TREATMENT OF OESOPHAGEAL VARICES IN PORTAL HYPERTENSION BY MEANS OF SCLEROSING INJECTIONS*

BY

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In 1949 I briefly described a method of treating oesophageal varices by sclerosing injections based upon nine cases (Macbeth, 1951). The purpose of the present communication is to describe further experience with the method in a total series of 30 cases, and to attempt to justify its use as a valuable means of treatment in patients suffering from portal hypertension.

Portal Hypertension

This term, coined by McMichael in 1932, is descriptive of an increase of pressure within the portal venous system. It may be intrinsic by reason of fibrosis of the liver, or extrinsic because of thrombosis of the portal vein or of one of its main tributaries.

The portal system anastomoses with systemic veins at a number of points, but the lower end of the oesophagus and the cardiac end of the stomach provide a site where back-pressure from the portal side is peculiarly apt to produce varicose dilatations.

Bellis (1942) compared the portal venous pressure with that in an ankle vein in 16 human subjects who showed no evidence of portal obstruction. He found that the portal pressure ranged from 14 to 22 cm. of saline, while that at the ankle was 5 to 12 cm. Where valves are present in the veins such a pressure differential would not be expected to cause any dilatation of the systemic veins of the oesophagus. Whipple (1949) states that the normal portal pressure is 6 to 14 cm. of saline, but that in hypertension is 40 to 60 cm. Where the pressure is so markedly raised on the portal side any valves present in anastomotic veins would soon become incompetent, the blood flow would be from both ends, and varicosities would develop. Gradually further valves would give way, and ultimately the blood would find its way into the main systemic veins draining the oesophagus.

Anatomy

A comprehensive description of the veins of the oesophagus has been given by Butler (1951). He classified the veins as (*a*) intrinsic, which include subepithelial, submucous, and perforating; (*b*) extrinsic (or subserous), which are formed by the union of groups of perforating veins; and (*c*) venae comitantes of the vagal nerves, which run longitudinally in the adventitia of the oesophagus.

The subepithelial intrinsic veins are present throughout the oesophagus, and are continuous with those of the stomach. They drain without the intervention of valves into the submucous group. The submucous veins lie beneath the muscularis mucosae throughout its length. In the neck they drain via the perforating veins into the internal jugular vein; in the thorax similarly into the azygos veins; at the lower end they increase in size, become tortuous, and descend to join those of the stomach. Valves are inconstantly present at the level of the cardia. The perforating veins traverse the muscular coats and join the extrinsic veins. At this point of junction they are guarded by valves which direct the blood outwards.

The venae comitantes of the vagal nerves run longitudinally and link the left gastric vein directly or indirectly with the azygos system.

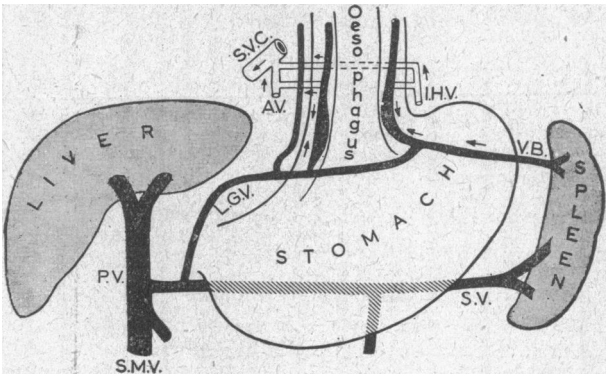

FIG. 1.—Schematic representation of portal system and anastomosis at oesophago-gastric junction (adapted from Learmonth). P.V.=Portal vein. S.M.V=Superior mesenteric vein. L.G.V.=Left gastric vein. A.V.=Azygos vein. S.V.C.=Superior vena cava. I.H.V.=Inferior hemiazygos vein. V.B.=Vasa brevia. S.V.=Splenic vein.

The extrinsic veins drain into the systemic veins except in the abdomen, where three or four join the left gastric vein.

There are, therefore, three routes in this area whereby portal blood may reach systemic veins.

Butler states that any or all of the veins of the oesophagus may become varicose in cases of portal obstruction, and this is borne out by the examination of necropsy specimens.

