blood glucose after injury

In 14 of the 31 children in whom blood glucose was measured in both of the periods 1·0−3·9 and 4−7·9 h after burn injury at least one value during the first

Table 1. Metabolite and hormone concentrations in blood or plasma of controls.

		Children		Adults		
	Units	Median	Range	Median	Range	P
Glucose	mmol/l	4·4(17)	3·7−5·2	4·2(42)	3·5−4·4	<0·01
Lactate	mmol/l	1·20(1)	−	1·18(42)	0·91−1·57	n.s.
NEFA	mmol/l	0·52(19)	0·13−0·83	0·50(42)	0·22−0·87	n.s.
Insulin	mU/l	11·8(11)	3−21	10·3(33)	7−28	n.s.
Cortisol	μmol/l	0·19(24)	0·16−0·24	0·33(33)	0·23−0·59	<0·001
Epinephr.	nmol/l	0·31(17)	0·10−0·57	0·17(22)	0·10−0·37	n.s.
Norepinephrine	nmol/l	1·6(19)	0·9−2·9	1·3(23)	0·6−2·0	n.s.

Concentrations of glucose are those in blood, concentrations of other compounds those in plasma. The number in each group is shown in parentheses. Some epinephrine concentrations were too small to measure, and were assigned the value 0·10 nmol/l. Ranges are as described in the Methods section. Not significant (P > 0·05), n.s.

period was higher than 10 mmol/l. All of these were among the 27 children less than 8 years old. The proportion with such values was much higher at every injury severity than in adults with non-burn injuries (Table 2). The high proportion at the lower severities is particularly notable.

In these 14 children there was a peaked response (Fig. 1), the concentrations falling by about 8 h to constant values. The peak value was usually before the start of resuscitation. The subsequent fall took place during infusion of dextrose-saline and FFP.

In Figure 1 the glucose levels in adults with non-burn injuries are indicated as time-invariant bands containing 90% of the values over the whole period. The justification for this is shown in Table 3. Within each ISS range there was no significant trend with time up to 24 h. This is itself evidence against any peak response in these patients. In 8 of these patients serial measurements were also made, with one in the period 1−4 h after injury and another at least 2 h after the first. The greatest fall was only 2·4 mmol/l.

There was little evidence from our data of a peaked response in the other groups. (Published data from children are considered in the Discussion section). In the 8 adults with burns in whom serial measurements were made concentrations

Table 2. Proportions of children with burns and adults with other injuries in whom blood glucose exceeded 10 mmol/l during the period 1·0−3·9 h after injury.

	ISS	4−8	9−14	≥16
Adults		0/59	1/112	5/26
Children		4/10	5/13	5/8
P		<0·001*	<0·001*	<0·05†

* Fisher's exact test; †Chi^2 with correction for continuity

Table 3. Blood glucose concentrations in adults with non-burn injuries. Values are shown as medians (N), with the 2−5 sextile ranges in mmol/l (see the Methods Section). When two or more measurements were made during a period in a single patient the value nearest to the centre of the time range was used. No differences within any range are statistically significant (Wilcoxon rank sum test, P < 0·05).

| Time (hr)	1·0−3·9	4·0−7·9	8−24
ISS			
4−8	5·2(59)	5·0(8)	5·0(6)
	4·5−5·9	4·3−5·6	4·3−6·3
9−14	5·8(112)	5·2(15)	6·2(14)
	4·8−7·8	4·2−6·7	4·9−6·7
≥16	8·0(26)	7·7(4)	7·1(10)
	6·1−10·4	3·9−8·6	5·4−8·5

varied up and down, but the greatest change before 8 h was only 3 mmol/l (Fig. 2). Only a single measurement was made in each child with other injuries, but it was made 0·5−2·5 h after injury, when a peak should have been revealed by a high concentration. Only one of the 7 children under 8 years old (ISS 4−13) had a concentration in blood above 10 mmol/1·2 mmol/l), and none of the 17 older children, 7 of whom were very severely injured (ISS 16−35).

From 8 h the glucose concentrations in children with burns nearly remained constant up to 24 h at levels that were usually well above normal, and similar to those found in the other groups shortly after injury (Table 4). (In calculating the values for children with burns only one value per child was used, that nearest 16 h, the centre of the period.) Concentrations in adults with burns were higher than in adults with other injuries at lower severities, but similar at ISS $\geqslant$ 16. For completeness Table 4 also shows values in children with burns at earlier times. The inclusion of peak values increases means and ranges.

