The present findings perhaps support the role of testosterone in a sexual feedback mechanism. Possibly one stimulus for testosterone production might be orgasm and ejaculation—the usual culmination of coitus. Since testosterone is an essential requirement for the production of functionally mature spermatozoa (Dawson *et al.*, 1957; Dawson and Rowlands, 1959; Bishop, 1961) the biological-adaptive nature of such a feedback mechanism becomes apparent. Some evidence for this interpretation has been provided by Ismail and Harkness (1967), who showed that in two sexually abstinent normal men basal testosterone levels rose markedly when coitus was resumed. While probably endogenous testosterone levels may fluctuate according to ejaculative sexual activity (as well as many other factors) (Ismail and Harkness 1967) it is still far from clear whether the steroid induces or is the consequence of sexual behaviour.

Most of the impotent persons with abnormally low urinary testosterone levels in the present study population failed to respond to exogenous testosterone administered in varying doses (15–30 mg. daily) for up to four months. (These findings will be reported in detail later.) One possible interpretation of this observation is that potency once established is not specifically dependent on testosterone activity, which may be importantly related to ejaculative sexual response instead. Nevertheless, quite possibly the therapeutic failure in these cases might be accounted for by: (a) unphysiological dose levels too high or too low, and/or (b) enzymic and/or receptor site dysfunction. The elucidation of the precise role of testosterone and other androgens in potency and impotence is clearly important, with aetiological and therapeutic implications.

Conclusion

Though the present series is small and may not necessarily be representative of impotents generally, the data reported here tend to support the clinically derived “constitutional” “psychogenic” impotence classification; these terms, however, may be inappropriate and aetiological misleading, since the single most important discriminatory feature, clinically, appeared to be the occurrence in the psychogenic impotents of regular alternative sexual outlets (masturbation) to orgasm and ejaculation, up to the time of referral. This, absent in the

constitutional impotents, indicated a definite physiological potential to respond erotically. It may be preferable to classify impotent men as “high,” “average,” or “low” testosterone excretors. At present, however, it is not known whether such a classification would have aetiological or prognostic significance.

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A Survey of Infantile Gastroenteritis

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Summary: In 1967 we admitted 339 cases of infantile gastroenteritis; one-third of these were dehydrated, and in this group the commonest biochemical abnormality found was hypernatraemia, sometimes with metabolic acidosis. A higher incidence of dehydration was found in the patients who had received oral glucose fluids before admission. Enteropathic *Escherichia coli* were isolated from the faeces of 16% of the cases. Associated infections, especially of the respiratory tract, were common. Treatment was aimed at the restoration of fluid and

electrolyte balance. Usually this was achieved with oral fluids, though intravenous fluids were used in the most severely dehydrated cases. Recovery was complete in 320 cases and a further 14 cases were discharged as carriers of enteropathic *E. coli*. There were five deaths (1.5%) in the series; three occurred immediately after admission.

Introduction

Gastroenteritis of infancy is still common in Great Britain, accounting for about 400 deaths in 1967 in those aged less than 2 years (General Register Office, 1969). Each year some 10,000 cases of infantile gastroenteritis are admitted to hospital, and it is estimated that only 10% of the cases seen in general practice are referred to hospital (Wheatley, 1968).

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The true incidence is not known, as the disease is not notifiable except in Northern Ireland (estimated population in 1967, 1,491,000), where 1,172 cases and 23 deaths were notified in 1967. The General Practitioner Group (Wheatley, 1968) found an overall incidence of 9% in babies aged under 13 months, though their reported incidence ranged from 3% in Southern England to 23% in Wales and Ireland. In most cases no causal agent has been found and enteropathic strains of *Escherichia coli* have been isolated in only 20-30% of cases (British Medical Journal, 1968). The carrier rate of enteropathic *E. coli* in healthy infants has been reported to be about 2% (Ramsay, 1968).

Recent publications have tended to concentrate on a single aspect of the disease, often investigations of the bacterial or viral aetiology (Ejercito *et al.*, 1966; Hughes *et al.*, 1968; Moffet *et al.*, 1968), the biochemical abnormalities (Cornfeld 1964; Harrison and Finberg, 1964; Teree *et al.*, 1965; Hirschhorn *et al.*, 1966; Taylor, 1968), or treatment (Barnes and Young, 1964; Cushing, 1967; Lamb, 1968; Warin, 1968; Valman and Wilmers, 1969). Recent experimental work has been directed to the problem of transferable drug resistance (Anderson, 1968; Moorhouse and McKay, 1968) and to the effect of *E. coli* on isolated segments of intestine in rabbits and other animals (Taylor *et al.*, 1961; Smith and Halls, 1967).

