numbers of human subjects are exposed, and it is interesting to study the immunological response in molecular terms. A general picture is beginning to emerge, and it will doubtless be filled out and clarified by investigations in the next few years.

Summary

Sera from Africans living in malarious and non-malarious regions of Kenya, and of patients with trypanosomiasis and leishmaniasis, were investigated for M-antiglobulins (rheumatoid-factor-like globulins) using the sensitised sheep-cell agglutination test (S.S.C.A.T.) and latex-fixation test (L.F.T.).

More subjects from the malarious region had M-antiglobulins than from the non-malarious region. This difference did not appear to be due to the ethnic background of the subjects or to treponemal infection.

Patients with *Trypanosoma rhodesiense* infection showed high titres of heterophile antibodies, agglutinating non-sensitised sheep red-blood cells. This was not found in patients with *T. gambiense* infections. Patients with trypanosomiasis more often had positive S.S.C.A.T. results, but not positive L.F.T. results, than other subjects from the same region.

Patients with chronic visceral leishmaniasis commonly showed high M-antiglobulin levels by both tests.

We are indebted to those who provided specimens, to Dr. A. E. Wilkinson (Venereal Diseases Reference Laboratory, London Hospital) for treponemal antibody tests, to Dr. K. N. Brown (National Institute for Medical Research, London) for sera from infected animals (results of which will be published in collaboration later), to Miss M. V. Mussett for statistical advice, and to Dr. D. R. Bangham and Dr. S. G. Anderson for helpful discussion.

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"... G.P.'s unrest has coincided with increased pressure from right-wing economists for a return to consumer choice and sovereignty in deciding how much we should spend on health. ... From the G.P.'s point of view a massive switch to consumer choice, even if most people could afford it, would be disastrous. If North American experience is anything to go by, and the liberal economists urge that it is, then the effect of free consumer choice would be to push the G.P. out of pædiatrics, obstetrics, and surgery, at least in urban areas. The medical profession has no more interest in consumer sovereignty now than in the past."—GORDON FORSYTH, *New Society*, March 17, 1966, p. 12.

THE EFFECT OF SUXAMETHONIUM CHLORIDE ON UTERINE ACTIVITY

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THE action of muscle-relaxant drugs on the uterus in late pregnancy and labour is not clear and the evidence is contradictory. Laborit and Chaillot (1949) claimed that curare stimulated uterine contractions while Scurr (1951) reported that it produced uterine relaxation. Alver et al. (1962) reported that suxamethonium produces uterine relaxation in the pregnant uterus at term but Wiqvist and Wåhlin (1962) observed no change in uterine activity after paralysing doses of succinyl choline in cats, and in women during the 3rd and 4th months of pregnancy.

On opening the abdomen at cæsarian section when suxamethonium has been used as a muscle relaxant, we frequently observed that uterine muscle activity seemed to be increased. We have investigated this finding further.

Patients and Methods

Patients

5 patients who were about to undergo cæsarean section were studied. The purpose and nature of the experiment were explained to them and their consent was obtained. Clinical details are given in table I.

TABLE I—CLINICAL DETAILS OF 5 PATIENTS

Patient no.	Age	Para	Gestation (weeks)	Indication for cæsarean section
1	21	1	40	Previous cæsarean section for disproportion
2	20	1	40	Previous cæsarean section for disproportion
3	30	1	39	Previous cæsarean section
4	25	2	38	Antepartum hæmorrhage (placenta prævia)
5	20	1	38	Previous cæsarean section for disproportion

Patients 1–4 were not aware of uterine contractions and therefore were considered to be " not in labour " but the 5th patient had been having regular painful contractions for 6 hours. No drugs had been given for the previous 8 hours except atropine sulphate 0·6 mg., subcutaneously administered as premedication 30 minutes before the start of the recordings.

Methods

Transabdominal amniocentesis was performed under local anæsthesia with an 18-gauge ' Teflon ' needle. After the metal obturator and stilette were withdrawn, the teflon needle filled with amniotic fluid and acted as an intrauterine cannula. The cannula was connected to a transducer and through an amplifier to an electrical recorder having curvilinear coordinates. A continuous record of the intra-amniotic pressure was obtained before, during, and after the induction of general anæsthesia. Recording was discontinued just before the start of cæsarean section except for patient 4 (see figure [*b*]) when the recording was continued until the uterus was incised and the membranes ruptured.

