The figures of Krant *et al.* (1968) for sebum excretion rate are expressed as mg. sebum/10sq.cm./3 hours, but after conversion to μg./sq. cm./min. their value for the mean excretion rate in postmenopausal control subjects (0·57 ± 0·06) was fairly close to our control figures (0·42 ± 0·08). Their value for control subjects also lies between our previous figures for normal women aged 40 to 70 years with and without previous adolescent acne—namely, 0·84 μg./sq.cm./min. ± 0·07 and 0·23 μg./sq.cm./min. ± 0·06 (Cunliffe and Shuster, 1969b). The sebum excretion rate in Krant's patients with advanced cancer (1·17 ± 0·16) was significantly higher than our value for patients with early cancer (0·61 ± 0·07). It is possible, therefore, that this represents a change in hormonal status as the cancer progresses, though methodological differences may be important. Another possibility is that, owing to chance sampling differences, more of their cancer patients had the persistent seborrhoea which is associated with previous adolescent acne.

The seborrhoea found in patients with breast cancer may be of relatively recent onset, but alternatively it may have been present for many years, in which case one might find an increased incidence of adolescent acne in women who later tend to develop breast cancer. Only two of our cancer patients and one of our control patients gave a history of acne, and since the incidence of acne in the adolescent female population in this district is at present in the region of 50% (Burton *et al.*, 1969) it seems likely that little reliance can be placed on our patients' memories in this respect. It is notable that the three patients who did give a history of acne all had seborrhoea, and it is probable that only the more severe grades of acne are remembered into middle age.

None of our patients had acne scarring, and it seems unlikely that the incidence of previous severe acne in our breast cancer patients was increased. These facts, together with the possibility of a greater seborrhoea in advanced than in early cancer, suggest that the increased sebum excretion is of recent onset and is progressive. Prospective studies will be required to test this idea.

The cause of this slight but significant increase in sebaceous gland activity is unknown. The sebaceous glands are highly sensitive to androgenic stimulation, and though oestrogens produce a decrease in sebaceous activity, the effect of even larger doses of oestrogen is prevented by the simultaneous administration of small doses of androgen (Strauss *et al.*, 1962). Bulbrook and Hayward (1967) observed that women who subsequently developed breast cancer had an abnormality of urinary steroid excretion which was multidirectional—that is, the variance was increased—though the trend was towards a subnormal excretion of androgen metabolites. This is difficult to reconcile with our finding of an increased sebum excretion in women with breast cancer, unless some other factor is operative. There is evidence for the existence of a pituitary sebotrophic factor in animals (Lasher *et al.*, 1955; Lorincz and Lancaster, 1957), but its role in man is unknown.

The possible causes of seborrhoea include increased levels of circulating or tissue sebotrophic hormones, or an enhanced end-organ response to such hormones. Alternatively, there may be decreased inhibition of sebaceous gland activity either by decreased levels of circulating or tissue inhibitors such as oestrogen or by diminished end-organ response to inhibition. Further study is required to elucidate the mechanism concerned, and particular attention should be given to the relation between sebaceous gland activity and the subsequent clinical course of the breast cancer, especially with regard to response to hormonal therapy.

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Acute Scorpion Pancreatitis in Trinidad

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S ummary: Over a two-month period 30 patients were admitted to hospital following stings of the scorpion of Trinidad, the Tityus trinitatis. In 24 cases acute pancreatitis developed soon after the sting, but in nine of these no abdominal pain occurred. All the patients made an uneventful recovery. Although such complications have been reported no pseudocyst formations or acute haemorrhagic pancreatitis occurred in this series.

