

patients who have large shunts and who show evidence of increased pulmonary pressure should be operated upon, if the shunt is still left to right. When the shunt becomes bi-directional, because of increased pulmonary vascular resistance, repair may still be advised if the pulmonary flow remains increased. Once blood shunts from right to left, operation is contraindicated.

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## RÉSUMÉ

Cet article porte sur les défauts de cloisonnement avec communication inter-auriculaire tels qu'ils se manifestent chez les malades âgés de plus de 40 ans. On doit penser à ce diagnostic chez les patients qui présentent une palpitation précordiale à chaque battement, un souffle pulmonaire

systolique d'éjection et un dédoublement fixe du second bruit pulmonaire. Ce diagnostic possible recevra une certaine confirmation de la découverte d'un bloc de branche à droite d'après le tracé électro-cardiographique, ainsi qu'une hypertrophie du ventricule droit et une accentuation de l'arbre pulmonaire vasculaire à la radiographie. Enfin il sera signé par la démonstration d'un shunt au niveau des oreillettes et de l'égalité de la pression dans ces deux cavités.

Alors que la chirurgie est presque toujours recommandée chez les enfants porteurs d'une lésion de quelque importance, on doit s'arrêter à considérer les risques que comporte ce traitement chez les malades âgés de plus de 40 ans. Dans une série réunie par l'auteur, de 14 opérés, trois sont morts et deux autres ont souffert d'embolie. Même si ces morts se produisirent au début de la série, on est encore sous l'impression qu'un malade de plus de 40 ans s'il ne présente qu'une dérivation minime et asymptomatique et une pression pulmonaire à peine augmentée, ne devrait pas être opéré. Certains malades par contre qui ont une large communication inter-auriculaire et qui montrent des signes de pression pulmonaire augmentée peuvent être soumis à l'opération si le shunt est encore orienté de gauche à droite. S'il existe dans les deux directions à cause d'une augmentation de la résistance vasculaire pulmonaire, on peut encore tenter l'opération lorsque le débit sanguin pulmonaire demeure élevé. Quand la dérivation a changé de direction et s'est établie de droite à gauche, l'opération n'est plus indiquée.

## PRIMARY PEPTIC ULCER IN CHILDREN REPORT OF 14 CASES AND REVIEW OF LITERATURE\*

ABDUL W. ALVI, M.B., B.S.† and  
ARNOLD G. ROGERS, M.D., M.Sc.(Minn.),  
F.R.C.P.[C],‡ *St. Boniface, Man.*

THE FREQUENCY of peptic ulcer in infants and children has been the subject of a great deal of controversy. Some say that the condition rarely occurs; others have reported surprisingly large series. The difficulty has arisen because of failure to differentiate between the acute, often catastrophic, peptic ulcer that may occur in early infancy or in association with severe stress and the onset in childhood of peptic ulceration as we recognize it in adults. In addition, the criteria for diagnosis have not been defined, so that case reports from one group may not be acceptable to another. Despite reports primarily based on post-mortem or roentgenographic studies illustrating the significance of peptic ulceration in children, clinicians are reluctant to appreciate its prevalence. If paediatricians were more conscious of this, case reports of peptic ulcer in childhood would appear more frequently.<sup>1</sup>

The present study was undertaken to determine the local hospital experience of peptic ulcer in children and to warn physicians of this possibility when faced with obscure abdominal pains or feeding problems in children.

The first case of peptic ulcer in a child was published in 1821.<sup>2</sup> In subsequent years, besides numerous instances of single cases,<sup>3-13</sup> many reports indicate the increasing awareness on the part of physicians and the value of roentgenology in establishing the diagnosis in children (Table I).

## METHOD AND MATERIAL

Case records of the paediatric department of St. Boniface Hospital for 1948-1957 were reviewed. Criteria for selection included typical or suggestive history, evidence of gastro-intestinal bleeding, roentgen signs of an ulcer crater or associated deformity, and response to medical therapy. Fourteen cases thus obtained form the basis of the present report. These patients were not seen by us personally. Sixteen years was taken as the upper age limit.

We have divided our patients into two groups:

*Group I:* Ten patients with a demonstrable ulcer crater on radiological examination, convincing history of pain, evidence of gastro-intestinal bleeding and response to therapy (Table II).

*Group II:* Four patients whose cases were similar to those in Group I, but with no demonstrable ulcer crater on radiographs (Table III).

In three cases a diagnosis of peptic ulcer was made without a typical history or radiological evidence. It was not felt justifiable to include these patients in the present report. In our review we encountered, but excluded, nine proven cases of peptic ulcer in ado-

\*From the Departments of Medicine and Clinical Investigation, St. Boniface Hospital, St. Boniface, Manitoba.  
†Resident in Clinical Research, St. Boniface Hospital. Present address: Firmin Desloge Hospital, 1325 South Grand Blvd., St. Louis 4, Mo., U.S.A.  
‡Physician, St. Boniface Hospital and Mall Medical Group, Winnipeg, Manitoba.