In all 5 cases, general anæsthesia was induced by the same technique: preoxygenation for 3–4 minutes, intravenous thiopentone 250 mg., and by suxamethonium chloride 50–60 mg. intravenously. After endotracheal intubation, anæsthesia was maintained by intermittent positive-pressure respiration with nitrous oxide (5 litres per minute) and oxygen (3 litres per minute). Complete paralysis was maintained by intermittent injections of suxamethonium.

Measurement of Uterine Activity

Each recording was divided into two sections of equal time, before (A) and after (B) the injection of suxamethonium.

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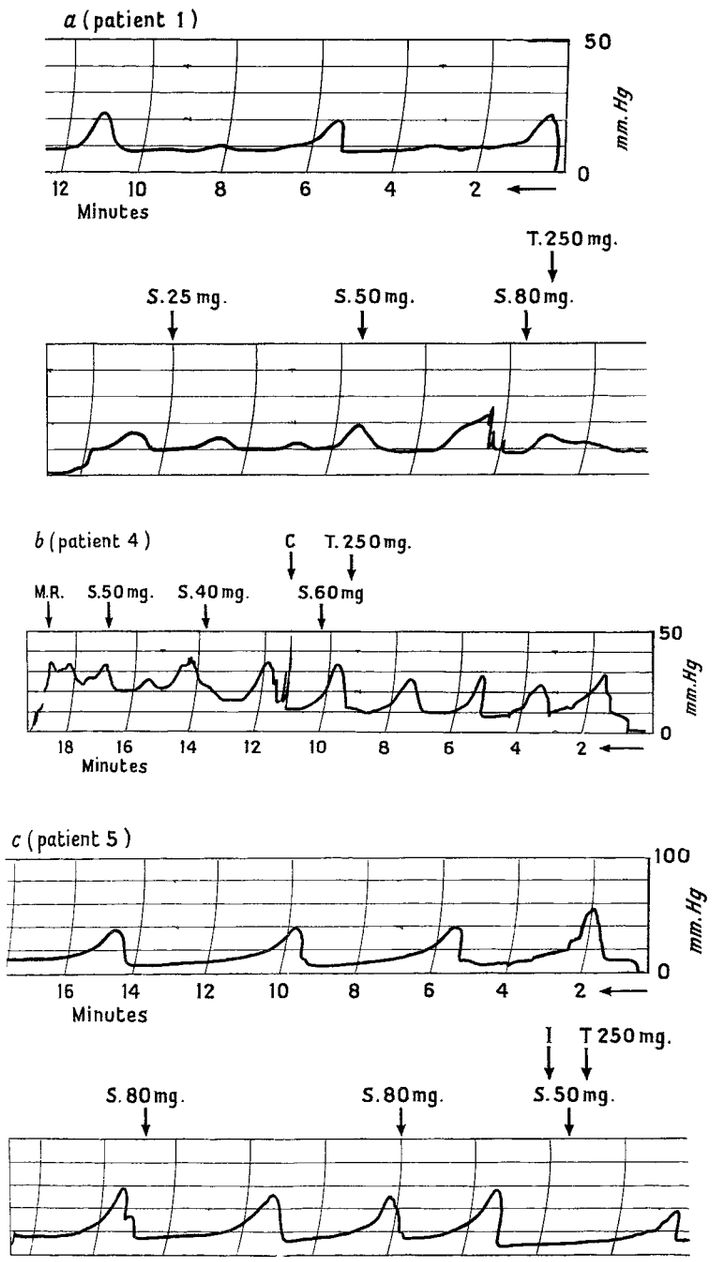
Uterine activity was measured for each section and the difference was expressed as a percentage (table II). For the purposes of comparison the uterine activity has been calculated for a period of 20 minutes because in practice the actual recording time varied from 12 to 29 minutes (table II).

We have related uterine activity to the concept of action in physics and calculated the activity during time T according to the equation:

$$\text{Activity during time } T = \int_{O}^{T} P \cdot V \cdot dt$$

where P is the pressure throughout the volume (V) of the uterus. For the times recorded, V is constant and so the uterine action will be proportional to the area under the pressure-time curve. This is expressed in mm.Hg minutes between the limits of time required. To exclude the component of uterine action due to resting uterine tonus, a base line was drawn representing this tonus and only the area above this line was measured.



