general similarity between the renal effects of aminometradine and of mersalyl suggests that the same mechanism of "resistance" might apply to both drugs. As shown in these results, the increase of chloride excretion exceeded that of sodium after mersalyl but was slightly less than the increase of sodium excretion in the case of aminometradine. This will lessen somewhat the liability of aminometradine to reduce the plasma chloride concentration and also render the development of "resistance" to this drug less probable.

Although the effect of mersalyl was greater than that of aminometradine during the first 24 hours after administration of either drug, the urine flow during the second 24 hours was frequently greater after aminometradine. Thus the net effect of the two drugs when they were administered at intervals of 48 hours was comparable. The more sustained and less violent diuresis caused by aminometradine given every 24 or 48 hours, as compared with that produced by mercurial diuretics, which are usually administered two or three times weekly, may be advantageous in some patients with heart failure.

The observations that the maximum diuresis from aminometradine often does not develop until the third or fourth day of administration, and that the diuresis caused by a single dose lasts more than 24 hours, suggests that a single dose of 400 mg. is not completely excreted in 24 hours. It is therefore probably advisable not to administer the drug daily but to allow one or two days of freedom from treatment each week.

It is possible that the main use of aminometradine may be found in the prophylaxis of oedema in those patients with chronically recurring cardiac failure who constantly require a diuretic. As pointed out by Spencer and Lloyd-Thomas (1953), assessment of the diuretic action of any drug in the treatment of heart failure is fraught with difficulty, owing largely to the tendency of the patients' clinical condition to fluctuate spontaneously, and this applies particularly to the prophylaxis of cardiac oedema. The evidence accumulated so far suggests, however, that a clinical trial of the prophylactic effect of aminometradine would be worth undertaking.

Summary

The effect of the oral diuretic aminometradine (mictine) on the urine flow and electrolyte excretion of 20 patients with congestive heart failure has been studied.

The increase of urine flow and the augmented excretion of sodium and chloride which resulted from 400 to 800 mg. of aminometradine were, in general, somewhat less than those caused by 2 ml. of mersalyl.

The drug produced a good therapeutic effect in eight patients, in five the response was fairly good, and in five it was negligible.

Aminometradine is regarded as a fairly effective agent in the treatment of congestive heart failure where an immediate diuresis is not urgently required.

Toxic effects were confined to the gastro-intestinal tract. In three patients the drug was discontinued owing to nausea and vomiting. Little advantage is gained by increasing the dose beyond 400 mg. daily in the majority of patients.

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SHIGELLOSIS IN THE FIRST TWO YEARS OF LIFE

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In infancy the classical picture of bacillary dysentery is often absent and the patient may present a variety of clinical patterns, and, moreover, in this age group the characteristic features of dysentery may be produced by other agents, infective or non-infective. In Yugoslavia, about 5,000 cases of bacillary dysentery are registered annually—a figure which is certainly far short of the actual total. The number of cases admitted in the first two years of life has steadily risen during recent years, among them many cases in infants, who are particularly susceptible to such infection. The variety

FIG. 1.—Yearly distribution (June 1-May 31) of bacillary dysentery. FIG. 2.—Seasonal distribution of bacillary dysentery (1949-53).

TABLE I.—Age Distribution of Cases of *Shigella* Infection

Age	No. of Cases	%
0-2 months	2	0.9
3-11	78	35.3
12-23	141	63.8
Total	221	100

of clinical pictures which can occur has led us to analyse our experience with such cases admitted to the Infectious Diseases Hospital in Zagreb between June, 1949, and May, 1953.

The distribution of the cases by year and by season is shown in Figs. 1 and 2. The latter illustrates the fact, already well known, that shigellosis is a disease of warm seasons. Table I gives the age distribution of the 221 cases included in our series and shows that the highest proportion of cases was in the second year of life. The majority of patients (158) came from the town of Zagreb; the remainder were from the surrounding country districts.

Bacteriological Examinations

Specimens of fresh faeces or rectal swabs were taken in every case, and were plated immediately on SS agar at the patient's bedside. At least two specimens were examined before treatment was started. Despite this rather intensive

search, proof of infection with shigella organisms was obtained in only 59% of the series. In the remainder the clinical diagnosis of shigellosis was supported by epidemiological evidence, since close contact with bacteriologically proved cases was known. (A number of patients, for example, were infected in an outbreak in a nursing-home and others were involved in an extensive cross-infection with *Shigella sonnei* in a scarlet-fever ward.) Three reasons may be offered for failure to identify the infecting agent: (1) With small infants, specimens were taken only at times when diapers were being changed. Possibly these specimens were not always sufficiently fresh at the time of plating. (2) Many patients were already in the second or third week of illness when admitted. (3) Sulphonamide treatment had often been given before the patient was admitted to hospital.

Table II gives the distribution of the different strains isolated. Flexner strains accounted for almost two-thirds of the proved cases and were isolated from patients living in the town and in nearby areas. Although *S. shigae* accounted for only 4.6% of the cases, it was interesting that all of these cases came from the country districts. Analysis of the bacteriological findings in respect of stool appearance showed that shigella organisms were cultured from 64.5% of those whose stool contained blood, whereas of stools which showed no blood 47.4% gave a positive bacteriological result. The latter finding emphasizes the importance of routine plating of stools in infants and young children, since it is evident that shigella infection may be present even in cases where blood is not visible in the stools.