TABLE I.

Author and year of report	Number of cases	Age	Duration	Site of lesion	Criteria for diagnosis
Holt, 1913 <sup>14</sup>	65	70% less than 5 mths.	Acute	Duodenal	Autopsy
Theile, 1918 <sup>15</sup>	248	0-16 years	Acute and chronic	Gastric and duodenal	Clinical and autopsy
Paterson, 1922 <sup>16</sup>	2	3-6 months	Acute	Duodenal	Autopsy
Proctor, 1925 <sup>17</sup>	3	2-14 years	Chronic	Gastric and duodenal	X-ray and operation
Berglund, 1928 <sup>18</sup>	20	0-13 years	Acute and chronic	Gastric and duodenal	Autopsy
Kennedy, 1933 <sup>19</sup>	6	4-11 years	Chronic	Duodenal	X-ray and laparotomy
Smythe, 1934 <sup>20</sup>	2	Newborn	Acute	Gastric	Laparotomy and autopsy
Burdick, 1940 <sup>21</sup>	10	4½-13 years	Acute and chronic	Gastric and duodenal	X-ray, autopsy and clinical
Moore, 1941 <sup>22</sup>	8	6-14 years	Chronic	Gastric and duodenal	X-ray and clinical
Bird, Limper and Mayer, 1941 <sup>23</sup>	243	0-15 years	Acute and chronic	Gastric and duodenal	X-ray, laparotomy and autopsy
Clyne and Rabinowitch, 1942 <sup>24</sup>	4	5-7 years	Chronic	Duodenal	X-ray
Franklin, 1942 <sup>25</sup>	2	4 mths-9 yrs.	Acute and chronic	Duodenal	X-ray and autopsy
Newman, 1942 <sup>26</sup>	6	4½-12 yrs.	Chronic	Duodenal	X-ray and clinical
Guthrie, 1942 <sup>27</sup>	9	0-1 year	Acute	Gastric and duodenal	Autopsy
Benner, 1943 <sup>28</sup>	8	2 days-11 yrs.	Acute and chronic	Gastric and duodenal	Autopsy
Donovan and Santulli, 1945 <sup>29</sup>	10	3 mths-12 yrs.	Acute and chronic	Gastric and duodenal	X-ray, laparotomy and autopsy
Karlstrom, 1949 <sup>30</sup>	6	3-14 years	Acute and chronic	Gastric and duodenal	X-ray
Dahl, 1949 <sup>31</sup>	3	9-14 years	Chronic	Gastric	X-ray
Tudor, 1950 <sup>32</sup>	3	0-14 years	Acute and chronic	Gastric and duodenal	X-ray and autopsy
Alexander, 1951 <sup>33</sup>	30	2-14 years	Chronic	Duodenal	X-ray
Badosa Gaspar, 1951 <sup>34</sup>	3	12-14 years	Chronic	Duodenal	X-ray
Aye, 1953 <sup>35</sup>	4	3-10 years	Chronic	Gastric and duodenal	X-ray
Girdany, 1953 <sup>36</sup>	45	1-11 years	Chronic	Gastric and duodenal	X-ray
McAleese and Sieber, 1953 <sup>37</sup>	16	6 wks.-14 yrs.	Acute and chronic	Gastric and duodenal	X-ray, laparotomy and autopsy
Bell, 1953 <sup>38</sup>	2	5 years	Acute and chronic	Duodenal	Operation
Chapman, Loeb and Young, 1956 <sup>39</sup>	5		Chronic	Duodenal	X-ray
Goldberg, 1957 <sup>40</sup>	20	7-15 years	Chronic	Duodenal	X-ray and operation

lescents between the ages of 17 and 19 years and a fatal case of gastric ulcer in a child with third-degree burns of 50% of body surface.

Peptic ulcers in children are either primary or secondary to other conditions. Kennedy's classification<sup>19</sup> of primary peptic ulcers in children has been widely accepted:

I. *Neonatal group* (from birth to a few weeks of age). The lesion is acute, gross melæna or hæmatemesis being the first signs. It either heals rapidly or causes death by hæmorrhage or perforation. At autopsy no cellular reaction or bacterial invasion is seen around the ulcer.

II. *Infantile group* (from a few weeks to one year of age). Diagnosis is rarely made until the onset of hæmorrhage; usually not until post-mortem examination.

III. *Childhood group* (1-16 years). The older the child, the more nearly does the picture resemble the pattern in the adult.

## RESULTS

All our patients had a primary ulcer and the cases correspond to Kennedy's childhood group. The youngest patient in our series is 10 years old, and we have included a 17-year-old boy in our analysis as his symptoms date back to the age of 14 years.

*Sex.*—Ten boys and four girls in our study confirm the reported predominance of males in the literature.

