

THE HYPERGLYCAEMIC RESPONSE TO DIFFERENT TYPES OF SURGERY AND ANAESTHESIA

BY

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SUMMARY

The rise in blood sugar during anaesthesia without surgery and during surface, thoracic and intra-abdominal surgery, was measured. In patients anaesthetized primarily with thiopentone there was no significant rise without surgery and the rise was, in general, proportional to the stress of surgery, the largest being during intra-abdominal operations. Findings were similar in another series of patients anaesthetized primarily with propanidid. Five anaesthetic techniques were also compared during intra-abdominal surgery. In all nitrous oxide and tubocurarine were used and there was a bigger rise in patients in whom anaesthesia was induced with propanidid than in those who had thiopentone. The addition of 1 per cent halothane or phenoperidine 5 mg to the thiopentone/nitrous oxide/tubocurarine technique, led to a significantly smaller response. When a technique using droperidol/fentanyl/tubocurarine was employed the hyperglycaemic response was similar to that with thiopentone induction.

During body surface surgery under thiopentone plus nitrous oxide anaesthesia (with or without relaxant) there is a small rise in blood sugar (Clarke, 1968). When propanidid is used as the main anaesthetic agent the hyperglycaemia is much greater than with thiopentone (Clarke, 1968). This is probably due to the lighter level of anaesthesia present after propanidid, rather than to a specific difference between the anaesthetic agents. When the induction agents alone were given there was no hyperglycaemia, so it seemed desirable to investigate the relationship between the degree of trauma and the rise in blood sugar.

Since propanidid and thiopentone differ in their ability to block the hyperglycaemic response to surgical trauma, the effect of other anaesthetics and analgesics has been studied. The field of surgery covered was mainly upper abdominal, and in the current practice in Great Britain this virtually excluded the use of diethyl ether, cyclopropane and spinal analgesic techniques. However, the agents available seemed to offer a chance of understanding the mechanism of the hyperglycaemia by determining which drugs or techniques reduce the response during abdominal surgery.

METHOD

The techniques and procedures were similar to those described by Clarke (1968). Blood samples were taken in all series before induction of anaesthesia and at 15-minute intervals thereafter, from a forearm vein via a Mitchell needle. The second sample was taken soon after the skin incision. Blood sugar was estimated by the standard auto-analyzer technique which measures total reducing substances in blood. The maximum error in an individual reading was 5 mg/100 ml and, in a consecutive series analyzed in one batch, about 2 mg/100 ml. Investigations were carried out on 150 patients of either sex, 20 of whom were included in the previous study (tables I and II). Premedication consisted of atropine 0.6 mg and pethidine 50–75 mg or morphine 10 mg. Anaesthesia was induced with thiopentone or propanidid, approximately 5.0 mg/kg, except in series 7 when droperidol and fentanyl were given instead. Further small doses of the induction agent or additional tubocurarine, phenoperidine or halothane were used for maintenance, as indicated in tables I and II.

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TABLE I
Details of techniques and of patients with average doses of intravenous agents in the series comparing types of surgery.

Series	Type of operation	Maintenance of anaesthesia	Thiopentone induction							Propanidid induction					Total dose (mg)	
			No. of patients	Age (yr)	Weight (kg)	Initial blood sugar* (mg/100 ml)	Induction dose (mg/kg)	Total dose (mg/kg)	Total dose (mg)	No. of patients	Age (yr)	Weight (kg)	Initial blood sugar* (mg/100 ml)	Induction dose (mg/kg)		Total dose (mg/kg)
1	Nil	Intermittent i.v. N ₂ O-O ₂	20	38	68	92 ± 5.0	5.0	12.4	820	10	46	72	73 ± 4.0	4.9	33.5	2300
2	Body surface	N ₂ O-O ₂ , tc	20	42	70	85 ± 2.2	5.0	7.1	510	10	47	63	79 ± 3.3	5.8	10.3	655
3	Thoracic	N ₂ O-O ₂ , tc	10	60	66	85 ± 3.3	5.5	6.3	410	10	62	63	87 ± 2.6	5.2	12.6	700
4	Intra-abdominal	N ₂ O-O ₂ , tc	30	52	62	91 ± 2.4	5.3	6.2	360	10	61	59	82 ± 3.2	5.1	13.3	778

* Mean and SE. tc=tubocurarine.

