4 was the most severely affected, while Case 3 was the least severely affected and could be regarded as a dull normal child.

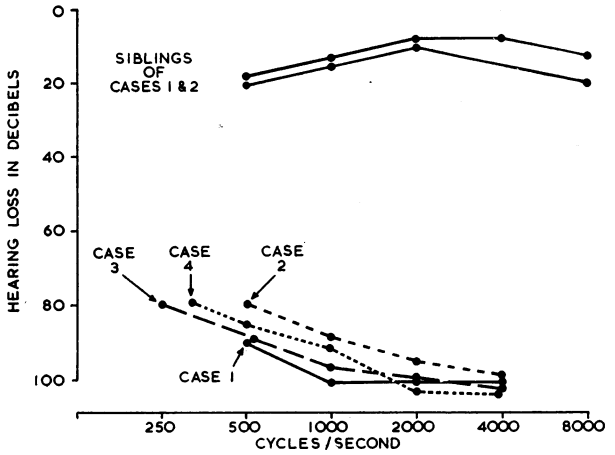

FIG. 2.—Audiograms.

Discussion

Goitre is endemic in Lebanon (Matovinovic, 1961; Interdepartmental Committee on Nutrition for National Defense, 1962). Cases of goitre with deaf-mutism, retarded linear growth, and mental retardation in such a country would be regarded as "endemic cretins," a sequel of endemic goitre. The cases forming the subject of this report demonstrate that this assumption does not always hold true. On the basis of radioiodine, otological, and genetic studies, these cases belong to the well-defined entity of Pendred's syndrome (Fraser *et al.*, 1960), a syndrome consisting of perceptive deafness and goitre, with or without hypothyroidism and inherited as a simple recessive trait. The main feature of the thyroid abnormality is a decreased rate of oxidation of the trapped iodine. All four cases described had perceptive deafness, all had a defect in organic binding of iodine by the thyroid gland as demonstrated by thiocyanate administration, and the genetic distribution in the two families was suggestive of a simple recessive trait. The rest of the goitrous population examined did not belong to this entity; in fact, 30 goitrous children and, of greater interest, the two goitrous siblings of Cases 1 and 2 did not have the defect of Pendred's syndrome. Deaf-mutism is rare among this particular goitrous population (Matovinovic, 1961). Preliminary studies suggest environmental factors as the cause of goitre in this population, mainly iodine deficiency (Najjar *et al.*, unpublished observations).

Although the number of cases is small it is apparent that, at least in Lebanon, a country where goitre is endemic, deaf-mutism with hypothyroidism may not be aetiologically related to endemic goitre. Genetic factors rather than iodine deficiency may be responsible for the symptom-complex that has been referred to as "endemic cretinism."

Summary and Conclusion

Four children with Pendred's syndrome belonging to two families residing in an endemic-goitre area are described.

Persons with deaf-mutism, goitre, and hypothyroidism who reside in a goitrous area, classically "endemic cretins," need not be the victims of the same aetiological factors responsible for the endemicity of the goitre, but may have genetic defects in their iodine metabolism.

I wish to express my thanks to Dr. Farid Karam for carrying out the otological studies; to Dr. Najib Abu Haydar, in whose laboratory the P.B.I. and radioactive iodine determinations were done; and to Dr. Calvin Woodruff for his advice in preparing the manuscript.

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Preliminary Communications

Potential Dangers of Morphine in Acute Diverticulitis of the Colon

Recent events have focused attention on the tragedies that may follow the use of newly discovered drugs whose properties are incompletely understood, but it should be remembered that other drugs which have been in widespread use for many years may have unsuspected side-effects. Morphine is the drug most often prescribed for the relief of severe pain, but it is possible that its beneficial analgesic action masks its other actions, some of which may be disadvantageous in certain circumstances.

During the course of investigations into the intraluminal pressures in the human sigmoid colon, both in health and in diverticulosis coli, the opportunity was taken to study the effect of morphine and other drugs on these pressures. The detailed results of these researches will be published elsewhere (Painter and Truelove, 1963; Painter *et al.*, 1963), but we feel that a brief résumé of certain of our findings is worth presentation in a general medical journal, as they appear to veto the use of morphine as an analgesic in acute diverticulitis.

METHOD OF INVESTIGATION

The intrasigmoid pressure patterns were recorded by means of water-filled open-ended "polythene" tubes introduced into the sigmoid colon through a sigmoidoscope, which was then withdrawn. The metal tips of these tubes were located radiologically. When patients with diverticulosis were being studied the relationship of these tips to the actual diverticula was ascertained, either by simultaneous cineradiography or by comparison with the relevant barium enema. The polythene tubes transmitted the intrasigmoid pressures to photoelectric pressure transducers. The resulting electrical signal was amplified by a Cambridge multi-channel recorder whose direct pen-writer registered the pressures on squared paper which moved at a set speed. Thus a permanent record of the intrasigmoid pressure patterns was obtained that could be studied at leisure. Patients were investigated for at least an hour under basal conditions—that is, at rest on a bed and abstaining from food and tobacco—and the resulting pressure tracing was called the "resting pattern of pressures." Morphine 1/6 gr. (11 mg.) was then given and the "post-morphine pattern of pressures" recorded for a further hour.