*Site.*—Twelve patients had duodenal ulcer, and ten of these had a demonstrable crater on radiological examination. Two cases had evidence

suggestive of gastric ulcer, although no crater was clearly noted.

*Signs and symptoms.*—All patients were between 10 and 16 years of age. Their symptoms were mainly those found in adults, with certain complications. The onset of symptoms was acute, i.e. in four patients there was a history of less than four months, and in ten others the duration varied from months to years, the longest duration being three years in three cases.

As their presenting complaint, eight of 14 patients described recurrent abdominal pain, usually post-prandial and relieved by ingestion of food, milk or alkalis. Abdominal pain was localized to the epigastric or peri-umbilical region by the majority of our patients. Nocturnal pain was strikingly rare, only two admitting such pain. Another child had pain on arising, relieved by milk. The patients' descriptions of abdominal pain varied considerably: some labelled it "gnawing"; others called it "burning", "prickly", "stabbing", "crampy" or "stomach ache". Two patients, both with gross gastrointestinal bleeding, denied having abdominal pain at any time.

Three patients presented with massive hæmatemesis or tarry stools. Another had occult blood in his stools during the hospital course. Anæmia due to blood loss was noted clinically in these patients, one developing shock soon after admission. Five patients gave no history of hæmatemesis or tarry stools in the past and showed no evidence of gastro-intestinal bleeding while they were in hospital. Two of these five patients

TABLE II.

No.	Initials	Sex and age	Duration of symptoms	Symptoms	G.I. bleeding	X-ray findings	Other complications	Therapy	No. of days in hosp.	Additional
1	K.P.	F 15	3 years	Recurrent abd. pain 2-3 times a month, relieved by Epsom salts	Hæmatemesis 3 days before admission	Active duodenal ulcer		Med.	10	
2	D.T.	M 13	2 years	Recurrent abd. pain relieved by alkali	Occ. melæna (history)	Duodenal ulcer		Med.	9	
3	R.K.	M 12	4 days	Anorexia, dizziness, weakness, diarrhoea, headache	Severe melæna	Duodenal ulcer with pylorospasm		Med. and 1900 c.c. blood	20	
4	F.P.	M 11	1 month	Weight loss of 9 lb. in one mth. Vomited blood on day of admission	Hæmatemesis + melæna	Duodenal ulcer with pylorospasm and retention		Med.	21	Rheumatic fever in past; appendectomy in 1953.
5	B.L.	M 13	2 weeks	Sudden onset of vomiting of altered blood and gross melæna on day of adm. Epigastric pain, relieved by food for 2 weeks	Hæmatemesis + melæna	Duodenal ulcer, spastic and deformed cap		Med. + 4500 c.c. blood	17	Appendectomy in past. Had abundant free HCl in gastric juice. Rheumatic fever in past.
6	K.T.	M 12	4 weeks to many years	Abd. pain, aggravated by starch; food and relieved by milk. Also nightly vomiting	Occ. blood in stools in hospital	Duodenal ulcer with deformed cap and irregularity		Med. (poor response)	31	Had free HCl in gastric juice—one year. Some relief.
7	D.D.	M 15	Several months	Pain after meals "gnawing" in character, relieved by milk, food		Duodenal ulcer with deformity of cap. Rapid transit time		Med.	13	
8	E.J.	M 16	3 years	Epigastric pain 2-4 hours after meals "burning" in character; started at age 13; relieved by food or baking soda	Vomited on day of admission	Duodenal ulcer		Med.	14	Free HCl in gastric juice. Follow-up at age 22. One episode of subsequent hæmatemesis, occ. melæna; radiographs at age 22 showed ulcer with deformed cap. Weight loss.
9	H.S.	M 17	3 years	Gradual onset of "prickly" periumbilical pain 3 yrs.; not related to meals; would wake patient at night. For 1 year pains 1 hour after meals, "stabbing" in epigastrium and lasting for a few minutes to one hr.; constant for 24 hrs. before admission	Occasional melæna 1 wk. before admission	Duodenal ulcer	Obstruction	Med.	18	Had free HCl in gastric juice. Course satisfactory until age 20 when readm. for pyloric obst. Had subtotal gastrectomy after a bout of massive hæmatemesis while in hospital.
10	P.D.	F 15	1 year	Epigastric pain 1½ hrs. after meals		Duodenal ulcer		Med.	9	Appendectomy — 1950. Gastritis? One year before present adm. had similar complaints, but had no radiographs.

TABLE III.

