operatively; new types of unit are at present being developed to meet the problem of competition between the natural and artificial pacemakers.

The analysis of E.C.G.s taken during the investigation of pacemaker failure can be carried out by reference to Table I. The importance of the deflection due to the pacemaker stimulus will be apparent, and it should be noted that the amplitude of this deflection is considerably less for bipolar stimulation than for unipolar stimulation.

Values for threshold voltage found under different conditions are given in Table II, and these were obtained with 2 msec. square-wave biphasic impulses provided by a pacemaker² with an output impedance of about 50 ohms (Fig. 5); the values

TABLE II

Pacing System	Threshold	Probable Cause	Action
Electrode catheter	< 2.5v	Normal	Nil
	2.5–5v	(a) Catheter malpositioned. (Coronary sinus, pulmonary artery, tricuspid valve, perforation of ventricle)	Reposition catheter
		(b) Faulty indifferent electrode	Check electrode or replace
Intramural electrodes	> 5v	Intermittent contact : With heart In wiring	Reposition catheter Check wiring
	< 3v	Normal	Nil
	3–8v	Sepsis	Exteriorize wires
Epicardial electrodes	> 8v	Broken wire	Use spare wire
	< 3v	Normal	Nil
	3–8v	Sepsis	Exteriorize wires
	> 8v	Broken wire	Use spare wire

If no spare myocardial wire is available it may be necessary to abandon a bipolar system in favour of a unipolar system or to consider attachment of new myocardial wires to the heart; the long-term use of an electrode catheter may be preferable to a second thoracotomy in some patients.

with different equipment may be slightly higher. These figures refer to the thresholds after the electrode has been in position for three weeks or more; differences in threshold between bipolar and unipolar stimulation may be ignored for present purposes.

The work on which these readings are based will be fully reported elsewhere.

Summary

This paper provides a scheme for the initial investigation of patients treated with artificial pacemakers who present with a history suggestive of failure of pacing. The techniques of

² Obtainable from Devices Ltd., Welwyn Garden City, Herts, England.

recording suitable E.C.G.s and x-ray films are described and the method of determining the approximate cardiac threshold with the aid of a simple adjustable pacemaker is reported. A rapid screening test of pacemaker function utilizing a portable radio is described. The interpretation of the results obtained is discussed in detail, with particular reference to some of the more common faults, including disturbance of pacing due to broken wires, battery failure, local infection, movement of electrode catheter position, and the return of A–V conduction.

FIG. 5.—Pacemaker used for simple threshold determination. The voltage calibration remains accurate over long periods and the fine control is graduated in $\frac{1}{4}$ -volt steps.

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× Outbreak of Typhoid Fever Connected with Corned Beef ×

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Typhoid fever has never been a major killing disease in the history of this country and deaths from it have always been greatly exceeded by those from such common ailments as measles or whooping-cough. Epidemics of typhoid are now rare, but between 1951 and 1962 an average of 134 cases a year were reported in England and Wales.

The following is an account of a sharp localized outbreak of typhoid fever in Harlow, Essex.

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The Outbreak

The infection came to light on 1 June 1963, when, as a result of laboratory tests, typhoid fever was diagnosed in four patients admitted to St. Margaret's Hospital, Epping, because of P.U.O. over the preceding two weeks. All general practitioners in the town were immediately alerted and asked to treat with suspicion every unexplained pyrexia. This resulted in more cases being suspected and confirmed during the ensuing days. In all, 26 persons were affected, but three of them had no clinical symptoms. Twenty-one came from eight households with two or more cases in each, and five were single cases. Their age and sex distribution is shown in Table I.

It must be pointed out that Harlow is a town with a predominantly young population, so that the high proportion of cases in the lower age-groups is not significant.

TABLE I

Age :	-5	-10	-15	-20	-25	-30	-35	-40	-45	-50	Total
Male ..	3	—	1	1	1	1	—	3	2	—	12
Female ..	1	2	2	1	2	1	2	2	—	1	14
Total ..	4	2	3	2	3	2	2	5	2	1	26

The dates of onset (Table II) could be established with a certain degree of accuracy in most of the 23 clinical cases. However, in some the early symptoms were so mild and vague that the patients could not be certain of the dates, which are therefore of necessity only approximate.

TABLE II

Date of Onset	May										June	
	15	16	17	18	19	21	22	23	25	26	1	3
No. of cases ..	5	2	2	4	1	2	1	2	1	1	1	1

The two cases which occurred in June could be either primary with a somewhat long incubation period or secondary. They were a man and his daughter in whose family two other children were confirmed cases of typhoid with onset on 23 and 26 May.