Thirty-two healthy subjects and 28 with diverticulosis were studied under basal conditions, and 21 of the former group and 25 of the latter group were given morphine. Nearly half of these subjects were investigated with simultaneous cineradiography to determine the behaviour of the sigmoid during the changes of pressure that were found to occur.

The effect of 100 mg. of pethidine given intramuscularly was studied similarly in six healthy subjects and in seven patients with diverticulosis.

RESULTS

Under resting conditions the normal sigmoid colon harbours a basal pressure that is within a few millimetres of mercury of atmosphere. Upon this baseline pressure waves of pressure are superimposed, the majority of which last for under 30 seconds. Eighty per cent. of these waves do not reach a height of 10 mm. Hg and only a few exceed a pressure of 20 mm. Hg. In diverticulosis an essentially similar pattern of pressure exists under basal conditions, whether or not the tip of the recording tube is situated in a segment of the sigmoid that actually bears diverticula. Under resting conditions the colon in diverticulosis does not produce higher waves of pressure than the healthy colon.

After morphine has been given to healthy subjects the number of waves of pressure of all dimensions is doubled, but the majority of these waves still fail to reach a height of 20 mm. Hg. In diverticulosis those segments of the sigmoid that do not bear diverticula behave in a similar manner to the healthy colon, except that waves of between 20 and 50 mm. Hg occur twice as frequently.

The intraluminal pressure patterns derived from segments that are beset with diverticula are different. After morphine these segments generate waves of very high pressure whose rise and fall is very abrupt. Frequently, several of these waves occur in rapid succession. Pressures of up to 90 mm. Hg have been registered during these bouts of activity. Even higher pressures sometimes occur, but we have not measured them precisely because our apparatus was set to cut out when this pressure was exceeded. Whereas the normal sigmoid colon generates waves greater than 50 mm. Hg only once in about five hours, the segments that bear diverticulosis produce such pressures on average every 24 minutes after morphine.

Once it was realized that morphine causes the diseased sigmoid to behave like this, cineradiographic studies were made to see whether these pressures affected the actual diverticula. Cineradiography showed that, although the necks of the diverticula were sometimes narrowed or intermittently occluded by morphine, at intervals the high intrasigmoid pressures forced sufficient bowel contents into them to cause them to be distended, sometimes to an alarming degree. At the same time the colon was observed to move to a greater extent than before the drug had been given.

Pethidine (100 mg. intramuscularly) was then investigated in a similar manner in the hope that it might not exhibit this undesirable effect. It was found that pethidine caused a diminution in the number and dimensions of the pressure waves, both in health and in diverticulosis. Very few waves of a pressure greater than 20 mm. Hg and none that exceeded 50 mm. Hg in height were recorded once the drug had taken effect. Cineradiography showed that after this drug no inflation of diverticula occurred. Pethidine also reduced the motility of the colon so that it remained still for longer periods than normal.

DISCUSSION

Peritonitis due to perforated diverticulitis carries a mortality of between 13 and 47% (MacLaren, 1957; McCollum, 1959; Brown and Toomey, 1960). The morbidity that attends this complication of diverticulitis is considerable, as those who survive this emergency are usually required to undergo two more operations—namely, resection of the sigmoid colon and closure of colostomy—neither of which is without risk. Hence the conservative treatment of acute diverticulitis aims to avoid these hazards. Both patient and colon are rested by sedation. Purgatives and enemas are withheld as these stimulate the bowel. It seems likely that morphine may have been responsible for some of the failures of this regime, as it leads to the actual distension of diverticula. The wisdom of giving it to patients with acute diverticulitis must therefore be questioned. Furthermore, the increased colonic movements evoked by the drug hardly favour the localization of a pericolic abscess. We therefore suggest that there is a prima facie case for withholding morphine from patients suffering from acute diverticulitis and giving pethidine instead, as the latter drug has neither of the disadvantages referred to above.

SUMMARY

Evidence is presented to suggest that morphine is contraindicated as an analgesic in acute diverticulitis.

Pethidine appears to be a suitable analgesic for use in this condition.

The cineradiographic studies mentioned in this article were carried out in collaboration with Dr. G. M. Ardran and Mr. M. S. Tuckey, of the Nuffield Institute of Medical Research, and we are grateful to them for allowing us to include this joint work in the present article.

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"Toothpaste makers doubled their sales in a few years, and one explanation is that they succeeded in large part by keeping a great number of people feeling uneasy about their teeth. They hammered at the wondrous new ways to kill bacteria and prevent decay. In the mid-fifties Crest toothpaste containing a fluoride was unveiled with typical modesty (for a toothpaste) as a 'Milestone of Modern Medicine' comparable to the discovery of means to control contagious diseases in the eighteenth century. The marketers themselves were less reverent in discussing the new fluorides among themselves. *Advertising Age* called the fluoride paste the latest gimmick of a series of big promises (ammoniated, chlorophyll, antienzyme) and added, 'The feeling persists that the public has responded appreciatively to every new therapeutic claim that has come down the pike in recent years. . . . The hope is that it will exhibit the usual alacrity at the sight of the fluorides.'" (*The Hidden Persuaders*, by Vance Packard.)