TABLE II
Details of techniques and of patients with average dose of intravenous agents in the additional series of intra-abdominal operations comparing types of anaesthesia.

Series	Anaesthesia		Number of patients	Age (yr)	Weight (kg)	Initial blood sugar† (mg/100 ml)	Induction dose (mg/kg)	Total dose	
	Induction	Maintenance						(mg/kg)	(mg)
5	Thiopentone	N ₂ O/O ₂ , tc, phenoperidine	10	48	64	82 ± 3.2	5.3	5.3	330
6	Thiopentone	N ₂ O/O ₂ , tc, halothane	10	64	63	88 ± 2.6	5.4	5.4	350
7	Droperidol/fentanyl	Droperidol/fentanyl/N ₂ O/O ₂ , tc	10	58	61	86 ± 4.3	0.30*	0.37*	22.5*

* The figures refer to droperidol dosage, that of fentanyl being 1/50 of this.

† Mean and SE. tc=tubocurarine.

There were seven groups of patients, as follows:

Series 1. Anaesthesia without surgery using intermittent thiopentone or propanidid and nitrous oxide.

Series 2. Body surface operations after thiopentone or propanidid induction, with nitrous oxide and tubocurarine maintenance.

Series 3. Thoracic operations with the same anaesthesia.

Series 4. Intra-abdominal operations with the same anaesthesia.

Series 5. Intra-abdominal operations after thiopentone induction, with nitrous oxide, tubocurarine and phenoperidine maintenance.

Series 6. Intra-abdominal operations after thiopentone induction, with nitrous oxide, tubocurarine and halothane maintenance.

Series 7. Intra-abdominal operations after droperidol and fentanyl induction, with nitrous oxide, tubocurarine, droperidol and fentanyl maintenance.

Those patients (series 1) who did not receive tubocurarine were given additional doses of the induction agent for maintenance when small movements of face or limbs indicated lightening of anaesthesia. Patients in series 2, 3 and 4 usually received some supplementary intravenous anaesthetic (thiopentone 50–100 mg; propanidid 50–500 mg) for similar indications in addition to

the tubocurarine. All patients given a muscle relaxant were intubated and, after a brief initial period of manual ventilation, respiration was controlled using a non-rebreathing circuit. In series 5 the tubocurarine was followed within the next 2-4 minutes by phenoperidine 5 mg. This was thought to be a dose likely to produce total analgesia for 1 hour and certainly the patients gave no sign of muscular activity during the first hour of surgery. Series 6 differs from the other relaxant studies only in that halothane 0.5-1.5 per cent was given from the onset of positive pressure ventilation. The aim was to maintain as high a level of inhaled halothane as was compatible with a systolic blood pressure of 80-100 mm Hg. It was usually necessary to

reduce the concentration when an additional dose of tubocurarine was given.

Patients in one series (7) were anaesthetized by a neuroleptanaesthetic technique in which droperidol 25 mg and fentanyl 0.5 mg were mixed and diluted to 20 ml. One ml of solution per 6.3 kg was then given slowly, followed by 2-ml increments at 3-minute intervals, until the patient fell asleep. Before unconsciousness supervened it was often necessary to exhort the patient to breathe at regular intervals. When the patient failed to respond to questions, nitrous oxide/oxygen (5/3 l./min) was given and at the same time tubocurarine 30 mg. Intubation and ventilation were performed in the usual manner but, because of the longer time for induction of