Other metabolites and hormones in children with burns.

Median values at ISS 4 and ISS 9 were never significantly different at the 5% level, so these two groups were combined (Table 5). Group sizes at ISS $\geqslant$ 16 were small, but the results are shown, since they are the only ones on children with burns.

Burn injury raised NEFA, cortisol and catecholamine levels, the latter very variably. Lactate levels were initially raised somewhat above control adult levels, but in most children had returned to normal by 8 h. Insulin levels were unchanged, while NEFA, cortisol and catecholamine levels rose, the latter very variably. The median cortisol level showed a marked dip at 4−8 h, which was not related to time of day.
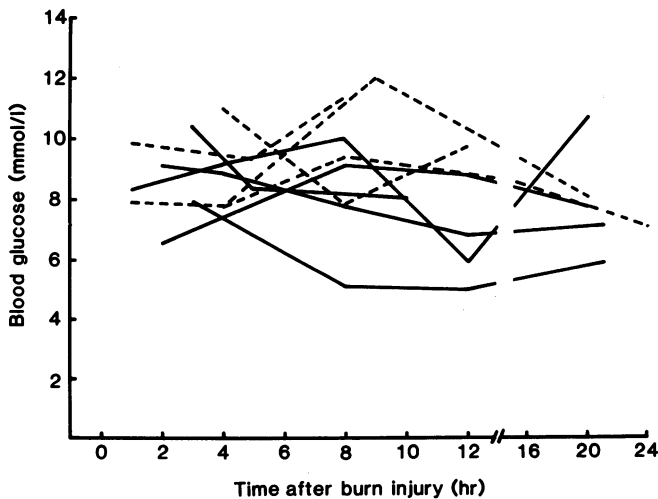
Fig. 2.   Blood glucose concentrations in adults with burn injuries from whom serial blood specimens were taken.
Results are shown as ————, ISS 9, and − − − −, ISS 16 and 25.

Table 4. Comparison of blood glucose concentrations at various times after burn injury in children with those shortly after injury in other groups. Conventions, and values for 'Other adults', are as in Table 3.

Group	Time (hr)	ISS range: 4−8	9−14	≥16
Children with burns	1·0−3·9	9·7(10)* 7·5−13·6	8·9(15)* 6·3−12·9	10·0(8)* 9·1−17·8
	4·0−7·9	7·1(8)* 5·7−9·3	6·5(11) 5·4−8·6	9·3(7) 7·9−13·6
	8−24	6·1(11) 5·0−7·8	5·6(14) 4·9−6·8	6·7(9) 5·8−8·2
Other children	0·5−2·5	7·2(2) 7·0−7·4	6·7(15) 6·5−7·1	8·8(7) 6·5−9·7
Adults with burns	1·0−4·0	6·5(1) −	8·3(5)* 7·9−10·8	9·4(4) 7·8−11·0
Other adults	1·0−3·9	5·2(59) 4·5−5·9	5·8(112) 4·8−7·8	8·0(26) 6·1−10·4

* P < 0·01 against 'Other adults'. Values from all children with burns are included, not only from those with values during each of the periods 1·0−3·9 and 4−7·9 hr. Numbers are therefore slightly greater than in Table 2.

Table 5. Plasma metabolites and hormones in children with burns.

Time (hr) ISS range	1·0−3·9 4−9	16−25	4·0−7·9 4−9	16−25	8−24 4−9	16−25
Lactate mmol/l	2·2(11) 1·7−2·6	1·6(3) 1·1−1·6	1·5(9) 1·0−1·9	1·0(4) 0·7−2·7	1·2(10)[†] 1·0−1·8	1·1(4) 0·9−2·4
NEFA mmol/l	0·81(17) 0·37−1·15	0·85(4) 0·36−1·53	0·88(12) 0·62−1·00	0·90(3) 0·53−1·15	0·74(16) 0·49−1·14	0·92(3) 0·44−1·11
Insulin mU/l	12(13) 9−21	10(2) 9−12	12(9) 6−22	17(2) 12−21	7(12) 5−14	24(2) 14−33
Cortisol μmol/l	0·77(20) 0·61−1·20	0·84(5) 0·75−1·11	0·36(13)* 0·27−0·70	1·03(3) 0·60−2·02	0·58(20) 0·16−1·04	0·69(5) 0·58−1·29
Epinephrine nmol/l	2·5(11) 0·4−6·5	15·5(5) 0·3−25·0	1·0(12) 0·7−2·0	4·1(2) 0·2−8·1	1·1(20) 0·3−2·0	3·2(5) 0·4−7·4
Norepinephrine nmol/l	2·3(13) 2·0−5·0	4·1(5) 0·8−12·5	2·6(12) 1·6−3·0	4·9(2) 1·2−8·6	3·2(20) 2·0−9·7	5·1(5) 1·0−7·6