Continuous record of uterine activity before and after the induction of general anæsthesia and the intravenous injection of suxamethonium for patients 1(*a*), 4(*b*), and 5(*c*).

Uterine activity measured by changes in intra-amniotic pressure records.

T. = Thiopentone.
S. = Suxamethonium.
C. = Cough at intubation.
I. = Intubation.
M.R. = Uterus incised and membranes ruptured.

TABLE II—UTERINE ACTIVITY BEFORE AND AFTER THE ADMINISTRATION OF SUXAMETHONIUM

Patient no.	Actual recording time (min.)	Total dose of suxamethonium (mg.)	Resting uterine tonus (mm. Hg min.)	Uterine activity (mm. Hg min.) (A) Before suxamethonium	(B) After suxamethonium	$\frac{(B)-(A)}{(A)} \times 100$
1	26	155	80·0	26·8	44·0	64·1
2	12	125	90·0	23·7	41·6	75·5
3	18	150	72·0	39·9	59·2	48·3
4	18	150	80·0	73·0	152·4	108·7
5	39	210	80·0	98·8	143·5	45·2

Results

Before Suxamethonium

The resting uterine tonus varied from 72 to 90 mm. Hg minutes (table II). Values of this order have been a constant finding in large numbers of recordings from patients in late pregnancy and the first stage of uncomplicated labour (Felton 1965) and agree with those of Alvarez and Caldeyro Barcia (1950) and Williams and Stallworthy (1952).

Uterine activity varied from 26·8 to 98·8 mm. Hg minutes (table II). In patients 1–3, who were not in labour, uterine activity was similar and typical of late pregnancy with painless contractions of 12–16 mm. Hg amplitude (see accompanying figure [*a*]).

In patient 4 (see figure [*b*]), uterine activity was greater than average in late pregnancy before the onset of labour. This patient was bleeding vaginally from a posterior placenta prævia, however, and for placental separation to happen there is presumably increased uterine activity, even in the absence of painful contractions.

In patient 5 who was in labour and had been having regular painful contractions for 6 hours, uterine activity was typical of the first stage of labour with contractions of much greater average amplitude (34 mm. Hg) than the other patients (see figure [*c*]).

After Suxamethonium

In all patients there was an increase in uterine activity. This increase varied from 45·2% in patient 5 to 108·7% in patient 4 (table II). The increase was due to a greater frequency of contractions and to a raising of uterine tonus between contractions. The increase in resting tonus in patient 4 is probably due to the greater frequency and prolonged duration of contractions.

Our results show a considerable increase in uterine activity after the intravenous injection of suxamethonium. We attribute this oxytocic effect to suxamethonium, since the dose of thiopentone was small and its effect, if any, would be transitory. Nitrous oxide and oxygen in the non-hypoxic concentrations used have been shown to have no effect on uterine contractility (Lindgren 1959, Vasicka and Kretchmer 1961).

Discussion

After curare was first used in obstetric anæsthesia (Whitacre and Fisher 1945, Gray 1947) reports of good uterine tone and retraction noticed at cæsarean section gave rise to the belief that it had an oxytocic action. This was denied by Scurr (1951) who measured the intra-amniotic pressure in 2 cases during cæsarean section. One received *d*-tubocurarine chloride and the other decamethonium iodide. There was a fall in pressure in both cases. Alver et al. (1962) claimed that suxamethonium produces useful uterine muscle relaxation at term and in labour, but their study is open to criticism since the results were classified according to the obstetrician's clinical impression of uterine activity. Furthermore, their

observations were made before and after paralysis of the abdominal musculature and may have been influenced by a reduction in the intra-abdominal pressure. Our results show a considerable increase in uterine activity, ranging from 45·7% to 108·2%.

Suxamethonium is the most commonly used muscle relaxant in obstetric anæsthesia. The intermittent injection technique with doses of 25–100 mg. is widely used. Since suxamethonium increases uterine activity mainly by raising uterine tonus, its use may be dangerous to the fœtus in utero because of the production of hypoxia due to interference with placental blood-flow. This danger would increase if there was any delay in the delivery of the baby after the start of anæsthesia or if the fœtus was already at risk due to placental insufficiency.

The important clinical implications of our findings are the possible disadvantages of using suxamethonium as a muscle relaxant in obstetric anæsthetic techniques: especially in cæsarean section and external or intrauterine manipulation of the fœtus.