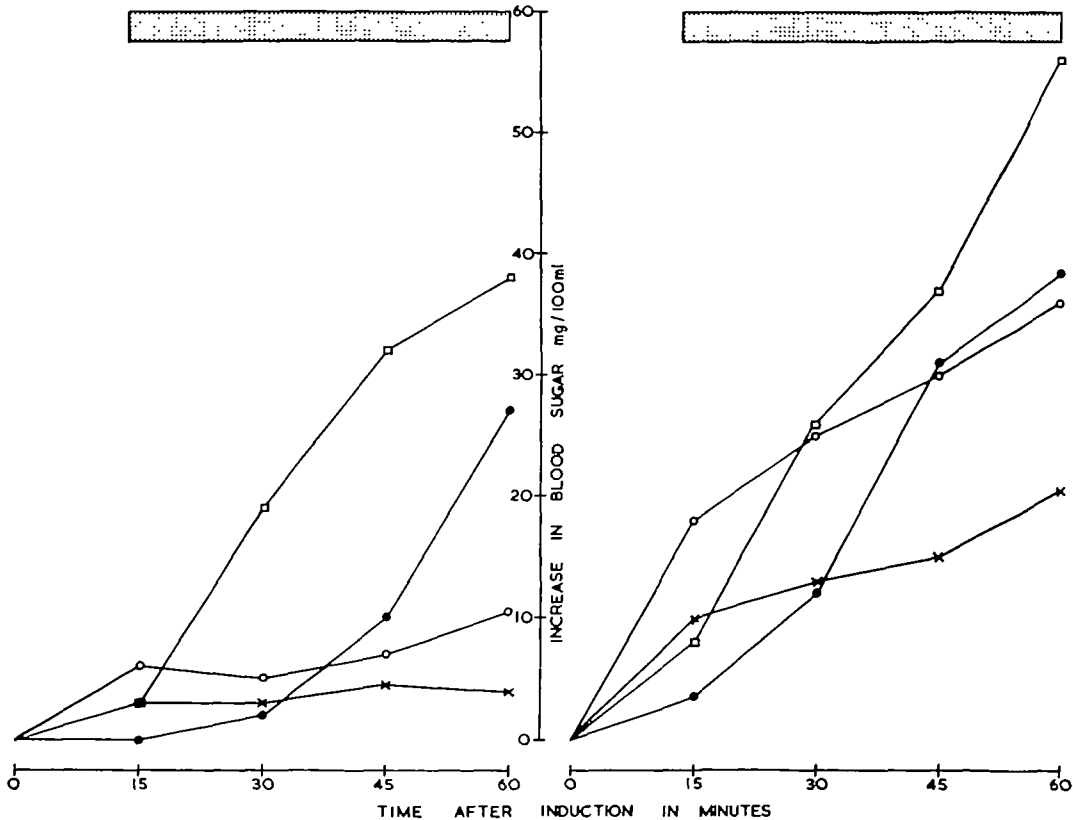


FIG. 1

Average increases in blood sugar during intra-abdominal surgery (squares), thoracic surgery (closed circles), body surface surgery (open circles) and anaesthesia without surgery (crosses). Results on the left are after thiopentone induction and those on the right are after propanidid induction. The stippled areas represent the period of surgery.

anaesthesia, the second blood sample was not taken until surgery had begun and later samples were delayed correspondingly. Maintenance in these patients was achieved using 1-ml increments of the above solution or tubocurarine 5 mg, according to the indications for anaesthesia or muscular relaxation.

The types of operation studied were restricted by the decision not to include patients who required blood during the first hour of surgery. Patients in the first series were studied pre-

operatively, or in some cases an examination under anaesthesia or cystoscopy was performed. The body surface operations consisted of ligation and stripping of varicose veins, herniorrhaphy and local mastectomy. The thoracic operations included lobectomy, pneumonectomy, exploratory thoracotomy, hiatus herniorrhaphy or Heller's operation. Cardiac surgery was not included. Most of the patients in the intra-abdominal groups underwent cholecystectomy or gastroenterostomy with or without vagotomy.

TABLE III
Details of results comparing the hyperglycaemic response to different types of surgery.