TABLE II.—Distribution of Strains of *Shigella* Isolated

Shigella Strain	Isolations	
	No.	%
Flexner	82	63
Sonne	38	29.2
Shiga	6	4.6
Schmitz	3	2.3
Etouse	1	0.8
Total	130	100

Clinical Data

More than half the patients in this series were children who were previously in perfect health (54.3%), but the remainder, including one 6-weeks-old premature infant, showed signs of undernutrition. In almost one-quarter of the series a history of frequent diarrhoea was obtained, and 17 patients (7.7%) had recently had an infectious disease such as whooping-cough, scarlet fever, measles, or pneumonia.

The onset of illness was sudden in 61% of the cases. The intensity of illness varied to some extent with age in that the older children had a milder form of infection. Table III shows the classification of intensity of illness according to age.

TABLE III.—Intensity of Illness According to Age

Intensity of Illness	Age (Months)				Total
	0-11		12-23		
	No.	%	No.	%	
Mild ..	33	41.2	104	73.6	137
Moderate ..	41	51.2	32	22.7	73
Severe ..	6	7.5	5	3.7	11
Total ..	80	100	141	100	221

The duration of treatment in hospital varied, but 134 patients were discharged after two to three weeks. The average duration of stay in those under 1 year was twice that in the older group (2.6 and 1.3 weeks).

In regard to the clinical aspects of the disease, we recognized four forms of illness:

(1) *Fulminant*.—The onset was abrupt, and toxic effects produced severe nervous and circulatory disturbance. Pyrexia and

signs suggesting colitis were more or less marked. This form, although infrequent in the series, occurred mostly in those in their first year. These cases were classified as severely ill.

(2) *Dysenteric*.—In this form mucus, blood, and pus were present in the stool. Abdominal pain, tenesmus, and vomiting with dehydration occurred, but toxic symptoms were less obvious than in the fulminant form. This was the commonest form of the disease in older children (63%), and accounted for the majority of the illnesses in infants. Most of the illness was mild in character.

(3) *Gastro-enteric*.—Vomiting and loose mucoid stools characterized this form of the disease. It was seen more often in infants than in older children.

(4) *Subclinical*.—Loose stools were noted, but constitutional upset did not occur.

Table IV shows the distribution of the four clinical forms of the illness in relation to the age of the patient.

TABLE IV.—Distribution of the Four Clinical Forms of *Shigella* Infection in Relation to Age

Clinical Form	Age (Months)				Total
	0-11		12-23		
	No.	%	No.	%	
Fulminant ..	5	6.25	1	0.7	6
Dysenteric ..	38	47.5	89	63.1	127
Gastro-enteric ..	34	42.5	35	24.8	69
Subclinical ..	3	3.75	16	11.3	19
Total ..	80	100	141	100	221

Pyrexia.—Fever was present in 50% of cases, and was usually high (100.4–104° F.—38–40° C.) but of short duration. In 44% of febrile cases the fever lasted three days or less. Many patients were admitted some time after the onset of illness, which may account for the absence of pyrexia or its short duration in hospital. It was noticeable that in the fulminant form of the disease fever was not usually a feature.

Diarrhoea.—This was a constant finding, but the frequency of stools varied between 2 and 40 in the first 48 hours of illness. More than one-third of the patients (36.1%) had up to 10 stools in the first 48 hours, and 12.2% had more than 10. Blood was noted in the stools during the first hours of illness in 41.6% of patients, but in 17.6% it did not appear before the third day. In 94 patients no blood was found in the faeces, but 7 of these had watery stools, 20 had loose stools, and in 67 loose stools containing mucus were noted.

Dehydration was a feature in half of those in the first year of life, and in one-fifth of those over 1 year. The weight was recorded daily in 46 children in the series. In infants there was an average loss of 71 g. daily, and in older children the daily weight loss averaged 92 g.

Vomiting occurred at the beginning of the illness in 36.3% of patients. This figure is not significant for dysentery, and indeed probably indicates only a non-specific response of the young patient to diverse insults.

Complications

Relapse was seen in 7.2% of the series, and was more frequent in infants than in older children. Diarrhoea without blood in the stools, and slight general disturbance unaccompanied by fever, were the basis for the diagnosis of relapse.

Four children were readmitted between one and two months after discharge. These cases were not bacteriologically proved at the second admission, but all had had a Flexner infection originally.

Otitis media occurred in 3.1% of patients, usually in the third and fourth weeks of the disease.

We also noted, in four cases, combined amoebic dysentery and shigellosis. These patients, in whom diarrhoea had continued for a long time, were found to be markedly undernourished. In these patients, and in a few others,

oedema of the feet was present. This we considered was probably due to hypoproteinaemia.

The fatality rate was low (2.3%). Of the five patients who died four were infants. All were bacteriologically proved cases, four being of Flexner and one of Shiga type. This low fatality rate is in keeping with our finding that the majority of cases were mild in character.