Introduction

There are seven species of scorpions in Trinidad. These belong to the families Chactidae and Buthidae (Kjellesvig-Waering, 1966). The *Tityus trinitatis* (Pocock, 1894) of the Buthidae family is the commonest scorpion in the island, accounting for almost 90% of the scorpion population. It is commonly found in forests under logs or debris, in sugar-cane fields, in banana, cocoa, and coconut plantations, and sometimes even in houses, mainly in the rural areas. Fatalities from scorpion stings, which occur only rarely, are more common in young children than in adults. Despite its aggressive appearance the scorpion is a shy creature and will use its sting only when roughly handled or trodden on. Nevertheless, there is a high incidence of scorpion stings in Trinidad. In the two months of July and August over 30 cases were admitted to the university unit of the Port-of-Spain General Hospital. Most of these had been referred from the small district hospitals of Arima and Sangre Grande, which serve a rural population. The most striking observation was the very high incidence of acute pancreatitis following the sting of the *T. trinitatis*. No previous reports have described this complication resulting from the sting of any other scorpion in the world.

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Material and Methods

Studies were carried out on 30 patients who were able to recognize with certainty the scorpion which stung them. Of these, six were able to kill the scorpion and bring it to the hospital. In each case the scorpion was identified as *T. trinitatis*. The ages of the patients, who comprised 20 males and 10 females, ranged from 9 to 57 years. Immediately on the patients' admission to hospital, blood was taken for estimation of serum amylase, blood sugar, serum alanine aminotransferase (S.G.P.T.), and serum bilirubin. On the following morning these investigations were repeated. The urine was also examined for glycosuria and proteinuria.

Serum amylase (normal 80 to 180 units/100 ml.) was estimated by the method of Somogyi (1960), serum bilirubin (normal up to 1 mg./100 ml.) by that of Powell (1944), and S.G.P.T. (normal 8 to 45 units/ml.) by that of Reitman and Frankel (1957). Blood sugar levels were determined in a Technicon AutoAnalyzer by means of the potassium ferri-cyanide-ferrocyanide oxidation reduction reaction.

Results

On receiving the sting the patients experienced a very sharp pain at the site of the puncture. In a few cases there was reddening and oedema over the affected area. Salivation occurred in 16 patients (53%) from 15 minutes to two hours after the sting, and at times was very profuse. In fact, a spot diagnosis of scorpion sting was often made from this sign alone. Sixteen patients (53%) complained of abdominal pain. This was epigastric in nature, radiated to the back in five patients, and occurred from half an hour to five hours after the sting. The pain, which varied in severity, was continuous or sometimes colicky, and lasted from 10 minutes to 24 hours. Vomiting occurred in 15 patients (50%) and was accompanied by pain in 13. In most cases the patient was free of symptoms within 24 hours. In this series there were no complications of shock or jaundice and all the patients made uneventful recoveries.

The results of the serum and blood sugar estimations are shown in the Table. The rise in serum amylase, which occurred in 24 (80%) cases, was found as early as one hour after the sting. Moreover, it was noteworthy that nine (30%) of the patients with hyperamylasaemia had no abdominal pain. The transaminase studies showed a raised S.G.P.T. in five cases. No case of hyperbilirubinaemia occurred. In four cases the fasting serums on the morning after admission was observed but showed no lactescence.

Discussion

The clinical picture of scorpion venom poisoning has been known for many years and is well documented. The main symptoms are localized burning pain, excessive salivation, nausea, vomiting, drowsiness, sweating, convulsions, dyspnoea, and cardiac irregularities. Death, which can occur, particularly in children, may be largely due to failure of the cardiovascular and respiratory systems. It has long been appreciated in Trinidad, however, that acute pancreatitis is a common complication of the sting of *T. trinitatis*. Waterman (1938) described two cases of acute oedematous pancreatitis, two of haemorrhagic pancreatitis, and 12 of pancreatic pseudocysts, all of which were found at laparotomy following stings by *T. trinitatis*. Within the past two years I have seen two similar cases of pseudocyst formation. Nevertheless, as yet no evidence indicates that chronic pancreatitis eventually develops.

It is noteworthy that in nine cases (30%) hyperamylasaemia occurred without abdominal pain. This confirms that acute painless pancreatitis may occur more often than is realized. Moreover, the severity of the abdominal pain did not correspond to the level of hyperamylasaemia. Joshi (1957) found that 36 (0.9%) out of 408 cases of pancreatitis had no symptoms referable to the abdomen. Evans (1958), reviewing 25 cases of acute or subacute oedematous (interstitial) pancreatitis, reported that abdominal pain was absent in 15 (60%) of them. All the patients had died of ailments other than pancreatitis.