No.	Initials	Sex and age	Duration of symptoms	Symptoms	G.I. bleeding	X-ray findings	Other complications	Therapy	No. of days in hosp.	Additional
1	E.G.	F 14	3 years to 1 year	Epigastric pain lasting for 2 hrs. Occ. emesis, relief with carbonated beverage. Similar pains 1 year ago. X-rays: spasm of duodenal cap		Ulcer high upon lesser curvature of stomach. Deformity of greater curvature		Med.	15	Appendectomy (acute supp. appendicitis).
2	J.S.	M 13	2 years	Intermittent low abd. pains for 2 yrs. lasting for 1 hr "Crampy" assoc. with distension, relieved by belching		Intravenous pyelogram neg. Pyloric spasm. Deformed cap spastic with unduly prominent folds and persistent rest of barium along greater curvature		Med.	6	Appendectomy (acute early appendicitis).
3	V.R.	F 15	1 day	Dull ache in epigastrium 1 day before adm. Nausea followed by sudden hæmatemesis and tarry stools	Hæmatemesis and melæna	Spasm of duodenum, rapid transit time		Med. + 2000 c.c. of blood	9	
4	G.F.	M 10	1 month	Upper abd. pain on arising in a.m. relieved by milk or food. Recurrence between meals. Nausea and early morning emesis		Considerable pylorospasm		Med.		Chorea in past "Nervous, high-strung child".

belong to group I—i.e., there was roentgenologic proof of an ulcer crater; the other three belong to group II. Anorexia was a prominent feature in one child. Another had lost 9 lb. in one month before admission. Pyrosis, eructation and flatulence were noted in two. Abdominal tenderness was the most constant sign in the present series. One patient exhibited generalized tenderness and guarding, but in the majority the tender area was in the epigastrium or around the umbilicus. In all four cases subjected to gastric analysis, free hydrochloric acid was present in the gastric juice, but only one showed a high concentration, reported to be a feature of duodenal ulcer in adults.

### *Radiology*

Radiographs were most helpful in arriving at the correct diagnosis even in cases where frank gastro-intestinal bleeding had forced the patient to seek medical advice. As already mentioned, an ulcer crater was clearly discernible on x-ray films in 10 cases (group I). Four cases (group II) had irritability, deformity and pylorospasm suggestive of peptic ulceration.

Three of 10 cases with a visible ulcer crater also had irritability and deformity of the duodenal cap. Five patients had noticeable pylorospasm during the radiological examination, and in two additional patients transit of barium through the small bowel was extremely rapid and associated with deformity of the duodenal cap. Two patients had gastric retention at the end of four hours, one of them requiring an operation for pyloric obstruction three years later.

### *Complications*

Massive gastro-intestinal hæmorrhage was encountered in three patients, one of whom developed shock soon after admission. They required respectively 1000, 2000 and 4500 c.c. of blood for replacement before bleeding was stopped. Six other cases had shown evidence of gastro-intestinal bleeding before admission or during their stay in the hospital, but in none was it considered serious enough to warrant transfusion.

Transient pyloric spasm during radiological examination was seen in five cases. One of the two patients showing gastric retention at the end of four hours responded to medical management; the other developed complete obstruction three years later and required subtotal gastrectomy for its relief. No case of perforation was encountered in this series. There was no fatality.

### *Therapy*

All patients were treated by the conventional medical regimen for peptic ulcer, namely by diet, sedation, antispasmodics and alkalis. Transfusions were required in three cases. One patient developed complete pyloric obstruction three years

later and underwent subtotal gastrectomy. All the others responded satisfactorily to medical management. Two patients were seen by surgeons in consultation who recommended continued medical management in the absence of complicating factors.

The hospital stay of our patients ranged from 10 to 21 days.

### *Psychological Factors*

Two children admitted dislike for school. One could not get along with the teacher; in the other, the symptoms started at the beginning of the fall term and recurred at the beginning of the fall term in the subsequent year. Abdominal pains were precipitated by financial worries in another child. No formal study of psychological factors was attempted. No hostility towards parents or siblings was recorded in the history, nor was a familial trend of peptic ulcer noted in our patients.

### *Previous Illnesses*

Five patients had had an appendectomy at one time or another before peptic ulcer was diagnosed. In only two of them was the pathologist able to detect changes of acute inflammation. Three patients had had rheumatic fever or chorea. Two patients gave a history of headaches with episodes of vertigo and transient loss of consciousness. Another patient had an abnormal electroencephalogram.

### DISCUSSION

There has been a gradual increase in the number of reports of peptic ulcer in children since the initial report. This has been brought about by greater awareness of peptic ulcer in children as a result of postmortem and particularly radiological studies.