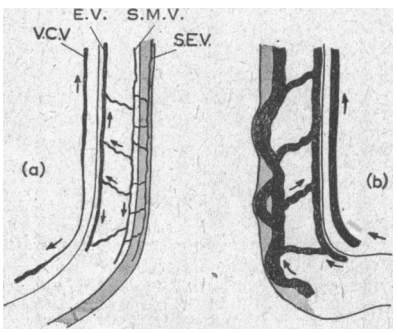

FIG. 2.—Schematic representation to show dilatation of veins. (*a*) Normal. (*b*) Abnormal. V.C.V.=Vena comitans of vagus. E.V.=Extrinsic vein. S.M.V.=Submucous vein. S.E.V.=Subepithelial vein.

The submucous veins of the stomach may also become varicose, but Learmonth (1951) states that this occurs later than in the oesophagus, and this observation fits in well with the clinical finding that gastric bleeding is rarer than oesophageal. The dangerous subepithelial varices of the oesophagus may develop by reason of the back-flow of blood coming into them indirectly via their own submucous veins, or because (as Learmonth says) the muscularis mucosae disappears by atrophy over submucous varices (Figs. 1 and 2).

Pathological Evidence

A mounted specimen of oesophagus taken from a patient who died of liver disease is shown in Fig. 3.

Sections of oesophagi have been specially prepared after injection of the portal veins of a recently dead infant and a similar young adult, following the method suggested by Butler (Figs. 4 and 5). The distribution of the veins as described by him is amply confirmed.

Further sections have been made of the oesophagi of patients who had died of liver failure, and in whom injection of varices had been carried out during life. In these it can readily be seen that the dilated varices impinging upon the lumen are in reality submucous veins over which the muscularis mucosae has disappeared (Fig. 6), as Learmonth

*Read in the Section of Otolaryngology at the Joint Annual Meeting of the British Medical Association, Canadian Medical Association, and Ontario Medical Association, Toronto, 1955.

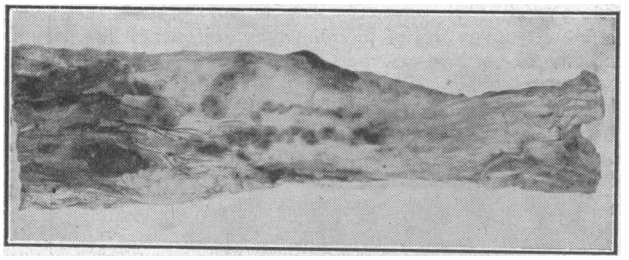

Fig. 3.—Mounted specimen of oesophagus from a patient who died of liver failure, showing injected and thrombosed veins, and one vein whose rupture was the cause of accompanying fatal haemorrhage.

(1951) suggests. Also there can be seen veins whose lumen has completely disappeared and been replaced with fibrous tissue (Fig. 7).

Methods of Treatment

It is obvious that methods of treatment must be aimed solely at relief of the varices from which these patients may bleed, since the underlying cause of the portal hypertension, whether intrinsic or extrinsic, is incurable anyway.

In many cases haematemesis is the only symptom of which the patients complain. Any method which results in control of the varices may prolong life in those patients with liver damage, and may give lasting relief to those without. The following methods have been used:

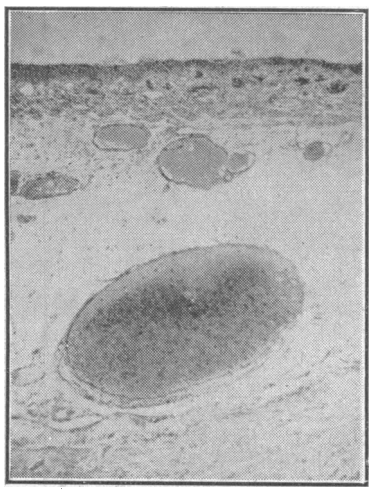

Fig. 4.—Oesophagus of child aged 3 months, congested but otherwise normal, full thickness. Showing subepithelial, submucosal, perforating, and adventitial (near vagus) veins.