Statistical significances against values in the first time range are denoted by † and * for p<0·05 and p<0·01 respectively

In some of the children with burns 3−6 measurements were made during the first 24 h, so that concentration-time curves could be sketched. Lactate levels always fell (14/14 children); NEFA and insulin levels fluctuated, with only one marked change (a rise in insulin in one child); and cortisol levels sometimes fell

steadily (6/22) but more often passed through a minimum at 4–8 h (10/22). Catecholamine levels fluctuated wildly, but tended to fall with time.

Correlations in children with burns

For brevity concentrations are denoted by square brackets. All the data within each period were used, i.e., when there was more than one measurement all were included. There were no such cases in the first period, and few in the second, but numbers in the third period were sometimes nearly doubled.

The results from simple correlations are shown in Table 6. [Glucose] was only weakly positively correlated with [epinephrine] during the first period, not at all during the second, and just significantly on a 1-tailed test during the third. There was little evidence of inhibition of insulin output by epinephrine, and from 8 h the two were positively correlated. [Glucose] and [cortisol] were never more than weakly correlated, but [insulin] was positively correlated with [glucose], weakly from 4 h and strongly from 8 h.

The weakness of the correlation between [glucose] and [epinephrine] casts doubt on the obvious explanation of the peak values, namely that they were caused by high [epinephrine], a reduction in which caused the subsequent fall in [glucose]. There was, in fact, only a marginally significant correlation ($P < 0.05$) between the fall in [glucose] and the fall in [epinephrine].

The strong correlation from 8 h between [glucose] and [insulin] (Kendall's tau = 0.54) accompanying persistent hyperglycemia suggests that by then insulin resistance had developed.

Blood glucose concentration, however, settles at the value at which the factors

Table 6. Simple correlations between concentrations of metabolites and hormones in children with burns and adults with other injuries.

| Time range (hr) | Probabilities | | | | | |
| | 1.0–3.9 | | 4.0–7.9 | | 8–24 | |
Compounds	Child	Adult	Child	Adult	Child	Adult
Glucose v. insulin	n.s.	<0.001	<0.05	<0.01	<0.001	<0.001
	(−,24)	(+,150)	(+,12)	(+,19)	(+,22)	(+,29)
Glucose v. cortisol	n.s.	n.s.	n.s.	<0.01	<0.05	n.s.
	(−,24)	(+,154)	(+,41)	(+,19)	(+,24)	(+,33)
Glucose v. epinephrine	<0.01	<0.05	n.s.	—	<0.05	n.s.
	(+,17)	(+,11)	(=,14)		(+,38)	(+,10)
Insulin v. epinephrine	n.s.	n.s.	n.s.	—	<0.01	—
	(−,10)	(−,10)	(+,9)		(+,20)	
Norepinephrine v. epinephrine	n.s.	n.s.	<0.05	—	<0.001	<0.01
	(+,17)	(+,17)	(+,14)		(+,38)	(+,10)

All values were used in those instances in which more than one measurement was made in a child within a period. Tests were by Kendall's rank correlation. Results are presented in the form P-value (sign of correlation, number of pairs). P > 0.05 is shown as n.s. significant by 1-tailed tests).

favouring glucose uptake balance those favouring output. Since output is increased by epinephrine and glucagon, while uptake is inhibited by epinephrine and cortisol [glucose] should be positively correlated with [cortisol], [epinephrine] and [glucagon]. Since insulin output is increased by glucose but suppressed by epinephrine, which also increases glucose output, no strong correlation is expected between [glucose] and [insulin]. The results in Table 6 did not accord with this view. It was, however, conceivable that underlying relationships may have been obscured by the simplicity of the analysis. Therefore, multiple regression analysis was carried out.