Earlier reports suggest that the chief difficulty in diagnosis is lack of the symptoms and signs usually encountered in adults. The diagnosis is frequently missed until severe hæmorrhage, obstruction or perforation has occurred.<sup>8, 17, 26-28</sup> This means that uncomplicated ulcers in children are usually not diagnosed. One-third of Holt's<sup>14</sup> cases were symptom-free during life, lesions being discovered at autopsy. Recent studies suggest that symptoms differ little from those seen in adults.<sup>31, 32, 34, 36, 40-42</sup> The history of abdominal pain, relieved by milk, alkalis or vomiting, and the response of our patients to conventional medical therapy leave little doubt that in children the symptoms simulate the adult pattern. Although the characteristic story of pain is often not volunteered, it can usually be elicited by direct questioning in older children.<sup>36</sup>

It is difficult to evaluate from the literature the true incidence of primary peptic ulcer in children. The number of reported cases is certainly far below the actual incidence, as not all cases are

reported. Many cases were missed in the days when radiological examination was not available or its use was limited. Sixteen of 1000 adults with gastric ulcer (1.6%) and 26 of 1000 adults with duodenal ulcer (2.6%) from the Mayo Clinic had symptoms dating back to their childhood.<sup>17</sup> This was essentially a select group. We know that there are many adult patients whose peptic ulcer is not complicated and who do not require hospitalization. Many more lesions are not diagnosed until autopsy. If this were taken into consideration, there would be a higher incidence of diagnosed peptic ulcer in children. Several large clinics have reported an incidence of 0.8-2.1% of children among their patients with peptic ulcer.<sup>30</sup> The incidence in children seems to be increasing in the same manner as in adults, although more thorough evaluation and roentgenological studies may be responsible for this increase.<sup>33, 36</sup>

The predominance of duodenal ulcer over gastric ulcer in our series corresponds to the ratio observed in reported cases.<sup>18, 22, 23, 27, 28, 31, 35, 37, 43</sup> In children 16 years or younger, Theile<sup>15</sup> reported a series of 248 cases of ulcers, half of which were located in the duodenum. Tudor<sup>32</sup> found 218 duodenal ulcers and 68 gastric ulcers in 286 cases collected from the literature. In Block's<sup>12</sup> critical analysis of chronic gastric ulcers in childhood, there were only 40 cases in over 100 years.

The striking preponderance of males over females in adult series also holds for children.<sup>12, 22, 24, 26-28, 30, 33, 40</sup> There are few reports to the contrary.<sup>17, 36, 41, 44</sup> The finding of ten boys and four girls in our series shows the increased incidence in the male sex. The reason for the male predominance is uncertain. Male hormones may increase gastric secretion; female hormones may inhibit gastric secretion (e.g., the remission seen in females in pregnancy).<sup>41</sup> It is known that the average acidity of the Ewald test meal is greater in males than in females between 20 and 50 years. The increase in incidence of peptic ulcer in males after the age of puberty may be due either to an increase in susceptibility or to an increase in exposure to the ulcerogenic factors in their environment. A lesser increase in the clinical incidence of and death rate from peptic ulcer also occurs in females after puberty.<sup>41</sup>

As in adults, the etiology of peptic ulcer in infants and children remains obscure. Prematurity has been mentioned as a cause, and cases have occurred in association with erythroblastosis fetalis.<sup>32</sup> Various theories of the production of secondary ulceration in infants and children have already been alluded to. Such factors as alcohol, tobacco and occupational strain are almost negligible.<sup>35, 44</sup> Constitutional factors should be evident before environmental factors operate. Some authors have suggested that ulcer in the newborn is due to retrograde thrombosis from the umbilical stump or emboli arising from it and passing through a patent foramen ovale, but thrombi are

not usually encountered on the border or the base of these ulcers. Others have suggested venous back pressure with congestion of mucosa and digestion of hæmorrhagic areas. Brain injury at time of birth has been mentioned as a cause, but Guthrie<sup>27</sup> failed to find evidence of brain lesions in her cases, all in children who had been delivered normally. Harvey Cushing<sup>45</sup> encountered acute ulcers after operations in the region of the cerebellum. In suppurative meningitis (acute or tuberculous) patients are especially prone to peptic ulceration. At one time, ulcers in infancy were considered to be infectious,<sup>46</sup> but it is unusual to find any evidence of inflammation in the margins of these ulcers. Local angiospasm as well as myospasm has been suggested.<sup>27</sup> In adolescents, peptic ulcer may be a psychosomatic disease. It has been suggested that there is an association between the anterior pituitary and peptic ulceration in adolescent boys.<sup>32</sup>

All the various theories of ulcer genesis have been used to explain peptic ulcer in infants, although no emphasis has been placed on the acid theory.<sup>41</sup> Cutter<sup>47</sup> noted a rapid increase in gastric acidity during the first year of life and a much slower increase from the end of that period until the fourth year of life, when the values almost reached adult standards. Miller<sup>48</sup> observed that the gastric juice even in early infancy possesses considerable powers of peptic digestion; its acidity is surprisingly high, reaching a maximum within 48 hours of birth, when it is equivalent to that of a healthy adult. Thereafter it falls rapidly, and remains low during infancy. At the end of the first year of life the reaction of the stomach to a test meal of milk closely resembles that of an adult. That some process or group of factors causes a change in the lining of the bowel wall which allows acid gastric juice and pepsin to destroy the mucosa is widely believed.

Reports of familial incidence of peptic ulcer are too few to lend support to the theory of hereditary influence. Barborka and Texter<sup>49</sup> report a family in which both parents and six children had complicated peptic ulcers requiring surgery. No such tendency was noted in the families of our patients.