There has been no recent general survey of the disease in the United Kingdom, though surveys have been published from other countries (Lie Kian Joe *et al.*, 1966; Moore *et al.*, 1966). The present study is a general survey of the disease as it occurs in a regional infectious diseases unit serving a large urban industrial area.

Methods

The survey was retrospective, and concerned patients aged under 2 years admitted to the infectious diseases department of Mونسall Hospital from 1 January to 31 December 1967 who were diagnosed as having gastroenteritis—namely, patients with an acute illness the main clinical features of which were diarrhoea and vomiting. If evidence of infection was present in other systems, patients were included in the survey only when the gastrointestinal disturbance was regarded as the most important aspect of the illness. Patients from whose faeces *Salmonella* sp. and *Shigella* sp. were isolated were excluded from the survey as these two groups were found to differ from the other cases, especially in the epidemiology, the clinical features, and the complication rates. The state of hydration was assessed clinically with a modified form of the Medical Research Council's (1952) grading.

Absent—No Dehydration.

Grade 1. Mild Dehydration.—An irritable baby with skin pallor and bright red lips whose eyes were slightly sunken.

Grade 2. Established Dehydration.—An ill-baby with a pale face and sunken black-ringed eyes, whose mouth was dry and whose fontanelle (when patent) was sunken. The skin turgor and elasticity were diminished. The peripheral pulses were palpable.

Grade 3. Shock Superimposed on Established Dehydration.—A limp baby who had the signs of established dehydration with, in addition, pale or mottled cold extremities and impalpable peripheral pulses.

These grades have been correlated (Medical Research Council, 1952) with the following percentage weight losses: grade 1, 2.5-5%; grade 2, 5-10%; grade 3, 10-15%.

Haemoglobin estimation and leucocyte count, culture of nose, throat, and rectal swabs, also microscopy and culture of the urine were carried out in all cases. In many of the dehydrated babies serum electrolytes and urea were measured, and in some cases the standard bicarbonate and pH of the capillary blood were also measured. Other investigations were carried out when indicated. The aim of the treatment was the restoration and maintenance of normal hydration

with oral or intravenous fluids. Antibiotics were given only when enteropathic *E. coli* were isolated or when associated infection was present.

Results

During the survey 323 patients were admitted, of whom 14 were admitted on two occasions and one on three occasions; therefore the data presented refer to 339 admissions. The age and sex distribution of the 339 admissions are shown in Table I in three-monthly age groups; boys predominated and accounted for 60% of the admissions. The youngest group (those aged less than 3 months) was the largest and comprised 91 admissions (27%)—62 boys and 29 girls. Half of the patients were under 6 months of age, and three-quarters were less than 1 year old. The numbers of cases admitted each month are shown in Table II; no fewer than 156 (45%) were admitted during the last three months of the year. In 70 admissions (21%) there was a history of contact with other cases of diarrhoea and vomiting. The contacts comprised 35 siblings, 8 mothers, 6 fathers, and 21 other relatives or neighbours.

The grade of dehydration recorded on admission is shown in Table III, which is presented in three-monthly age groups. Of the 91 babies aged less than 3 months the percentage of dehydrated cases (24%) was less than in the whole series (33%). Of the 15 cases admitted on more than one occasion, dehydration was present in only 4 out of 31 admissions, an incidence of 13%, which was significantly less than the remainder of the series ($P < 0.01$). In 49 patients who were given glucose fluids before admission the incidence of dehydration at the time of admission was 58%, compared with a 29% incidence of dehydration in the 290 who had not received glucose fluids at home (Table IV). This difference is statistically significant ($P < 0.001$).

Fever was found to be more common among the dehydrated cases, of whom 38 (36%) had an axillary temperature above 100° F. (37.8° C.) compared with 31 (14%) of the non-dehydrated cases. The percentage of patients with tachycardia of 140 beats per minute or more rose with increasing severity of dehydration. The respective percentages were: absent 13%; grade 1 18%; grade 2 40%; grade 3 80%. Of the 62 cases with tachycardia 32 were afebrile. Heart rates below 100 beats/minute were found in only three patients, none of whom was dehydrated. On admission 22 of the non-dehydrated group (10%) and 16 of the dehydrated group (15%) had haemoglobin levels below 9.6g./100 ml. (65%), a difference which was not statistically significant.