The rise in S.G.P.T. which occurred in this study is also noteworthy since it has been shown that transaminase levels may be normal or raised in patients with pancreatitis. Moreover, these levels can be correlated positively with serum bilirubin values, but not with the degree of pancreatic necrosis (Foulk and Fleisher, 1958). These observations and the low concentration of transaminase in pancreatic tissue indicate that increased serum transaminase levels may result from associated obstruction of the common bile duct. There was, however, no rise in the bilirubin levels in this series, and liver biopsy specimens were not taken.

Electrocardiographic changes are well known to occur in acute pancreatitis. Poon-King (1963) found E.C.G. evidence of " myocarditis " in 34 out of 45 patients stung by *T. trinitatis*. Some of the E.C.G. changes he observed may have been secondary to acute pancreatitis, though in some of these cases

Details of Cases

Case No.	Age	Previous Sting	Salivation	Vomiting	Abdominal Pain	Amylase (Somogyi units/100 ml.)	Fasting Blood Sugar (mg./100 ml.)	Urine Sugar	S.G.P.T. (units/100 ml.)	Serum Bilirubin (mg./100 ml.)
1	27	2	+	−	+	800	114	Neg.	40	0·7
2	9	—	+	−	−	457	64	Neg.	20	0·5
3	32	2	+	−	−	400	148	Neg.	23	0·5
4	32	—	−	−	−	800	82	Neg.	10	0·8
5	54	3	−	−	−	180	74	Neg.	96	0·7
6	12	—	−	+	+	320	120	+	30	0·5
7	57	2	+	+	+	1,600	104	+	30	0·7
8	20	1	−	−	−	400	80	Neg.	32	0·6
9	12	—	+	+	+	3,200	300	+ +	96	1·0
10	9	—	+	+	+	1,600	232	+	96	1·0
11	14	—	−	−	−	914	88	Neg.	30	0·6
12	11	—	+	+	+	1,000	550	+	30	1·0
13	14	—	+	−	+	640	120	Neg.	40	0·5
14	14	—	+	−	−	533	82	Neg.	50	0·8
15	11	—	+	+	+	100	92	Neg.	40	—
16	23	—	+	+	+	1,067	200	+ + +	34	0·7
17	9	—	+	+	+	3,200	144	+	45	0·5
18	39	—	+	+	+	1,067	100	Neg.	70	0·7
19	9	—	−	−	−	800	68	Neg.	40	0·5
20	12	—	−	+	−	1,067	98	Neg.	23	0·5
21	52	2	+	−	+	400	116	+	20	—
22	35	1	−	−	−	180	138	+	23	1·0
23	14	—	−	−	−	400	120	Neg.	30	0·5
24	21	—	−	−	−	160	94	Neg.	20	1·0
25	54	—	−	−	−	160	120	Neg.	35	0·5
26	11	—	+	+	+	800	128	+	30	0·5
27	38	1	+	+	+	290	324	+	32	0·7
28	16	—	+	+	+	640	94	Neg.	23	0·3
29	24	—	−	+	−	160	116	Neg.	30	1·0
30	25	5	−	+	+	800	84	Neg.	35	1·0

there was no clinical or biochemical evidence of pancreatitis.

The pharmacology and toxicology of scorpion venoms have shown that the venom has a powerful effect not only on the somatic but also on the autonomic nervous system. Samaan and Ibrahim (1959), studying the action of purified samples of " scorpion toxin " on the salivary glands of dogs, concluded that small doses of toxin had no direct action on the salivary gland cell. On the other hand, the toxin stimulated the salivary centres of the central nervous system and enhanced the response of the peripheral neurosecretory salivary mechanism to chorda tympani impulses. The venom of scorpions contains a macromolecular protein fraction which is responsible for its neurotoxic properties. There is, however, little proof that acute pancreatitis is caused primarily by a purely neurogenic mechanism.