The effects of glucagon had to be assumed constant, since it had not been measured. The effects of epinephrine were tested using either [epinephrine] or $\sqrt{}$ [epinephrine] as independent parameters. The latter gave a more symmetrical statistical distribution than the usual logarithmic transform, and had the advantage that all values were positive. Two equations were used:

[Glucose) = A + B[Insulin] + C[Cortisol] + D[Epinephrine] .. (1)
[Glucose] = A + B[Insulin] + E[Cortisol] $\sqrt{}$ [Epinephrine] ... (2)

where A, B, C, D, and E are the parameters to be evaluated. Eqn(2) represents the synergistic action of epinephrine and cortisol.

In all three periods the only significant dependence was on [insulin].
When terms in [insulin] were removed there was a weak relationship with [epinephrine] ($P < 0.02$, DF = 33) after 8 h, but none with [cortisol] or [cortisol].$\sqrt{}$ [epinephrine].

The changes in [glucose] during the fall from peak values (>10 mmol/L) were analysed similarly by relating them to the changes in [insulin], [cortisol] and [epinephrine]. The only significant dependence was on change of [epinephrine], and then only when the terms in [insulin] and [cortisol] were removed from the regression equation.

DISCUSSION

The immediate effects of burn injury in children showed some differences to those in adults with other injuries (Stoner *et al.*, 1979; Vitek *et al.*, 1979; Frayn *et al.*, 1985). In the children lactate levels rose less, cortisol levels were not so well sustained and epinephrine levels appeared more variable (Frayn *et al.*, 1985), but the most marked difference was the peaking of glucose levels in half of the children.

Both the peak values and their incidence were probably underestimated, since it is unlikely that the timing of a blood specimen would have coincided with a peak, and in children in which the first measurement was not made until 2−3 h after injury the peak may have been missed.

In 15/36 of a group of children with closed head injury very high glucose levels, averaging about 18 mmol/l, have also been reported (Parish & Webb, 1988). Mortality was not related to glucose level. Such levels were rare (2/37) in children with non-head injuries of similar severity. (We have converted levels in serum to levels in blood.) The data were only presented in a very condensed statistical form,

and the time that the high levels persisted can only be stated as less than 24 h, with the highest values usually after 4 h, unlike in children with burns. The general pattern, however, is not unlike that which we have found. About half the group of children with burns showed high levels, and the proportion was independent of severity. In children with non-burn injuries, who were also as it happened without head injuries either, levels were much lower. Thus many children can respond to non-fatal injuries by producing very high glucose levels, but the response seems only to be elicited by burn and head injury. It is not known at what age after 8 years the capacity is lost.

Analysis of data on adults with non-burn injuries in our database showed no tendency for those with head injury to produce unusually high glucose levels; and in adults in general levels above 10 mmol/l were rare after non-fatal injury, whether burn or non-burn, and there was little evidence of peaking. The distinction, therefore, appears to be between children and adults.

Further discussion of children is confined to those with burns, in which the time-course of the response is clearer.

The source of the glucose at the peak could have been hepatic glycogen. There is no need to postulate enhanced gluconeogenesis, for which there is evidence in injured adults (Barton, 1981; Saccà *et al.*, 1983), but which seems less likely in the children in many of whom lactate levels were barely above normal (For calculation organ weights at various ages were taken from Scientific Tables: Pharmaceutical Geigy and glycogen in liver is expressed as mmol glucose/kg liver. The glucose distribution volume was taken to be 250 ml/kg, and the liver to body wt ratio as 4·5%.). Hepatic glycogen in post-absorptive adults ranges from 50−400 mmol/kg liver (Nilsson, 1973). Since few of the children were, presumably, postabsorptive, concentrations in their livers were probably at least as high (Shelley, 1961). The highest blood glucose concentration measured, 16 mmol/l blood above the control value, could be accounted for by a release of only 90 mmol/kg liver. The brain would require a further supply equivalent to 7−10 mmol/h.kg liver (Gottstein *et al.*, 1965)).