The results of the biochemical investigations are summarized in Tables V-VII. Serum electrolytes were estimated in 53 out of 55 cases of grade 2 dehydration and in six out of seven cases of grade 3 dehydration. The serum electrolytes were estimated in only 16 out of 50 cases of grade 1 dehydration, but as there was no deliberate selection of cases it is believed that the electrolyte levels were representative of each grade of dehydration. In the 75 dehydrated cases in which the serum sodium was measured hypernatraemia—that is, >150 mEq/l. sodium—was found in 47 cases (63%), normal sodium levels (130-150 mEq/l.) were found in 24 cases (32%), and hyponatraemia (<130 mEq/l.) was found in 4 cases (5%). Thus the commonest electrolyte abnormality was hypernatraemia. The mean sodium levels in the dehydrated cases were grade 1 144 mEq/l., grade 2 154 mEq/l., and grade 3 161 mEq/l. The urea levels in 73 dehydrated cases are shown in Table VI; in 64 (88%) this was above the upper limit of normal (40 mg./100 ml.). Again the rise in the blood urea was greater in the more severe grades of dehydration. Mean levels were grade 1 52 mg./100 ml., grade 2 104 mg./100 ml., and grade 3 152 mg./100 ml. The standard bicarbonate (normal levels 17-

TABLE I.—Age and Sex Distribution

	Age in Months								Total
	0-2	3-5	6-8	9-11	12-14	15-17	18-20	21-23	
Males ..	62	37	32	27	12	14	13	8	205
Females ..	29	42	24	16	11	6	2	4	134

TABLE II.—Month of Admission

Month of admission No. of cases	J. 29	F. 26	M. 13	A. 26	M. 9	J. 24	J. 15	A. 16	S. 25	O. 42	N. 64	D. 50	Total 339
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TABLE III.—State of Hydration (339 Cases) on Admission

Dehydration	Age in Months								Total	
	0-2	3-5	6-8	9-11	12-14	15-17	18-20	21-23	No.	%
Absent ..	69 (1)	60	30	25	12	16	7	8	227	67
Grade 1 ..	9	6	11	7	5	4	4	4	50	15
Grade 2 ..	13 (1)	13	14	9	3	—	3	—	55	16
Grade 3 ..	—	—	1	2	3 (2)	—	1 (1)	—	7	2

No. of deaths in parentheses.

TABLE IV.—Association of Glucose Feeds with Dehydration

	Glucose Feeds		Remainder of Series	
	No.	%	No.	%
Not dehydrated ..	21	42	206	71
Dehydrated ..	28	58	84	29
Total ..	49	100	290	100

TABLE V.—Serum Sodium Levels in 75 Dehydrated Cases

Dehydration	mEq/l.						Total
	<130	130-140	141-150	151-160	161-170	171-180	
Grade 1 ..	—	6	5	5	—	—	16
Grade 2 ..	4	4	8	24	10	3	53
Grade 3 ..	—	—	1	2	2	1	6
Total ..	4	10	14	31	12	4	75

TABLE VI.—Blood Urea Levels in 73 Dehydrated Cases

Dehydration	mg./100 ml.										Total
	<40	40-60	61-80	81-100	101-120	121-140	141-160	161-180	181-200	>200	
Grade 1 ..	7	5	3	1	—	—	—	—	—	—	16
Grade 2 ..	2	7	7	8	10	9	5	—	2	1	51
Grade 3 ..	—	—	—	1	1	—	3	—	—	—	6
Total ..	9	12	10	10	11	9	8	—	2	2	73

27 mEq/l.) was measured in 27 dehydrated cases (Table VII). Metabolic acidosis was present in 15 (56%). There was no correlation between the degree of acidosis and the grade of dehydration, the mean bicarbonate levels being 15 and 16 mEq/l. and the mean pH values being 7.28 and 7.25 in grades 2 and 3 dehydration respectively.