Apart from the protein fraction, the venom of scorpions contains numerous free amino-acids (Fisher and Bunn, 1957) and also an appreciable quantity of serotonin (Adam and Weiss, 1956). Diniz and Gonçalves (1960), using paper and starch zone electrophoresis, fractionated the venom of T. serrulatus and of T. bahiensis and showed that they were mixtures of proteins with toxic, smooth-muscle-stimulating, and hyaluronidase components and that they increased capillary permeability. It is possible that the venom of T. trinitatis acts on the pancreas through an enzymatic property. McHardy et al. (1963) thought that the intrapancreatic conversion of trypsinogen to trypsin was the most important if not the sole cause of pancreatitis. Trypsin increases the permeability of pancreatic blood vessels and causes oedema (Dragstedt, 1943). More work recently has shown that free trypsin in the pancreas releases kallikrin, another proteolytic enzyme found in the pancreas and the parotid glands; this acts on known precursors to produce a powerful hypotensive vasodilating polypeptide identical in physiological action to bradykinin.

Despite the high incidence of acute pancreatitis in this series (80%) the true incidence of T. trinitatis pancreatitis may be even higher when it is considered that normal values for amylase do not entirely eliminate the possibility of acute pancreatitis. Moreover, the scorpion does not always inject venom when it stings, since it can control its ejaculation so that this is total, partial, or non-existent (Junqua and Vachon, 1968). It is apparent that no immunity to the scorpion toxin develops following a sting, since pancreatitis occurred in seven patients who had been stung previously.

The scorpion sting is by far the most frequent cause of pancreatitis in Trinidad. Nevertheless, the venom of T. trinitatis has not been so widely recognized. The frequency of acute pancreatitis, however, is evident from this short study. Apart from being of clinical and public health interest, the venom of T. trinitatis may throw some light on the pathogenesis of acute pancreatitis.

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Preliminary Communications

Multiple Halothane Exposure and Hepatic Bromsulphthalein Clearance

Summary: Multiple exposures to halothane have been shown to have delayed effects on bromsulphthalein (B.S.P.) clearance. Rats were exposed to repeated halothane anaesthetics, and their livers were subsequently isolated and perfused. B.S.P. retention in the perfusate of these isolated livers was greatly increased one to three weeks after the last halothane exposure. In similarly pretreated animals at the same time period the B.S.P.–glutathione conjugating enzyme activity in homogenates of the livers was found to be depressed. These findings did not occur after multiple diethyl ether exposures or following a single exposure to halothane.

INTRODUCTION

The question of multiple exposures has become an extremely important one relative to the mechanism by which liver damage may be caused following halothane anaesthesia (Little, 1968). Attention has again been drawn to this problem by several recent reports (Trey et al., 1968; Klatskin and Kimberg, 1969; Rodriguez et al., 1969), in addition to many previous individual surveys and case reports (Tygstrup, 1963; Sherlock, 1964; Morgenstern et al., 1965; Griner, 1966; Subcommittee on National Halothane Study, 1966).

The controversy surrounding the possible role of halothane in the causation of postoperative liver dysfunction has centred on, among other factors, the inability of clinical and statistical surveys to eliminate the numerous potential causes of liver dysfunction during this period (viral hepatitis, blood transfusion, intraoperative hypotension and hypoxia, septicaemia, and the concurrent administration of potentially hepatotoxic drugs).

The present investigation was designed in an attempt to eliminate these other potential causes of liver dysfunction by the study of isolated perfused livers and liver homogenates from animals previously exposed to halothane on several occasions. Abnormalities of bromsulphthalein (B.S.P.) handling by the livers of such animals were observed, and the study was modified to confirm the findings and to attempt to isolate the abnormality present in the liver.

MATERIALS AND METHODS

ANIMALS

Male albino rats (weight 375-400 g.) of Wistar and Sprague-Dawley strains, housed in conditions of controlled temperature