Diagnosis

The most difficult disease to differentiate is salmonellosis, in which also blood is often found in the stools at onset. The only accurate means of diagnosis is by bacteriological culture. Amoebic dysentery may be identified by finding the cysts or vegetative forms of *Entamoeba histolytica* in the stools, or from knowledge that the patient comes from an area where such infection is endemic. Infections of the central nervous system may be diagnosed in shigellosis, especially in the early, pre-diarrhoeal stage of the fulminant type of infection, when the picture suggests an encephalitis. Diarrhoea due to parenteral infection or alimentary upset may be differentiated by finding a focus of infection elsewhere—for example, otitis, nasopharyngitis, pneumonia, or pyuria—or by the response of the patient to correct dietary regime.

Conclusions

The younger the child the more difficult is the diagnosis of shigellosis, because in infancy the disease more often suggests gastro-enteritis than dysentery, and because diarrhoea of other aetiology (alimentary, parenteral, or salmonella infection) may present the same clinical features as the dysenteric form of shigellosis. The disease is an important one in summer, especially in Yugoslavia, where standards of hygiene are low, and should be regarded as the most probable cause of enteric illness in infants and young children. The disease has an acute onset in children and lasts longer and is more severe in infants than in the older group. The most efficient method of diagnosis is the finding of shigellae in the stool.

Spread of the disease is by means of infected food. This is suggested by the fact that only small numbers of cases are seen in infants in the first three months of life when breast-feeding is usual, whereas older children are frequently affected. As the child becomes older and receives cow's milk and solid foods, especially when these are uncooked, opportunities for infection increase. In addition, with increasing activity the child himself may put infected objects into his mouth.

The small number of infections we saw during the winter months were probably exacerbations of chronic shigellosis, an uncommon condition under the age of 2 years, but more frequent in adults. The survival of shigella organisms in adult cases throughout the winter months ensures that there is a reservoir of infection from which epidemics may appear in children in the summer. As the number of cases of chronic shigellosis in adults increases, greater opportunity of infection in childhood occurs.

Summary

An analysis has been made of 221 cases of shigellosis in children up to 2 years of age in Zagreb, Yugoslavia. In 59% there was bacteriological proof, and in the remainder the epidemiological data suggested shigella infection as the cause of illness. The Flexner type of organism was most frequently found.

The majority of cases were mild in character. Five children in the series died—a fatality rate of 2.3%.

Four clinical forms of the disease were noted, of which the most severe were seen in infancy. The importance of the variation of the disease in infants from the classical description, and the importance of routine stool plating in this group, are emphasized.

The diagnostic difficulties are discussed.

ABDOMINAL MIGRAINE IN CHILDREN

BY

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Considerable interest has recently been shown in the condition variously known as cyclical vomiting, abdominal migraine, abdominal epilepsy, or the periodic syndrome. By whatever name it may be called the clinical manifestations are of a remarkable constancy, consisting in recurrent attacks of abdominal pain, vomiting, and headache, occurring alone, consecutively, or in combination. Laboratory investigations and radiological examination seldom help in the diagnosis, which remains in doubt unless this syndrome is recognized. The importance of the condition is indicated by its frequency—one case in ten patients attending a paediatric clinic (Kempton, 1956)—and by the number of children who are unnecessarily subjected to operation because of it. The aetiology remains in doubt, but an inherited constitutional abnormality is admitted by most writers on the subject, and a close association between migraine and, more recently, epilepsy has been recorded.

Hurst (1924) thought that bilious attacks in children were most often due to migraine or appendicitis, and could detect no difference between these attacks and so-called "psychical vomiting." Riley (1937) emphasized the importance of suspecting migraine as the cause of obscure abdominal symptoms in children. Piper (1951) described a case of abdominal migraine, and regarded it as indicating the similarity between cyclical vomiting in childhood and the abdominal variant of migraine. Krupp and Friedman (1953) analysed the case histories of 50 children suffering from all forms of migraine and found that they were weighted with attacks of biliousness, vomiting, and abdominal pain. In their series 84% of the parents suffered from headaches and 70% from migraine.

This association between migraine, cyclical vomiting, and abdominal pain seems to be so common that records have been kept of the incidence of familial headaches and migraine in a series of cases. It is the purpose of this paper to describe the series, to quote typical cases, and to put forward the evidence in favour of a migrainous aetiology for the symptoms.

Mechanism of Attack

It is necessary first to define the term "migraine." There is no known method of proving the diagnosis of migraine, though certain investigations, such as electroencephalography, may be suggestive. It is therefore fortunate that the classical syndrome is so precisely delineated that little doubt about the diagnosis need arise. The cause of migraine itself is still not known, but the mechanism of an attack is now fairly well established. There is good reason to believe that the onset of the attack is due to a vasoconstriction of the arteries supplying the head and brain. This vasoconstriction leads to anoxia of the cortex and so to the aura of migraine, which is often visual. This is followed by a reactionary vasodilatation of the vessels that can sometimes be seen in the superficial vessels of the scalp. It is this stretching of the blood vessels which is believed to cause the headache, and since this vasodilatation can be confined to one carotid artery it is often unilateral.