Series	Type of operation/ anaesthesia	Statistical parameter	Increase in blood sugar (mg/100 ml) at (min)			
			15	30	45	60
1	No surgery (thiopentone)	Mean	3	3	5	4
		SE	1.7	1.9	1.9	2.2
2	Body surface (thiopentone)	Mean	6	6	7	10
		SE	1.5	2.2	2.3	2.0
		Significance of increases above initial values				
		$t =$ $P <$	4.39 0.001	2.61 0.02	3.26 0.005	5.22 0.001
3	Thoracic (thiopentone)	Mean	0	2	10	17
		SE	1.7	2.8	3.4	3.9
		Significance of increases below intra-abdominal series				
		$t =$ $P <$	1.42 0.001	4.48 0.001	5.42 0.001	4.82 0.001
4	Intra-abdominal (thiopentone)	Mean	3	19	32	38
		SE	1.4	2.8	2.5	2.4
		Significance of increases above body surface series				
		$t =$ $P <$	1.50 NS	3.78 0.001	7.60 0.001	9.12 0.001
1	No surgery (propanidid)	Mean	10	13	15	20
		SE	1.9	3.4	4.6	5.2
		Significance of increases above initial values				
		$t =$ $P <$	5.63 0.001	3.94 0.005	3.36 0.01	4.22 0.005
2	Body surface (propanidid)	Mean	18	27	30	36
		SE	3.5	4.6	5.2	8.5
		Significance of increases above initial values				
		$t =$ $P <$	5.34 0.001	6.05 0.001	4.86 0.001	4.36 0.005
3	Thoracic (propanidid)	Mean	8	16	34	40
		SE	1.9	4.9	5.6	4.9
4	Intra-abdominal (propanidid)	Mean	9	27	37	56
		SE	2.8	5.0	7.0	7.9

RESULTS

Influence of the type of surgery.

Figure 1 (left graph) shows the changes in blood sugar levels during anaesthesia with thiopentone, nitrous oxide and oxygen in the three groups undergoing different types of surgery and in the group in whom surgery was not performed. For purposes of comparison it may be taken that the anaesthetic technique was the same in all (table I). The patients anaesthetized but without surgery showed no significant rise, those undergoing body surface surgery a small but significant rise, those having chest surgery a greater rise and those having intra-abdominal surgery showed the largest rise (for details of significance see table III). There was a difference between the findings during body surface and intra-abdominal surgery which was highly significant at 30, 45 and 60 minutes. The findings during chest surgery were intermediate between the two series, but although they could presumably be classed with intra-abdominal operations as major surgery, the blood sugar increases differed significantly from those in series 4 (abdominal surgery) at all times. During all these operations the 15-minute sample was taken soon after the skin incision, so there could be no difference in blood sugar relating to the type of surgery, at this time.

The responses to propanidid anaesthesia with similar types of surgery are seen to the right in figure 1. There was a small but significant rise in blood sugar in the series without surgery, a highly significant rise during body surface surgery, but the blood sugar level again rose most in the intra-abdominal series (for details of significance see table III). Also, findings during chest surgery were intermediate between the other two series and those during anaesthesia without surgery fell below those in the body surface series at 45 and 60 minutes. Because of the wide scatter of results and the relatively small numbers in each series the blood sugar increases, during surgery after propanidid induction, were not significantly different from each other.

Influence of the type of anaesthesia during upper abdominal surgery.

It was shown previously that there was a significant difference in the blood sugar rise