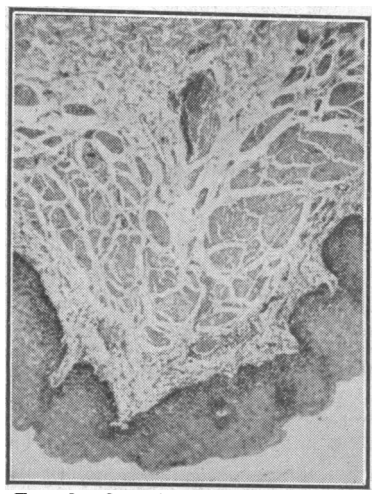

Fig. 5.—Oesophagus of young man (killed in road accident), inner half. Showing normal appearance of veins with much thicker adult epithelium and muscularis mucosae.

1. *Splenectomy* has been credited with diminishing the blood supply to the portal veins by 20–40% (Pemberton, 1931; Adams, 1951). This results in a temporary decrease in the portal pressure, but the pressure soon rises and varices may recur and bleed after an interval of freedom from trouble. Learmonth (1951) recommends splenectomy as preventing external anastomoses in relation with the swollen spleen.

2. *Ligature* of the short gastric, coronary, and diaphragmatic veins has proved useless because other venous channels open up.

3. *Gastric transection* aims at interrupting the veins in the walls of the abdominal oesophagus near the cardia. An encircling incision is made down to the mucosa, all veins are ligated, and the incision is then sewn up. This is not a minor procedure and is attended by a significant mortality rate. Other surgeons use a similar encircling incision of the oesophagus. These operations belong essentially to the same category as subdiaphragmatic venous ligature, and suffer from the same likelihood that new venous channels may open up. I have been told of one patient who developed a sudden intractable ascites after this type of operation; and of another who developed peritonitis, possibly because ascitic fluid became infected. Both died.

4. *Total gastrectomy* is an even more heroic procedure belonging to the same group.

5. *Porto-caval venous anastomosis* would appear to be the most logical method of relieving portal hypertension by a direct transfer of blood from the one system to the other. Blakemore (1951) reported 111 cases up to May, 1950, with a 16.2% mortality due to the operation. He states that "the operative risk is inversely proportional to the normality of the liver," and therefore it has its greatest application in extrinsic cases. In successful cases it seems undoubted that varices become smaller or disappear. Unfortunately the operation is technically difficult and thrombi may form at the anastomotic site.

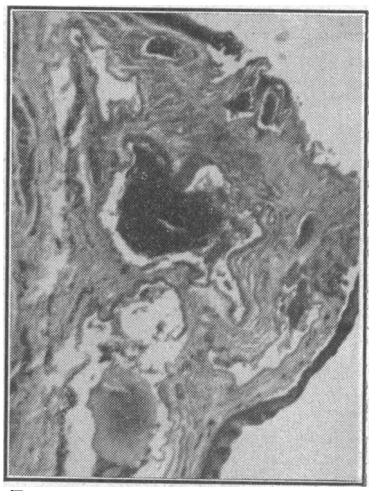

Fig. 6.—Dilated submucosal veins breaking through muscularis mucosae, which appears atrophic over them. Subepithelial veins not very large.

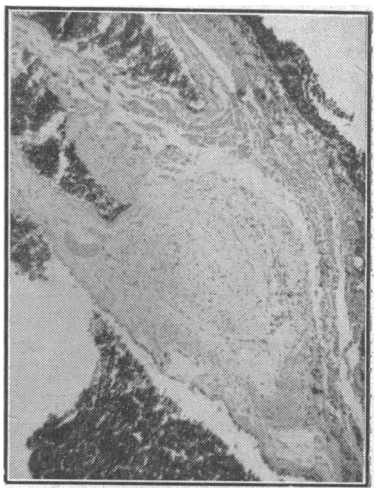

Fig. 7.—Old thrombosed submucosal vein close beside new varix.

6. *Sclerosing injections* have been carried out since Crafoord and Frenckner (1939) reported a successful case. Success with the method has not been uniform, but those who have tried it and given it up may either have used unsuitable techniques or have encountered hopeless cases, and in consequence have failed to persevere. The most recently published series was that of 20 cases by Kempe and Koch (1954). They stress the value of splenectomy as a preliminary procedure. The present series of 30 cases has been treated by injection in the last 12 years in the department of otolaryngology at the Radcliffe Infirmary.