In 56 cases enteropathic *E. coli* were isolated from the faeces. The relative frequencies of the different serotypes

TABLE VIII.—*E. coli* Serotypes Isolated From 56 Cases

<i>E. coli</i> ..	026	055	0111	0119	0125	0126	0127	0128	Total
No. of cases ..	6	5	10	1	25	6	4	5	62*

*Six had two serotypes in the faeces on admission.

isolated are shown in Table VIII. Six patients had two serotypes isolated from their admission specimens. Cross-infection with *E. coli* occurred in eight cases, of which six were due to serotype 0125. The cases in which enteropathic *E. coli* were isolated were not found to differ in any other respect from the remaining cases of the series. For example, the incidence of dehydration in the enteropathic *E. coli* group was 32%, compared with 33% in the rest of the series. In four cases (1%) cysts of *Giardia lamblia* were identified in the faeces.

In 64 cases (19%) an associated respiratory tract infection was found at the time of admission. These cases were subdivided as follows:

Upper respiratory tract infection ..	28 cases
Otitis media ..	16 cases
Upper respiratory tract infection and otitis media ..	6 cases
Lower respiratory tract infection ..	10 cases
Lower respiratory tract infection and otitis media ..	4 cases

In three patients (1%) there was an associated urinary tract infection; one further case developed acute renal failure, from which he subsequently recovered. Convulsions occurred before admission in seven cases, but possible predisposing causes were observed in six of these, of which two were fatal. In four cases these were febrile upper respiratory tract infections. In one of the fatal cases there was bronchopneumonia and grade 3 dehydration, and in the other cortical vein thrombosis. Within 48 hours of admission convulsions occurred in a further six cases, but previous brain damage was a predisposing cause in two of these. The other four were dehydrated, with hypernatraemia, and one of these patients died from grade 3 dehydration and bronchopneumonia.

Half-strength Darrow's solution (which contains sodium 60 mEq/l., potassium 18 mEq/l., chloride 53 mEq/l., lactate 25 mEq/l.) was used initially to restore and maintain fluid and electrolyte balance. The basic amount given was 150 ml./kg./day; in dehydration, increments of 50 ml./kg. were given in cases of grade 1 dehydration, and of 100 ml./kg. to cases of grades 2 and 3 dehydration, in the first 24 hours. Fluids were given intravenously only to borderline or definite cases of grade 3 dehydration and to the very few others who did not immediately tolerate oral fluids. Oral fluids were used exclusively in 329 cases and 10 were given intravenous fluids, including the four patients with grade 3 dehydration who survived long enough for resuscitation to be instituted. In the dehydrated children treated orally, fluids were given every 15 minutes for the first two to three hours in amounts not exceeding 60 ml. and then at hourly intervals in amounts calculated to complete the daily fluid requirement. It was usually possible to rehydrate the children satisfactorily in the first 24 hours and to reintroduce dilute milk feeds gradually during the next day. In the non-dehydrated children fluids were given at hourly or two-hourly intervals for 24 hours, after which dilute milk feeds were usually tolerated.

TABLE VII.—Standard Bicarbonate Levels in 27 Dehydrated Cases

Dehydration	mEq/l.																	Total
	<9	<10	<11	<12	<13	<14	<15	<16	<17	<18	<19	<20	<21	<22	<23	<24	<25	
Grade 1 ..	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Grade 2 ..	1	—	1	1	4	3	—	3	1	4	1	—	—	—	1	1	—	21
Grade 3 ..	—	1	—	1	—	—	—	—	1	—	—	—	—	—	—	—	—	5
Total ..	1	1	1	2	4	3	—	3	2	6	1	—	—	—	1	1	—	27

Antibiotics were not used routinely for the treatment of gastroenteritis but were given to 47 patients to eradicate enteropathic *E. coli*, and to a further 63 for associated infections.

The duration of stay in hospital ranged from 1 to 70 days (average 12.5 days); 166 infants (49%) were discharged between the 6th and 10th days. Prolonged stay in hospital was more often due to bad home or social conditions than to severe illness. Recovery was complete in 320 cases, and a further 14 were discharged as symptomless carriers of enteropathic *E. coli*. There were five deaths in the series, of which three occurred immediately after admission. These immediate deaths were all in children with grade 3 dehydration, two of whom also had bronchopneumonia. Another baby was unconscious on admission, had a bulging fontanelle, third and sixth cranial nerve paralyses, and blood-staining of the C.S.F. This infant died 24 hours later; the cause of death, confirmed at necropsy, was cortical vein thrombosis. The fifth death was of a premature infant who had had persistent diarrhoea and vomiting from birth; death occurred three weeks after admission following a period of irreversible hypothermia at a time when hydration and serum electrolytes were normal.