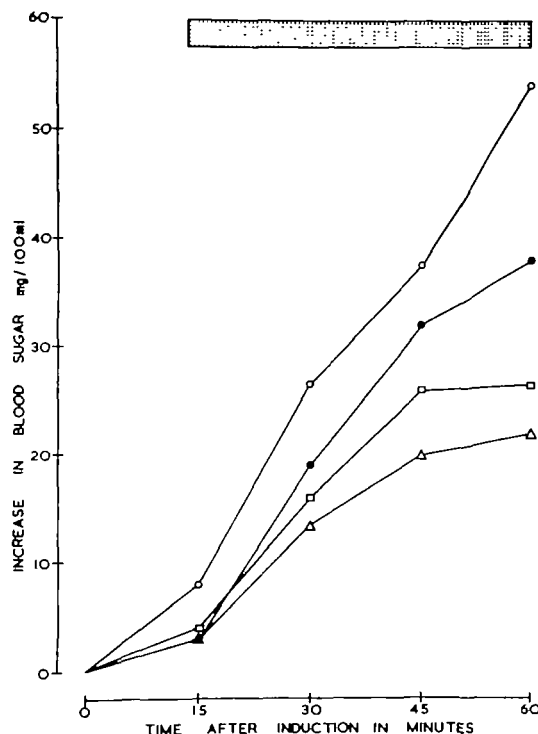


FIG. 2

Average increases in blood sugar during intra-abdominal surgery under anaesthesia with propanidid/tubocurarine (open circles), thiopentone/tubocurarine (closed circles), thiopentone/tubocurarine/halothane (squares) and thiopentone/tubocurarine/phenoperidine (triangles).

during body surface surgery using intermittent thiopentone from that using intermittent propanidid anaesthesia (Clarke, 1968). On the other hand, it made little difference whether these drugs were given intermittently throughout the period of surgery or were given for induction and followed by tubocurarine. Since the hyperglycaemic response to intra-abdominal surgery is larger than that to body surface surgery it seemed more fruitful to study the influence of different techniques in the former field. Figure 1 shows that the rise with propanidid induction was very great and that with thiopentone was smaller; these results are replotted in figure 2. There was, in fact, a significant difference only at 15 and 60 minutes.

Phenoperidine was added as an analgesic to the thiopentone / nitrous oxide / tubocurarine

TABLE IV
Details of results comparing the hyperglycaemic response with different anaesthetic techniques for body surface and intra-abdominal surgery.

Series	Type of operation/ anaesthesia	Statistical parameter	Increase in blood sugar (mg/100 ml) at (min)			
			15	30	45	60
2	Body surface (thiopentone <i>v.</i> propanidid)	Significance of increases with propanidid com- pared with thiopentone $t =$ $P <$	3.27 0.005	4.34 0.001	3.51 0.005	3.06 0.005
4	Intra-abdominal (thiopentone <i>v.</i> propanidid)	Significance of increases with propanidid com- pared with thiopentone $t =$ $P <$	2.03 0.05	1.47 NS	0.07 NS	2.31 0.05
5	Intra-abdominal (+ phenoperidine)	Mean SE Significance of increases below intra-abdominal (thiopentone) series $t =$ $P <$	3 1.9 0 NS	13 2.5 1.66 NS	20 4.0 2.68 0.02	22 4.0 3.61 0.001
6	Intra-abdominal (+ halothane)	Mean SE Significance of increases below intra-abdominal (thiopentone) series $t =$ $P <$	4 2.3 0.38 NS	15 3.7 0.82 NS	21 5.1 2.03 NS	25 5.9 2.16 0.05
7	Intra-abdominal (neuroleptanalgesia)	Mean SE Significance of increases compared with intra-abdominal (thiopentone) series	12 4.3 NS	25 7.0 NS	38 6.5 NS	43 8.1 NS

technique and the blood sugar changes were measured (series 5). The rise in blood sugar was much smaller than in the series without phenoperidine, although the differences were significant only at the 45 and 60 minute readings. In series 6 halothane (0.5–1.5 per cent) was added to the basic technique. The difference between the blood sugar rises in series 4 (thiopentone) and that in series 6 (halothane) was only significant at 60 minutes, though it just failed to reach the 5 per cent level at 45 minutes.

The series of patients having intra-abdominal surgery under neuroleptanalgesia with nitrous oxide and tubocurarine (7) showed a slightly larger rise in blood sugar at all times than those

having thiopentone / nitrous oxide / tubocurarine (4) though there was no significant difference between the increases in the two series. The results are omitted from figure 2 for the sake of clarity but are given in table IV.