Material

Two main groups of patients have been recognized—those with and those without liver damage. Of the 30 cases, 14 have been classified as belonging to the former category and 16 to the latter. On occasions it may be difficult to give a hard-and-fast opinion on this point without a liver biopsy, but the biochemical liver-function tests will usually give reasonably accurate information. Almost invariably a severe haematemesis requiring emergency treatment is the event which leads to the diagnosis of portal hypertension.

G. J. Fraenkel (1955, personal communication) has made a survey of all admissions to the Radcliffe Infirmary in the years 1948–52 suffering from haematemesis, and finds that bleeding from oesophageal varices accounted for 23 out of a total of 540 such admissions (4.26%).

Cases with Liver Damage.—These have a very much worse prognosis than have the undamaged group. Such patients may already be far advanced in their disease before they bleed, and may be actually jaundiced. For this reason, because they lack thrombocytes, because they are also anaemic, and in consequence their metabolism is poor, haemorrhage is likely to be profuse. Such an event of itself seems to lead to hepatic incompetence and death from liver failure.

Cases with Liver Damage (14)

Age range	5–72 years
Injected as emergency	4
Lived days after first injection	1
„ weeks „ „ „	2
„ months „ „	4
„ one year or more	7
Not traced	1
Longest survival	7½ years
Average number of injections	3

Cases Without Liver Damage.—The occurrence of portal hypertension in this group is sometimes obscure in origin. A thrombosis of the portal vein or of the splenic vein must be postulated. One patient in this series had had a retrocaecal appendicitis, with localized peritonitis, and later a cholecystectomy for gall-stones. Another patient had had tuberculous peritonitis which had been cured by streptomycin. A third had received a blow in the abdomen in a motor accident. A fourth was a boy aged 5 years who had had haematemeses since the age of 2 years; in his case it must be supposed that a thrombosis had ascended from the umbilical vein through the ductus venosus to the portal vein.

Cases without Liver Damage (16)

Age range	5–60 years
Injected as emergency	0
Not traced	1
Alive and well	14
Longest survival	11 years
Average number of injections	7
Subsequent shunts	2

Technique

The technique employed in the present series has varied somewhat as to detail, but has conformed generally with that described in 1949 (Macbeth, 1951). The sclerosing fluid has latterly been sodium morrhuate 5%, and 3–4 ml. has been injected at each venepuncture. No harm seems to come of making about six injections of this size at any one session.

A general anaesthetic is given, and the largest Negus type oesophagoscope which can be passed is used. It is important to use as large an oesophagoscope as possible, because thereby the veins are put upon the stretch, and because the oesophagoscope can be used to obliterate the vein after injection by passing it beyond the injected point. Theoretically the varices nearest the cardia should be injected first. This should be done if a patient has bled recently, when the offending vein can often be recognized and injected above and below the bleeding point. But in a quiescent phase it is more convenient to take the veins in groups from above downwards.

A long needle-carrier, mounted upon a bayonet-type fitting and locking into a 10- or 20-ml. syringe, is used. The needle is screwed into the distal end of this and should be very sharp. The vein is steadied on the stretch by the beak of the oesophagoscope, and the needle is slid down the wall of the tube until it punctures the vein. The sodium morrhuate is injected and, with the needle still in place, a "mastoid strip" of gauze is passed downwards in an alligator forceps and pressed upon the vein. The needle is withdrawn and the gauze held in place for a full minute. The oesophagoscope is slid downwards for a centimetre or so and the manœuvre is repeated four or five times.

In cases where there is marked bleeding as a result of venepuncture or where the injection therapy is undertaken as an emergency measure during an active haemorrhage, the bleeding can usually be controlled after injection by some form of hydrostatic bag. The simplest form is the Miller–Abbott bag, but this suffers from the disadvantage that it is made of very thin rubber which readily tears. A useful bag is that known as the Sengstaken triple lumen tube. This has two fluid compartments, the smaller of which is the distal and passes into the stomach, and the larger fills and stretches the lumen of the oesophagus. It is inflated with normal saline and left in position for one to two hours.

The routine is to repeat the treatment every one to two weeks until no veins remain uninjected. The patients are then examined after three months and, if no varices are found, in a further six months. They are then examined every six or twelve months according to whether they show new varices.

Possible Complications

Further and Immediate Haemorrhages.—These can be avoided or controlled by the use of hydrostatic bags.

Ulceration.—This was seen in one case in which liver damage was considerable and where the outlook was probably hopeless.