Elective cæsarean section is often carried out for suspected placental insufficiency when the fœtus is premature. Usher et al. (1964) concluded that the procedure predisposed to the respiratory-distress syndrome. It has been suggested on the basis of clinical and animal studies (James 1959, Cohen et al. 1960, Reynolds et al. 1965) that intrauterine hypoxia may contribute to the development of the respiratory-distress syndrome in the newborn. Raised intrauterine tonus, by producing fœtal hypoxia and acidosis just before delivery, may therefore contribute to the development of this disease in premature infants.

Many obstetricians favour the use of suxamethonium for external cephalic version in breech presentation and for intrauterine manipulations in transverse lie. If uterine activity is increased as a result of the general anæsthetic technique, these potentially dangerous procedures are made more difficult.

Summary

The effect of suxamethonium chloride on uterine activity in 5 patients about to undergo cæsarean section under general anæsthesia has been studied. Uterine activity has been measured from records of the intra-amniotic pressure. There was a notable increase in uterine activity after the intravenous injection of suxamethonium. When suxamethonium is used as a muscle relaxant for obstetric operations, there is a danger of intrauterine hypoxia from interference with placental blood-flow.

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URINARY EXCRETION OF 5-HYDROXY-INDOLEACETIC ACID IN NIGERIANS WITH ENDOMYOCARDIAL FIBROSIS

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Endomyocardial fibrosis (E.M.F.) is a relatively common form of heart-disease found both in East and in West Africa (Ball et al. 1954, Abrahams 1959, Davies 1960), but its ætiology remains obscure. It occurs predominantly among Negro people at the lower levels of the socio-economic scale whose staple diet includes foods (such as plantain and banana) which contain large amounts of 5-hydroxytryptamine (5-H.T.). This substance is absorbed from cooked plantain (Crawford 1962, Foy and Parratt 1962) and is excreted as 5-hydroxyindoleacetic acid (5-H.I.A.A.); in parts of Western Nigeria the oral ingestion of 5-H.T. from plantain may be as much as 200 mg. a week (Foy and Parratt 1960). 5-H.T. is capable of producing cardiac lesions in laboratory animals, especially when given over long periods (Bulle 1957, Kaverina 1965, McKinney and Crawford 1965) and is believed to be responsible for such lesions in carcinoidosis (Goble et al. 1955, 1956). The suggestion has been made (Arnott 1959, Crawford 1962, Foy and Parratt 1962) that the ingestion of large amounts of 5-H.T. may be responsible to some extent for the lesions in E.M.F. Crawford (1963) concluded that " at the moment there is no conclusive evidence either for or against the possibility of a common denominator between E.M.F. and carcinoidosis ". This is partly, as Crawford points out, because of the difficulty of accurate diagnosis in the early stages of the disease.

Over the past two years we have studied some twenty patients with confirmed E.M.F. and we have compared their ability to metabolise 5-H.T. with that of healthy Nigerians and Europeans and with that of patients with other cardiopathies. The results of these investigations are reported here.

Methods

The methods were similar to those used in an earlier study (Foy and Parratt 1962). The investigation was carried out in two stages. Firstly, 24-hour urine samples were collected from

TABLE I—EFFECT OF EATING A SINGLE PLANTAIN MEAL ON URINARY EXCRETION OF 5-H.I.A.A.

—	Normal		E.M.F. (20)	Other cardio-pathies (10)
	Nigerians (20)	Europeans (6)		
Basal excretion 5-H.I.A.A. (mg. per 24 hr.) ..	3·9±0·8	3·7±0·7	2·6±0·8*	2·2±0·8*
Amount plantain eaten (g.)	397±95	380±121	336±68	309±74†
Estimated amount 5-H.T. ingested (mg.)	19·9±4·8	19·6±6·2	16·7±3·2	15·6±4·0†
5-H.I.A.A., above basal levels, excreted within 20 hr. after plantain meal (mg.)	8·5±3·1	8·1±4·1	6·8±2·9	4·1±1·6*
Percentage of 5-H.T. excreted as 5-H.I.A.A. ..	41·6±6·5	42·7±7·9	39·1±9·1	25·5±5·6*
Urine volume (litres) over 20 hr.	1·26±0·43	2·07±0·89	1·41±0·20	1·04±0·22

Values are means ± standard deviations.
* † Significantly different from normal individuals at a probability level of P = < 0·001(*) and of P = < 0·01(†).