DISCUSSION

It appeared likely from previous work (Clarke, 1968) that the hyperglycaemic response to surgery was related to its duration and the extent of its stress. A single dose of an intravenous anaesthetic was accompanied by no rise in blood sugar, a minor gynaecological operation by a transient response, and a body surface operation lasting an hour or more by a moderate though significant

rise. The findings with the wider range of surgery presented here support the same general conclusion, namely that the more severe the stress the greater the response. The pattern of findings was similar with the two induction agents, though the higher level and greater scatter of blood sugar results with propanidid made the differences due to the type of surgery less marked.

Two slightly anomalous results should be discussed. There was a small rise in blood sugar in the absence of surgery, if light anaesthesia with propanidid was maintained for an hour, whereas there was no such rise during maintenance with thiopentone. As in the case of body surface operations carried out under the two anaesthetic agents it seems likely that when the level of anaesthesia with propanidid becomes light, minor stimuli are sufficient to initiate a hyperglycaemic response. The second point of note was that the blood sugar rose more during intra-abdominal surgery than during thoracic surgery with both induction agents. This perhaps suggests that traction on the peritoneum and mesentery is a stimulus of particular importance.

The technique of anaesthesia used in the first series (without surgery) consisted of intermittent injections of the intravenous agent compared with a full relaxant technique in all other series. However, it was found in the previous work during body surface surgery (Clarke, 1968) that the hyperglycaemic response under the two types of anaesthesia was very similar.

One possible difference between operations in the various series was in the amount of blood loss. This was small in all cases, being about 100–300 ml, as judged by swab weighing performed on five of them. In addition, some gastrectomies and pneumonectomies requiring blood transfusion in the first hour had to be excluded from the series. It has also been shown by Lawrence and Plaut (1942) that slow bleeding in blood donors (400 ml) did not produce a statistically significant effect on blood sugar.

There is a large literature on the effects of anaesthesia and surgery on the blood sugar, but in much of the early work the two factors were confused. The earliest report that diethyl ether caused hyperglycaemia in the dog is by Seelig (1905). All the findings by numerous workers, and particularly those with animals led Harris (1951)

to state that "the most striking, the most constant and one of the most consequential disturbances of metabolism during anaesthesia is the rise in the glucose and lactic acid content of circulating blood". In recent years this view has not been confirmed in man and, in the absence of abdominal surgery, anaesthesia with diethyl ether (Cullingford, 1966), halothane (Hunter, 1959), methoxyflurane (Gottlieb and Sweet, 1964) and thiopentone (Dundee and Todd, 1958) has not been shown to lead to a significant rise in blood sugar.

There do not appear to have been many studies comparing the hyperglycaemic response to different operations, but Weddell and Gale (1934) showed that under anaesthesia with diethyl ether, intraperitoneal surgery led to an average rise in blood sugar of 93 mg/100 ml, compared with 52 mg/100 ml during superficial operations. Griffiths (1953) found no rise in blood sugar during superficial operations, whereas there was a small but significant rise during partial gastrectomy (average 6.1 mg/100 ml) during the first hour. The findings of Gottlieb and Sweet (1964), that anaesthesia with methoxyflurane did not raise the blood sugar, are balanced by those of Roberts and Cam (1964) that surgery (mainly abdominal) under this agent did raise it.

In spite of these findings it was surprising, in the 60 patients having intra-abdominal surgery, to observe a consistent rise in blood sugar in every patient, whatever the anaesthetic technique. This is quantitatively at variance with the previously published series on Europeans by Griffiths (1953), Keating (1958) and Cullingford (1966), using thiopentone/nitrous oxide/relaxant/adjuvant techniques. All these workers did, however, find a small rise in blood sugar, varying on average from 7 to 18 per cent of the pre-operative value, and it may be that minor differences in technique influenced the extent of the hyperglycaemia. The premedication in the cases described here was light by many standards, and even pethidine 75 mg has much less sedative effect than the papaveretum 20 mg plus hyoscine 0.4 mg or the pentobarbitone 50–150 mg plus morphine 10 mg or pethidine 50–100 mg used by Cullingford. Since the type of anaesthesia influences the response, it seems likely that heavy

sedation pre-operatively could reduce it slightly.