Substernal Pain.—This is usual, but slight.

Venous Embolism.—This has not been seen.

Allergy to the Injection Fluid.—This has not been seen.

Discussion

Reynell (1951) points out that where adequate transfusion therapy is available haemorrhage from varices in patients without liver damage is not so serious as was originally thought, and that the more severe the liver damage the worse the prognosis of a haemorrhage. Not only do patients with liver damage tend to bleed for haematological reasons, but the effect of a massive haemorrhage is in itself to "decompensate" the liver, and such patients die of hepatic coma. At best, therefore, a haemorrhage may have a high nuisance value, and at worst it may result in death.

It has been fashionable among writers on the surgery of portal hypertension to dismiss thrombosing injections as not having justified themselves, and as unlikely to do so because new venous channels continually open up (Walker, 1949; Whipple, 1949; Learmonth, 1951). It may well be that those who make the first contention have remained in ignorance of successful work in this field because this has been published in otolaryngological journals; or possibly they may have become distrustful of unsatisfactory techniques. The contention about new venous channels must surely apply with equal force to any operation involving gastric or oesophageal transection and ligation of veins, with resuture.

As has been said, the veins of the oesophagus are specially apt to dilate in an attempt to carry the portal blood into the systemic venous channels, and one would imagine that, with the exception of those prolapsing into the lumen, they are in fact serving a useful purpose and should be given every encouragement to continue.

The only veins, therefore, which are a danger to the patient and whose control is necessary are the subepithelial veins. Whether they are subepithelial *ab initio* or are in reality submucous veins which have become more superficial is immaterial.

The thin-walled veins prolapsing into the lumen are obviously at risk, but it has not been determined why they bleed. Local injury by food, sepsis, sudden increase in intrathoracic pressure, and muscular movements have all been invoked. Digestion by regurgitated gastric juice has been suggested as a cause for erosion of these veins, but if this were so one would expect a greater incidence of bleeding from gastric veins, which does not seem to be the case. Learmonth (1951) rejects the acid-juice view and notes that haemorrhages often occur soon after physical exertion.

In the case of patients suffering from severe liver damage the results of injection therapy have been disappointing. It has often been possible to control a particular haemorrhagic incident and apparently to prolong life, but these patients readily pass into a vicious circle of liver damage with jaundice leading to haemorrhage, which in its turn seems to predispose to liver failure. In fact when patients admitted apparently with severe liver damage are controlled readily by transfusion and injection we begin to think that perhaps their portal hypertension is extrahepatic after all. It is always worth while to attempt to control even the least hopeful case, especially if active bleeding has recently occurred, until the diagnosis becomes clear or until the patient goes into liver failure.

In the group of patients without demonstrable liver damage the outlook is very different. All of the cases quoted have remained alive and well from eleven years to four months after being controlled. Of these, three have had abdominal operations.

One patient who had been controlled by injection for six years bled again and had a porto-caval shunt. This was unsuccessful, so he had a gastric transection. He later had no varices.

A second patient bled again at about the time he was due for oesophagoscopy; he was taken into another hospital, where he had a porto-caval shunt. This man reported that he was well.

A third patient was sent by her physician after one injection to a surgeon, who did a porto-caval shunt. Her spleen was not removed, and recent oesophagoscopy showed no further development of varices.

When controlled these patients are so well that they can live normal lives—one, a schoolboy, plays football and is a cross-country runner; another is a hospital nurse; others lead full and ordinary lives. The main disadvantage of this method is that the patients need to be oesophagoscoped once or twice a year as a routine, and this must be firmly emphasized. Kempe and Koch (1954) have noted that patients who fail to attend for examination may be running a risk. I would echo this, and would instance the case of a man who had been well for three years, but not checked by oesophagoscopy in that period. He was examined in March, 1955, and found to have a number of varices which needed injection. Further experience may show that some of these cases can be completely and permanently cured.

I would also agree with the observation made by the same writers that splenectomy is a valuable adjunct to injection therapy. If bleeding has recently occurred it is best to inject such veins as were probably responsible, then to have a splenectomy done, and finally to complete the injection course. This was the method employed in a number of cases, and it was noteworthy how much more controllable were the varices after splenectomy. If bleeding has not occurred recently the operation may immediately precede an injection course, as recommended by Kempe and Koch.