Most of the reports indicate that the information obtained from gastric analysis in children is of little value in the diagnosis of peptic ulcer.<sup>22, 25, 26, 34, 44</sup> Too few of our patients had gastric analyses to warrant any conclusions.

The great number of factors known to cause ulcer in man and in experimental animals suggests that there is no common etiology, and the problem in children as in adults is as yet unsolved.<sup>33</sup>

The most important factor in diagnosis is awareness that peptic ulcer, acute and chronic, occurs in children. One must consider peptic ulcer in every case of obscure abdominal pain, especially if it lasts for more than several days. Naturally

a good history and physical examination with particular reference to symptomatology are indispensable. Nevertheless, barium meal roentgenography is the single most dependable factor in the diagnosis of peptic ulcer in children.<sup>26, 34, 44</sup>

The roentgenological signs of duodenal ulcer in children include pylorospasm, deformity of the duodenal bulb, folds radiating towards a crater, and a niche with a radiolucent zone surrounding it.<sup>36, 42</sup> Ulcer craters demonstrated in children are usually smaller than those seen in adults.<sup>36</sup> Techniques of radiological examination are the same as in adults. Right oblique anterior erect and prone projections will give a satisfactory delineation of this area.<sup>33</sup> Spot films of the duodenum are especially important, since this is the most common site of peptic ulcer in childhood.<sup>42</sup> Irritability of the bulb cannot be used as a roentgenographic criterion of ulcer in children, since it is a usual finding, according to Girdany.<sup>36</sup> On the other hand, Alexander<sup>33</sup> feels that a greater degree of bulbar deformity is usually found in pre-adolescent patients with symptoms similar to those of ulcer of longer duration in adults; irritability of the duodenal cap and the intermittent pyloric spasm during the early part of the examination are very prominent features. Borderline situations in interpretation will occur in which the barium meal may show pylorospasm and delayed emptying, or in which the duodenal bulb may reveal irritability and irregularity without the actual formation of a crater. In cases in which these changes persist after the administration of atropine, the diagnosis can only be presumptive; routine therapy should be ordered and periodic roentgenography should be performed.<sup>26, 34, 44</sup>

During fluoroscopic examination the child frequently points to the site of the pain, although he has previously given a story of pain referred to the epigastrium or peri-umbilical region.<sup>36, 42</sup>

Fractional test meals are apparently of little or no diagnostic value in children. Tests for occult blood in stools, if done repeatedly, are an aid to diagnosis in otherwise obscure cases; periodic blood counts may also be of some value.<sup>44</sup>

In the neonatal sub-group when there is serious bleeding from the gut without discoverable cause, peptic ulcer should be considered as the possible diagnosis, as the ulcer may be microscopic. The occurrence of hæmatemesis or melæna in a young infant whose condition otherwise suggests pyloric stenosis should suggest the possibility of peptic ulcer.<sup>44</sup> Regardless of the age of the child, indefinite and prolonged abdominal discomfort particularly epigastric in situation, even if unaccompanied by other characteristic symptoms, may be caused by ulcer, and roentgen examination is justifiable.<sup>32, 44</sup>

By omitting the radiological examination the diagnosis may be missed. Presumably if roentgenological studies were made routinely in all

children with digestive complaints, peptic ulcer would be diagnosed more frequently.<sup>34</sup> Hæmorrhage from the stomach or bowel is the most characteristic sign of peptic ulceration in children.<sup>32</sup> The roentgenographic examination is of much value not only in confirming the diagnosis, but also in following the result of therapy.<sup>37</sup>

In differential diagnosis, one must exclude ingestion of blood from the nose or mouth, and in the case of nursing infants, from the mother's nipple. In the newborn, hæmorrhagic disease of the newborn, septicæmia, leukæmia, purpura, syphilis and fibrinopenia should be considered. Hæmophilia rarely manifests itself during the newborn period. Melæna neonatorum is due to peptic ulceration in 50% of cases, according to Bradlow.<sup>44</sup> Duodenal ulcer in infants may simulate severe pylorospasm, hypertrophic pyloric stenosis, congenital duodenal stenosis or gastroenteritis. In older children other causes of intestinal hæmorrhage such as intussusception, colitis, rectal polypi, Meckel's diverticulum and intestinal parasites must be considered. Malignant neoplasms of the bowel are very rare in this age group. Children were thought to have acute appendicitis in some instances, and the true nature of the lesion became known only after removal of a normal appendix suggested that further investigations were desirable.<sup>24</sup>

As mentioned already, five patients in our group had had appendectomy for abdominal symptoms before the diagnosis of peptic ulcer was established. In three of these, no evidence of acute inflammation of the appendix could be determined on histological examination, suggesting that it was not the cause of symptoms. It is almost certain that the ulcer was responsible for the symptoms that led to the appendectomy.