The studies with different anaesthetic techniques were designed to throw further light on the stimulus required to evoke hyperglycaemia. The first group of studies suggested that the lighter the anaesthesia, the greater the response, and the results from series 6, in which halothane was added to the basic technique for intra-abdominal surgery, supported this view. The addition of phenoperidine 5 mg had a similar effect to that of halothane, and this suggests that no rigid line can be drawn between anaesthesia and analgesia in this respect. In the concentration given (0.5–1.5 per cent) halothane produces light anaesthesia, but it can only be said that in sub-anaesthetic concentrations it is not analgesic (Dundee and Moore, 1960). Its hypotensive action restricted the use of higher concentrations which might have reduced the hyperglycaemic response more significantly. Phenoperidine 5 mg is a powerful analgesic (Rollason and Sutherland, 1963) but clinical observation during its use for suppression of respiration suggests that it does not produce deep sedation. The technique of neuroleptanaesthesia as used here clearly had no inhibitory effect on the response and it might be suggested that an adequate dose of an analgesic such as phenoperidine, the effect of which lasts for at least 1 hour, is more effective in this respect than the short-lasting fentanyl. Furthermore, it cannot be shown that droperidol is of any value in abolishing the hyperglycaemic response to stress.

Taking all the above findings into consideration, it appears likely that any painful stimuli, but particularly those arising from traction on abdominal viscera, transmit impulses centrally to spinal cord and/or mid-brain. There they can be partly suppressed by profound anaesthesia or analgesia but probably only drugs blocking the spinal cord itself or the afferent or efferent pathways in its neighbourhood could block it effectively. Findings on the motor side will be discussed elsewhere but suggest that release of cortisol plays a large part in initiating the hyperglycaemia.

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LA REACTION HYPERGLYCEMIQUE CONSECUTIVE A DIFFERENTS TYPES D'INTERVENTION CHIRURGICALE ET D'ANESTHESIE

SOMMAIRE

L'auteur a mesuré l'augmentation du taux de sucre sanguin durant l'anesthésie sans chirurgie et pendant des interventions superficielles, thoraciques et intra-abdominales. L'augmentation chez les malades anesthésiés principalement au thiopentone, n'est pas significative sans chirurgie, et l'hyperglycémie est en général proportionnelle au stress chirurgical: elle est la plus marquée durant les opérations intra-abdominales. Des observations similaires ont été faites

chez une autre série de patients, anesthésiés principalement au propanidid. Cinq techniques anesthésiques ont également été comparées durant la chirurgie intra-abdominale. On a administré à tous les malades du protoxyde d'azote et tubocurarine et l'augmentation était plus grande chez les patients où l'anesthésie avait été induite au propanidid, que chez ceux où thiopentone avait été utilisé. L'addition d'halothane 1 pourcent ou phenoperidine au mélange thiopentone/protoxyde d'azote/tubocurarine causait une réaction significativement moins forte. La réaction hyperglycémique était similaire à celle observée lors de l'induction au thiopentone, lorsqu'on appliqua la technique droperidol/fentanyl/tubocurarine.

DIE HYPERGLYKÄMISCHE REAKTION AUF VERSCHIEDENE ARTEN VON OPERATION UND NARKOSE

ZUSAMMENFASSUNG

Das Ansteigen des Blutzuckers während einer Narkose, sowohl ohne nachfolgenden chirurgischen Eingriff als auch nach oberflächlicher, thorakaler sowohl intra-