In the absence of insulin resistance (insensitivity), however, the liver would also have had to supply glucose to balance the increase in uptake caused by the raised glucose levels. The hepatic output required can be calculated from the measured glucose and insulin concentrations if the kinetics of glucose uptake are the same in children as in the adults in which they have been studied (Jackson *et al.*, 1986; Yki-Järvinen *et al.*, 1987). In some children, in whom glucose levels stayed above 10 mmol/l for over 8 h, the requirement would have exceeded 200 mmol/kg, after allowing for the dextrose infused. Over-all, it is likely that insulin resistance had developed within an hour or two, as it does in adult humans (Little *et al.*, 1981) and animals (Frayn 1976; Heath 1986).

Why glucose levels shortly after burn injury in children should be so much more variable than in adults, and why the highest levels should fall, is far from clear. Some features are explicable if hepatic glycogenolysis is more readily stimulated by epinephrine in children than in adults, and maintenance of hyperglycemia depends upon synergism between epinephrine, cortisol (Eigler, 1979) and sympathetic stimulation. Epinephrine concentrations in injured adults are usually

below those that cause the maximal hyperglycemic response in normal adults (Clutter *et al.*, 1980). If this were not the case in children the glucose level reached would depend less on epinephrine concentration and more on the glycogen reserves, which appear to be very variable (Shelley 1961; Nilsson 1973). The fall from peak values would then be attributable to the lowering of cortisol concentrations, and the reduction of sympathetic drive by analgesia and partial restoration of blood volume (Walker *et al.*, 1959; Folkow & Neil, 1971).

On this hypothesis, however, one expects all injuries in children to lead to massive hyperglycemia, not just burn and head injury. Perhaps a more thorough study of glucose, epinephrine and insulin relationships shortly after injury might throw light on this matter. There are, however, a number of other factors, such as the action of vasopressin, angiotensin and glucagon, which have not been studied, and which might provide other, truer, explanations.

From 8 h the presence of insulin resistance in children with burns was shown by the marked hyperglycemia and its positive correlation to insulin levels. The resistance did not, however, appear to be caused by the mechanism usually postulated, the synergistic action of epinephrine, cortisol and glucagon (Heath, 1980; Barton, 1981; Shamoon *et al.* 1981; Bessey *et al.* 1984; Gelfanal *et al.*, 1984; Heath, 1986). Other mechanisms must exist, since resistance is very marked in adults a few days after non-burn injury, when epinephrine concentration are normal, and those of cortisol and glucagon nearly so (Frayn, 1986). It is not known how soon this type of resistance develops in adults. It appears that it may be present in children 8 h after burn injury.

ACKNOWLEDGEMENTS

REFERENCES

Baker S. P., O'Neill B., Haddon W. Jr. & Long W. B. (1974) The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *Journal of Trauma* **14**, 187–96.

Barton R. N. (1981) Neuroendocrine mobilization of body fuels after injury. *British Medical Bulletin* **41**, 218–25.

Bessey P. Q., Watters J. M., Aoki T. T. & Wilmore D. W. (1984) Combined hormonal infusion simulates the metabolic response to injury. *Annals of Surgery* **200**, 264–81.

Bradley J. V. (1968) *Distribution-free statistical tests*. Prentice-Hall International Inc., London, U.K.

Copes W. S., Lawnick M. M., Champion H. R. & Sacco W. J. (1988a) A comparison of abbreviated injury scale 1980 and 1985 versions. *Journal of Trauma* **28**, 78—86.

Copes W. S., Champion H. R., Sacco W. J., Lawnick M. M., Keast S. L. & Bain L. W. (1988b) The injury severity score revisited. *Journal of Trauma* **28**, 69—77.

Clutter W. E., Bier D. M., Shah S. D., & Cryer P. E. (1980) Epinephrine plasma metabolic clearance rates and physiologic thresholds for metabolic and hemodynamic actions in man. *Journal ·of Clinical Investigation* **66**, 94—101.

Eigler N., Saccà L., Sherwin R. S. (1979) Synergistic interactions of physiologic increments of glucagon, epinephrine and cortisol in the dog. *Journal of Clinical Investigation* **63**, 114—23.

Folkow B. & Neil E. (1971). *Circulation*. Oxford, University Press, Oxford, 320—39.

Frayn K. N., Little R. A., Maycock P. F., & Stoner H. B. (1985) The relationship of plasma catecholamines to acute metabolic and hormonal responses to injury in man. *Circulatory Shock* **16**, 229—40.

Frayn K. N. & Maycock, P.F. (1983) Sample preparation with ion exchange resin before liquid-chromatographic determination of plasma catecholamines. *Clinical Chemistry* **29**, 1426—8.