For children under one year of age, prognosis is generally poor because of the acuteness of the lesion. A few heal spontaneously. In older children the outlook for healing is generally excellent, and symptomatic relief, if not cure, is obtained in a great majority of cases by routine therapy.<sup>44</sup>

Most authors agree that the indications for medical and surgical treatment of ulcer and its complications in children are the same as in adults. For older children, frequent meals of bland diet, chiefly milk, together with the use of alkali powder and antispasmodics, are the essentials of medical treatment. In infancy most of the cases present with complications initially and thus are unfit for medical therapy; prompt surgery is most often necessary. Yet often even those who need surgery cannot be operated upon because of their poor general condition.

The indications for surgical intervention in the treatment of peptic ulcer in children are much the same as in adults.<sup>13, 37, 38, 44</sup> For the most part they are pyloric obstruction, perforation, persistent hæmorrhage or intractable pain. The mortality from surgery is very high in children under one

year of age; for those past the age of six, the mortality rate is about 5%;<sup>44</sup> 70% of patients between 7 and 15 years, reported by Bird,<sup>23</sup> were operated upon, mostly for stenosis (53 cases), for perforation (43 cases), a few for hæmorrhage (12 cases), and some for persistent pain (11 cases). Simple closure was performed in 37 cases, pyloroplasty and gastro-enterostomy in 55 cases and resection in 17 cases. The total mortality was 11%. Pyloroplasty, gastro-enterostomy and closure of perforation have all been attempted by various workers. Apparently vagotomy has never been performed in children.<sup>13, 37</sup> There is controversy among surgeons regarding gastric resection.<sup>13, 26, 37</sup> There are case reports of stomal and jejunal ulcers complicating gastro-enterostomy operations in childhood,<sup>13, 23, 41</sup> but long-term studies are needed to evaluate the problem.

Psychiatric studies have not been reported on large groups of children with peptic ulcer. Available observations reveal a division of opinion on the role of emotional problems in the etiology of peptic ulcer in children.<sup>17, 33, 34, 40, 42</sup> Girdany's patients<sup>36</sup> were bright and tense, and characterized by their parents as "nervous", often lacking outward emotional lability, with a tendency to keep things to themselves.

In a more recent psychiatric study by Chapman *et al.*,<sup>39</sup> of five children with duodenal ulcers, the findings were similar to those in adults with peptic ulcer. Their common features were a marked inability to be comfortable, with expression of any hostile or aggressive feelings; resultant passivity and subnormal assertiveness, with a strong need to attempt to obtain endless amounts of affection and approval by being servile and obliging to all persons around them; their marked conflicts over unmet needs for a secure, anxiety-free relationship with a warm and affectionate mother figure; and a distant and emotionally ineffective relationship with the father.

#### SUMMARY

Available literature on the subject of peptic ulcers in children has been reviewed. The case records of ten boys and four girls between the ages of 10 and 16 years admitted during 1948-1957 to St. Boniface Hospital were selected and reviewed. Twelve patients had duodenal ulcer. The incidence corresponds well with the reported increased frequency in males and predominance of duodenal over gastric ulcer.

The symptoms seemed to follow the adult pattern, and bleeding from the gastro-intestinal tract seemed to be common. However, five patients had no bleeding but had radiological evidence of peptic ulcer. The importance of roentgenological examination in children with abdominal complaints of obscure nature has been clearly defined. Radiological criteria for diagnosis of peptic ulcer in children have been discussed.

Children usually respond satisfactorily to a conventional medical regimen.

It is suggested that in children with a history of long-standing abdominal pain not obviously fitting

into the usual childhood ailments, peptic ulcer should be included in the differential diagnosis and gastro-intestinal radiographs should be obtained. A similar diagnosis should be considered when a normal appendix is removed from a child with abdominal complaints. Such a method will yield a greater number of cases of peptic ulcer, and early diagnosis with prompt treatment may reduce the percentage of complications and mortality. The incidence of uncomplicated peptic ulcer in children must be far greater than is apparent from studies of hospital patients with complicated ulcer.

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#### RÉSUMÉ

Les auteurs ont passé en revue la littérature médicale traitant de l'ulcère peptique chez les enfants. Ils ont de plus résumé les dossiers de 10 garçons et de 4 fillettes âgés de 10 à 16 ans admis à l'hôpital de St-Boniface entre 1948 et 1957. Douze d'entre eux souffraient d'ulcère duodénal. Cette fréquence illustre bien la prépondérance de l'ulcère duodénal et de l'atteinte masculine.

La symptomatologie chez l'enfant correspond à celle de l'adulte et les hémorragies gastro-intestinales sont fréquentes. Cependant, cinq patients n'accusaient aucun saignement mais offraient une image radiologique d'ulcère peptique. On doit reconnaître l'importance de l'examen radiologique chez les enfants accusant des symptômes abdominaux d'origine obscure. Les critères radiologiques du diagnostic d'ulcère peptique chez les enfants sont présentés.