Size and profusion of varices in the oesophagus should not deter one from attempting injection, provided that the patient is a hopeful case otherwise; in fact one of the most successful cases in this series presented numerous veins the size of a fourth finger when first seen. But, as a prophylactic measure, it may be advisable in such cases to leave a hydrostatic bag in the oesophagus for two hours after injection.

In conclusion, I would say that sclerosing injections of oesophageal varices in combination with splenectomy provide a method of treatment which may palliate hopeless cases of liver damage, and which should be considered as a safe and satisfactory alternative to more complicated and hazardous procedures in cases of extrahepatic portal hypertension.

Summary

Portal hypertension indicates an increase of pressure within the portal venous system; this may be intrinsic due to liver disease, or extrinsic due to a thrombosis of the portal vein or a main radicle.

In both types of case the most troublesome symptom is haematemesis due to rupture of oesophageal varices. In intrinsic cases the cause of death is almost always liver failure, but this may be precipitated by a massive haemorrhage. In extrinsic cases patients may be incapacitated solely by the haemorrhages.

Treatment is aimed at preventing haemorrhage. Splenectomy alone gives temporary relief. Ligature and transection of veins and viscera may lead to opening of new channels. Venous porto-caval shunt operations are the most logical method of relieving portal pressure, but not minor procedures.

The only veins at risk are those prolapsing into the oesophageal lumen. Sclerosing injections of such varices are capable of controlling them indefinitely in extrinsic cases, and for limited periods in intrinsic cases. It is emphasized that patients must submit to oesophagoscopy once or twice a year, because new varices may form.

Experience in 14 cases with liver damage (intrinsic) and 16 cases without (extrinsic) is discussed and injection technique is described.

Splenectomy makes the veins more readily controllable, and should be carried out as an adjunct to injection therapy.

The method is a safe and satisfactory alternative to major surgery.

I am indebted to the physicians of the United Oxford Hospitals and other colleagues who have kindly invited me to treat their patients in this way, and in particular to Professor Leslie Witts, who has provided more of them than any other. I also acknowledge with gratitude the permission given by my colleague, Mr. Gavin Livingstone, to include in this series seven patients treated by him. Finally, I should like to record my thanks to Dr. Hugh Cowdell, of the department of pathology, for his kindness in making the photomicrographs.

REFERENCES

Adams, H. D. (1951). *Surg. Clin. N. Amer.*, **31**, 803.
Bellis, C. J. (1942). *Proc. Soc. exp. Biol. (N.Y.)*, **50**, 258.
Blakemore, A. H. (1951). *J. Amer. med. Ass.*, **145**, 1335.
Butler, H. (1951). *Thorax*, **6**, 276.
Crafoord, C., and Frenckner, P. (1939). *Acta oto-laryng. (Stockh.)*, **27**, 422.
Kempe, S.-G., and Koch, H. (1954). Ibid., Suppl. 118, 120.
Learmonth, J. (1951). *Edinb. med. J.*, **58**, 1.
Macbeth, R. G. (1951). *Proceedings of the Fourth International Congress of Otolaryngology, 1949*, **1**, 294. London.
Pemberton, J. (1931). *Ann. Surg.*, **94**, 755.
Reynell, P. C. (1951). *Lancet*, **2**, 383.
Walker, R. M. (1949). *Practitioner*, **162**, 211.
Whipple, A. O. (1949). *Advanc. Surg.*, **2**, 155.

The total number of epileptics on the register of disabled persons was 16,267, or nearly 2% of the total register, said Sir GODFREY INCE, Permanent Secretary, Ministry of Labour and National Service, in his address at the annual general meeting of the British Epilepsy Association in June. The decrease in the total number of unemployed on the register over the past five years was 103, a disappointing figure, though it was affected by the number of newly registered epileptics. The decrease in the number of the severely disabled unemployed was 343; this was due in great part to the fine work of Remploy Ltd., who employ over 400 epileptics in special factories for the severely disabled. The Ministry gave about 300 epileptics a year an eight-weeks course at the industrial rehabilitation units, and over 80% of the 250 who completed it were placed in employment or training. Sir Godfrey pointed out that once an epileptic "appreciates that a fit is not going to cause consternation to anyone, a steady improvement sets in and the frequency and duration of the fits diminish. With many, the fits disappear entirely."