Discussion

Until 1930 infantile gastroenteritis was considered to be mainly an epidemic summer disease (Wilson and Miles, 1964; Ramsay and Emond, 1967). This regular pattern no longer occurs though severe local outbreaks are still apt to arise at irregular intervals (Smith, 1955). In this survey there were more cases in the winter months, but the pattern remained sporadic apart from a small episode of cross-infection in the unit due to *E. coli* serotype 0125. There were more boys than girls in the survey, but the male predominance was most noticeable in the group aged less than 3 months. Though the reasons for this male predominance are not known, it has been described in other surveys (Wheatley, 1968) and exceeds the normal sex ratio for this age group in the community.

The survey included infants up to 2 years of age, but 79% were in the first year of life and more than half were less than 6 months old. Similarly, 76% of the dehydrated cases were in the first year of life. Fewer patients under 6 months of age were dehydrated, and probably admission of these smaller infants was sometimes requested because of maternal anxiety or the family doctor's suspicion that these infants might deteriorate rapidly. The worst cases (grade 3 dehydration) were mainly aged 9-14 months and tended to be well-nourished children in whom the early stages of dehydration might have been difficult to recognize. Only one baby in the series was breast-fed, and he was not dehydrated. The incidence of dehydration among the readmitted cases was significantly lower, but several of these babies belonged to well-known "problem" families and tended to be admitted for social reasons.

A significantly higher incidence of dehydration was found among the babies given "glucose drinks" before admission and confirmed the view that these fluids seriously aggravated the disease. There was no evidence that the patients given glucose drinks were different from the others, with respect to the severity of the symptoms or the state of hydration, up to the time when the glucose was started. In many cases the mothers changed the babies' feeds from milk to glucose drinks without seeking medical advice. From the descriptions of the fluids it was clear that they were not isotonic solutions such as 5% glucose or 1/5 N saline in 4% glucose. Usually the fluids were either commercial effervescent glucose preparations (containing about 25% liquid glucose), or were prepared in the house by substituting glucose for the usual

amount of milk powder, again producing a hypertonic solution. It is suggested that aggravation of the disease may have resulted from the osmotic effects of these hypertonic solutions.

Some writers have suggested that severe dehydration may be associated with either tachycardia or bradycardia (Medical Research Council, 1952). In this series the percentage of cases with tachycardia rose with increasing severity of dehydration, but bradycardia was not found in any case of dehydration. Though iron-deficiency anaemia was commonly found there was no increased incidence of dehydration or other complications among the anaemic cases.

Since 1947 hypernatraemia has been recognized as a common biochemical abnormality in gastroenteritis, with a reported incidence of 10-30% (Macaulay and Blackhall, 1961) in different series. In the present series serum electrolytes were estimated in three-quarters of the dehydrated cases and hypernatraemia was found to be the commonest abnormality. Several surveys have shown a mortality rate of 10-20% in hypernatraemia often associated with convulsive encephalopathy (Finberg and Harrison, 1955; Macaulay and Blackhall, 1961; Morris-Jones *et al.*, 1967). In this series of 47 cases of hypernatraemia there were two deaths (4% mortality). If one further infant who died before serum electrolytes were estimated, and who may also have been hypernatraemic, was included this would raise the mortality to 6%. Of the two known hypernatraemic deaths, one patient with hyperpyrexia, convulsions, and grade 3 dehydration (serum sodium of 157 mEq/l.) died immediately after admission. The other child was unconscious on admission with convulsions and grade 2 dehydration (serum sodium 152 mEq/l.), and died after 24 hours from severe cortical vein thrombosis.

The most serious effect of hypernatraemia is neurological damage associated with convulsions, often appearing during the first 48 hours of treatment in hospital. It has been postulated that this is due to rapid dilution of the hypertonic extracellular fluid during rehydration with a subsequent shift of water into the hypertonic cells, thus causing water intoxication with its neurological sequelae. Two surveys have recorded the incidence of neurological damage following hypernatraemia (Macaulay and Blackhall, 1961; Morris-Jones *et al.*, 1967); in these the preadmission incidences of convulsions were 3% and 6% respectively, a finding that is similar to the 4% recorded in this series. These other papers, however, reported the incidence of convulsions during rehydration to be 30% in each, compared with an incidence of 6% in the present series. As the three series were not entirely comparable for the age and selection of cases, no definite conclusions may be drawn from these results. A major difference in the present series, however, was the greater use of oral fluids in rehydration (92% of the dehydrated cases were rehydrated by the oral route), and it is suggested that rehydration with oral fluids may reduce rapid changes of osmolarity in the extracellular fluid and so reduce the incidence of convulsions.