Frayn K. N. (1976) Insulin secretion after injuries of differing severity in the rat. *British Journal of Experimental Pathology* **57**, 316—20.

Frayn K. N. (1986) Hormonal control of metabolism in trauma and sepsis. *Clinical Endocrinology* **24**, 577—99.

Gelfand R. A., Matthews D. E., Bier D. M. & Sherwin R. S. (1984) Role of counter-regulatory hormones in the catabolic response to stress. *Journal of Clinical Investigation* **74**, 2238—48.

Gottstein U., Held K., Sebening H. & Walrunger G. (1965) Der Glucoseverbrauch des menschlichen Gehirns unter dem Einfluss intravenoser infusionen von Glucose, Glucagon und Glucose-Insulin. *Klinische Wochenschrift* **43**, 965—75.

Heath D. F. (1980) Carbohydrate metabolism after injury. The development and maintenance of hyperglycaemia. In: *Homeostasis in Injury and Shock*. Bíró Zs., Kovách A. G. B., Spitzer J. J. & Stoner H. B. (Eds). 63—70. Pergamon Press

Heath D. F. (1986) Experimental studies on energy metabolism after injury and during sepsis. In: *The Scientific Basis for the Care of the Critically ill*. Little R. A. & Frayn K. N. (Eds). Manchester, University Press, Manchester, 75—101.

Heath D. F., Corney P. L. (1973) The effects of starvation, environmental temperature and injury on the rate of disposal of glucose in the rat. *Biochemical Journal* **136**, 519—30.

Jackson R. A., Hamling J. B., Blix P. M. *et al.*, (1986) The influence of graded hyperglycemia with and without hyperinsulinemia on forearm glucose uptake and other metabolic responses in man. *Journal of Clinical Endocrinology Metabolism* **63**, 594—604.

Little R. A., Stoner H. B. & Frayn K. N. (1981) Substrate oxidation shortly after accidental injury in man. *Clinical Science* **61**, 789—91.

Morgan C. R. & Lazarow A. (1963) Immunoassay of insulin: two antibody system. Plasma insulin levels of normal, subdiabetic and diabetic rats. *Diabetes* **12**, 115—26.

Muir I. F. K. & Barclay T. L. (1962) Treatment of Burn Shock. In: *Burns and their Treatment*. Lloyd-Luke, London 28—30.

Nilsson L. H:son. (1973) Liver glycogen content in man in the postabsorptive state. *Scandinavian Journal of Clinical and Laboratory Investigation* **32**, 317—23.

Parish R. A. & Webb K. S. (1988) Hyperglycemia is not a poor prognostic sign in heed-injured children. *Journal of Trauma* **28**, 517—22.

Saccà L., Vigorito C., Cicala M., Corso G. & Sherwin R. S. (1983) Role of gluconeogenesis in epinephrine-stimulated hepatic glucose production in humans. *American Journal of Physiology* **245**, E294—302.

Scientific Tables: Geigy Pharmaceuticals (1975) 8th edition. Diem K. & Lentner C. (Eds)

Shamoon R., Hendler R. & Sherwin, R. S. (1981) Synergistic interactions among antiinsulin hormones in the pathogenesis of stress hyperglycemia in humans. *Journal of Clinical Endocrinology Metabolism* **52**, 1235—41.

Shelley H. J. (1961) Glycogen reserves and their changes at birth. *British Medical Bulletin* **17**, 137—43.

Stoner H. B., Frayn K. N., Barton R. N., Threlfall C. J. & Little R. A. (1979) The relationships between plasma substrates and hormones and the severity of injury in 277 recently injured patients. *Clinical Science* **56**, 563—73.

Vitek V., Lang D. J. & Cowley R. A. (1979) Admission serum insulin and glucose levels in 247 accident victims. *Clinica Chimica Acta* **95**, 93–104.

Walker W. F., Zileli M. S., Reutter F. W. Shoemaker W. C., Friend D. & Moore F. D. (1959) Adrenal medullary secretion in hemorrhagic shock. *American Journal of Physiology* **197**, 773–80.

Yki-Järvinen H., Young A. A., Lamkin C. & Foley J. E. (1987) Kinetics of glucose disposal in whole body and across the forearm in man. *Journal of Clinical Investigation* **79**, 1713–9.