abdominaler Operation wurde gemessen. Bei vornehmlich mit Thiopenton narkotisierten Patienten wurde ohne nachfolgende Operation kein wesentliches Ansteigen des Blutzuckers beobachtet; im allgemeinen entsprach die Blutzuckererhöhung dem operationsbedingten Streß, der bei intra-abdominalen Operationen am bedeutendsten war. Ähnliche Befunde wurden bei einer anderen Untersuchungsreihe festgestellt, wo die Narkose der Patienten mit Propanidid durchgeführt wurde. Ebenfalls verglichen wurden fünf verschiedene Narkosemethoden während operativer Eingriffe am Abdomen. Bei allen Methoden wurde Lachgas und Tubokurarin angewendet; in den Fällen, in denen zur Induktion der Narkose Propanidid gegeben wurde, war der Blutzuckeranstieg höher als bei den Patienten, die zur Narkose-Induktion Thiopenton erhielten. Der Zusatz von 1 Prozent Halothan oder 5 mg Phenoperidin zu der Narkose mit Thiopenton/Lachgas/Tubokurarin führte zu einer wesentlich geringeren Reaktion. Wenn die Narkose mit Droperidol/Fentanyl/Tubokurarin durchgeführt wurde, war die hyperglykämische Reaktion ähnlich wie bei einer mit Thiopenton induzierten Narkose.

BOOK REVIEW

Modified Gelatins as Plasma Substitutes. Edited by P. Lundsgaard-Hansen, A. Hässig and Hs. Nitschmann. Basel: S. Karger AG (distribution in UK: Academic Press). Pp. xiv+610; 237 figs.; 110 tables. Price 150s.

This book is published as No. 33 in the *Bibliotheca Haematologica* series, and records the papers and discussion at a meeting held at Berne in October 1967. Although the editors and the vast majority of the contributors are either Swiss, German or Swedish, the whole is written in English and, apart from a few infelicities, the standard of translation is excellent.

Artificial plasma substitutes have been with us for several years, but detailed scientific interest in their properties and uses is still expanding. There is no doubt that, in this field, the major advances have stemmed from Scandinavia and the European mainland countries, and interest in them has been slow to kindle in the United Kingdom. This may be due, in no small part, to the fact that the preparations initially available in this country were atypical, and unsuitable as plasma substitutes. BP Dextran was unsatisfactory, because of difficulties with blood cross-matching and allergies; "Rheomacrodex" was too hyperoncotic to be used as a substitute, and was promoted for rheological properties, which are now realized to be largely mythical. The harm done is difficult to measure. In the reviewer's experience, it is quite unusual to find trainees in anaesthesia who can clearly distinguish between the properties, uses and toxic effects of the various molecular weight dextran preparations. Perhaps this may now prove to be a blessing. As a study of the proceedings of this conference reveals, modified gelatin preparations appear to be as acceptable as dextrans as plasma substitutes, but have significant advantages in terms of lesser toxicity and fewer unwanted side effects.

The rather laggard interest in this field in the United

Kingdom is reflected in the fact that, although these papers discuss at least three preparations of gelatins which appear to be widely available on the Continent, there is—as yet—none available commercially in this country. However, as their advantages appear to be considerable, one supposes that this situation will soon be remedied.

This book is divided into nine major sections, each of which has an excellent review of the field of that section. These introductory reviews, and the whole of the first section, which contains a review of the development and clinical context of the use of plasma substitutes by two of the editors, would be excellent reading for examination candidates and anyone wishing to be "updated" as quickly as possible. The second section on chemistry and immunology is mainly for the specialists in these fields, although there is considerable general interest in the findings that gelatins do not appear to have a structure which could allow them to become antigenic.

Section III is concerned with distribution, retention and excretion, and the effects of gelatins on blood volume. Section IV is mainly animal experimentation, and includes some interesting studies on the physiological limitations to replacement of blood by cell-free colloids of various kinds. Two adjacent papers demonstrate very clearly the importance of experimental design to the interpretation of results. Both experimenters were comparing the mortality in dogs associated with using either dextrans or gelatins to replace large volumes of acutely shed blood. In one case, the volume of plasma substitute was that required to maintain normal arterial blood pressure, and centrifuged plasma was re-transfused to produce an anaemia of 4.5 g%. Under these conditions, no significant difference existed between the two types of preparation. The other workers replaced shed volume with

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