Ces jeunes malades ont bien répondu au régime médical habituel. On suggère que l'ulcère peptique soit inclus dans le diagnostic différentiel des douleurs abdominales chroniques chez les enfants, surtout si elles ne cadrent pas dans les maladies infantiles communes. Il est alors important de pratiquer un repas baryté. Les mêmes recommandations s'appliquent lorsqu'un appendice normal est enlevé chez un enfant se plaignant de douleurs abdominales. Cette

méthode permettra de découvrir un plus grand nombre de cas d'ulcère peptique et grâce à un diagnostic précoce et à un traitement immédiat elle contribuera à diminuer le pourcentage des complications et des mortalités. La fréquence des ulcères peptiques sans complication chez les enfants doit être bien supérieure à ce que les travaux sur les malades hospitalisés avec complications nous permettent d'entrevoir.

## SUSTAINED-RELEASE NICOTINIC ACID (Nicospan)\* EFFECT ON (1) CHOLESTEROL LEVELS AND (2) LEUKOCYTES

P. O. O'REILLY, M.B., B.Ch.,†  
North Battleford, Sask., and

M. J. CALLBECK, R.N.‡ and

A. HOFFER, Ph.D., M.D.,¶ Saskatoon, Sask.

### INTRODUCTION

RECENT INVESTIGATIONS of the administration of nicotinic acid to humans have shown that nicotinic acid lowers serum cholesterol levels.<sup>3, 4, 8, 9, 10</sup> Altschul<sup>1, 2</sup> has also demonstrated that in rabbits, normal or artificially raised serum cholesterol levels can be lowered by large doses of nicotinic acid and the well-known experimental atherosclerosis inhibited. The minimum effective dose in humans is one gram three times a day, and doses up to six grams a day have been used. Hoffer, O'Reilly and Callbeck<sup>6</sup> in a recent study showed how specific the hypocholesterolaemic action of nicotinic acid is. Neither nicotinamide nor nicotiny alcohol (Roniacol) is active. The question of safety of prolonged medication with 3 to 6 g. per day of nicotinic acid has been studied by Hoffer and Callbeck.<sup>7</sup> They found that following at least one year's continuous treatment with nicotinic acid no liver dysfunction or significant shift in leukocyte pattern occurred, indicating the safety of the medication.

Of immediate concern are the side reactions which accompany the taking of the drug. They are: (a) The marked flushing and pruritus which occur in all cases. Associated with this, some persons report a numbness and weakness of the lower limbs and dizziness. Generally these reactions diminish and usually disappear after the first few days of treatment. However, some persons on prolonged medication report this reaction occurring sporadically throughout the treatment period. (b) Gastro-intestinal disturbances occur in a cer-

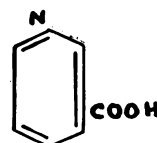
tain number of cases and may lead to interruption or discontinuation of the treatment. These gastric disturbances are believed by Altschul and Hoffer<sup>5</sup> to be due to the high acidity — that is, an un-specific factor — rather than to a specific action of nicotinic acid. They suggest that a solution of nicotinic acid buffered with NaHCO<sub>3</sub> and KHCO<sub>3</sub> may eliminate the gastro-intestinal disorders.

These side effects are possibly due to a very rapid absorption of nicotinic acid into the blood. We had earlier observed that after the intravenous administration of nicotinic acid there was a very marked vasodilatation. When the vasodilatation subsided, a short period of time followed during which the subject was refractory to further vasodilatation. In some instances no flush followed the taking of 2 g. of nicotinic acid orally, after the flush induced by 200 mg. of intravenous nicotinic acid had subsided. Furthermore, after some days of steady administration the vasodilatation tended to disappear. It thus seemed likely that the vasodilatation depended upon high serum levels of nicotinic acid and was independent of its hypocholesterolaemic effect. These findings suggested that adequate blood levels could be attained by some slow-release mechanism without producing a flush.

The purpose of this paper is to report on the action of a sustained-release form of nicotinic acid (Nicospan). The areas of investigation are: (a) the vasodilatation, (b) the effect on serum cholesterol levels, (c) the effect on leukocytes, (d) the side reactions.

### Composition of Tablet

The structure formula of nicotinic acid may be represented as follows.



The sustained-release tablet (Nicospan) contains 500 mg. nicotinic acid in a special base which is liberated over a period of 7 to 11 hours after ingestion.

\*Nicospan is the trademark of Wm. S. Merrell Company for its special nicotinic acid sustained-release tablet.  
†Research co-ordinator and senior specialist, Saskatchewan Hospital, North Battleford, Sask.  
‡Chief research psychiatric nurse, psychiatric research, Psychiatric Services Branch, University Hospital, Saskatoon, Sask.  
¶Director, psychiatric research, Psychiatric Services Branch, University Hospital, Saskatoon, Sask.