Doctors have differed about the value of antibiotics in treating gastroenteritis, some holding that they are of real value in the individual case and in controlling the spread of infection (Valman and Wilmers, 1969) while others believing that they play little part in management except in cases complicated by septicaemia (Ramsay, 1968). In this series various antibiotics were given to patients from whom enteropathic *E. coli* were isolated, but in spite of this 25% of these cases were still excreting the organisms on discharge from hospital and cross-infection was not eradicated. Antibiotics were used in the treatment of associated infections such as otitis media and appeared to be of value. Severe gastroenteritis complicated by dehydration was not considered to be an indication for antibiotic treatment. It appeared unlikely that the use of antibiotics would have reduced the mortality rate of the series since three out of five

deaths occurred immediately after admission, the fourth was from a non-infective cause, and the fifth followed prolonged non-specific gastroenteritis. So it is suggested that antibiotics are of real value in treating associated infection but play little part in the severe case or in the control or spread of infection.

Even in the developed countries gastroenteritis is still one of the commonest diseases of infancy, with a hospital mortality rate of over 1%. It is therefore remarkable that the aetiology is unknown in most cases, that the chemical pathology of the disease is still imperfectly understood, and that there is little agreement on the optimum treatment.

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Rifampicin-induced Immune Thrombocytopenia

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Summary: A case is reported in which severe thrombocytopenia occurred during administration and readministration of rifampicin. The patient's erythrocytes gave a positive direct antiglobulin test due to complement on the red cell surface; in the serum, complement-fixing antibodies were detected which were directed against the drug.

Immunological studies showed antibodies, of both IgG and IgM type, capable of fixing complement to both normal and the patient's platelets, but only in the presence of rifampicin. In addition the IgM type of antibody (but not the IgG) was capable of fixing complement to normal red cells; again only in the presence of the drug.

Introduction

Rifampicin is a most useful and effective oral antituberculosis agent of great therapeutic promise. It has hitherto been considered of remarkably low toxicity and, together with ethambutol, is probably the combination of choice in the treatment of tuberculosis resistant to the primary drugs (Canetti *et al.*, 1968; Verbist and Gyselen, 1968; Pines *et al.*, 1970).

In the present report we describe the case of a patient who developed thrombocytopenia while receiving ethambutol plus rifampicin, and in whom readministration of rifampicin resulted in an acute, severe thrombocytopenia. Thrombocytopenia is a well-known complication following the administ-

ration of many different drugs and chemicals (Horowitz and Nachman, 1965), and is characterized by a rapid lowering of the platelet count whenever the offending drug is taken by the sensitized individual. The aetiological relationship between the thrombocytopenia and the drug in such instances is often difficult to confirm. In the present case, however, antibodies in the patient's serum were detected which could fix complement to normal red cells and platelets only in the presence of the offending drug. It is believed, therefore, that this patient had an immune thrombocytopenia due to antibodies directed against rifampicin. To our knowledge this represents the first report of thrombocytopenia due to rifampicin, despite its use in tens of thousands of patients since 1967.

Clinical Findings

The patient, a 56-year-old West Indian woman, came to this country in 1964. Essential hypertension was diagnosed in 1965 and has been treated continuously since then with methyl dopa and frusemide. The following year she developed tuberculous peritonitis with ascites and an associated pleural effusion; acid-fast bacilli were isolated from both pleural and ascitic fluids. She received 18 months' therapy with streptomycin, sodium para-aminosalicylate (P.A.S.), and isoniazid. In 1968 a diagnosis of maturity-onset diabetes was made and managed with appropriate dieting only.

In December 1968 she had a sudden onset of left hemiparesis and left homonymous hemianopia with focal fits leading to grand mal seizures. Acid-fast bacilli were found on direct examination of her sputum on one occasion, but cultures for *Mycobacterium tuberculosis* were negative. A diagnosis of tuberculous meningitis was made, and over the following seven months she received, owing to toxicity and hypersensitivities, various combinations of streptomycin, pyrazinamide, ethionamide, ethambutol, and

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