Laboratory Diagnosis

All strains of *Salmonella typhi* isolated during the outbreak were sent to the Enteric Reference Laboratory for confirmation and bacteriophage-typing. They belonged to Vi-phage type A, which is of world-wide distribution and is the second commonest type encountered in the world as a whole (Felix, 1955).

The Harlow strain was sensitive to the following chemotherapeutic and antibiotic substances by the dry disk method: sulphonamide, furazolidone, streptomycin, chloramphenicol, neomycin, colimycin, framycetin, ampicillin, polymyxin, and paromomycin, and was poorly sensitive to tetracycline. In addition, tube sensitivity tests were carried out using serial dilutions of chloramphenicol pure powder and three of the newer antibiotics in broth. The following bacteriostatic levels were determined: chloramphenicol 2 µg./ml., colimycin methyl sulphionate 2 µg./ml., kanamycin 3.5 µg./ml., ampicillin 2.5 µg./ml.

Preliminary diagnosis of suspected cases was carried out in St. Margaret's Hospital, Epping, and screening of contacts in that hospital and the Public Health Laboratory, Chelmsford. Criteria accepted for bacteriological diagnosis were the isolation of *Salm. typhi* from the blood or stool or a high or rising titre of antibody to *Salm. typhi* in the patient's serum. Agglutination tests were set up against the following three antigens: *Salm. typhi* H, *Salm. typhi* O, Vi, and the following titres accepted as positive: *Salm. typhi* O 1:125; *Salm. typhi* H 1:125, Vi 1:10. A raised H agglutination titre is not generally accepted as proof of infection in people who have been inoculated with T.A.B. vaccine, owing to the occurrence of anamnestic rises, and while a raised O agglutination titre in such cases is accepted it cannot be regarded as diagnostic of infection with *Salm. typhi*, as the somatic antigens of *Salm. typhi* are common to all members of Kauffmann's salmonella group D. Vi antigen also occurs in *Salm. paratyphi C* among others. In this series of cases all three antibody levels were determined, but no case was regarded as positive on serological grounds alone unless the titres of H or Vi antibody reached the levels stated and the O titre was at least 1:125.

In all, 26 cases fulfilled these conditions: 23 were clinical cases and three had no symptoms but were excreting the

organism. All cases, with the exception of four who fell ill outside Harlow and were treated in different hospitals, were admitted to St. Ann's Hospital, Tottenham (13 cases) or Rush Green Hospital, Romford (nine cases).

Of the 22 cases investigated and treated by us only three fulfilled all three criteria, eight fulfilled two only, and 11 fulfilled only one, although one symptomless excreter did not have blood cultures taken and one case had no Widal test carried out. The 11 cases fulfilling only one criterion consisted of five with positive stool cultures, four with positive Widal reactions, and two with positive blood cultures. The eight cases fulfilling two criteria consisted of three with positive stool cultures and Widal reactions, two where the organism was isolated from the blood and stool, two with a positive blood culture and positive or rising titre Widal reaction, and one with a positive stool culture and a rising titre of antibodies.

All samples from all but one patient and a few blood cultures from another case were taken after the latter part of the second week of illness. It is advisable, therefore, that in this country at least, when screening close contacts and suspected clinical cases of typhoid fever, blood and stool cultures and Widal examination should be carried out regardless of the stage of the illness. It is noteworthy that nine of these 22 cases had positive blood cultures; indeed, in four of them the organism was isolated only from the blood. Of these nine positive cultures, only one was taken during the first week of illness, one during the second, and five during the third week. Two others were from a symptomless case and a mild case, and were probably taken during the third week. This observation confirms those of Huckstep and others quoted by him (Huckstep, 1962). Blood culture should be performed even if the subject is apparently asymptomatic, as is illustrated by two cases mentioned later.

Isolation of the organism from the blood is, of course, diagnostic, but the Widal reaction requires care in its interpretation as discussed above. The following instance could easily have set the epidemiological investigation of this outbreak on a completely false scent.

A large number of food-handlers in the shopping area, described below, had their Widal tests carried out in addition to faecal examination. One man giving a history of gastrointestinal illness in Spain was found to have the following agglutinins in his serum: *Salm. typhi* O 1:512; *Salm. typhi* H nil, Vi nil. He was employed in a food shop close to the butcher's shop finally implicated. His serum was promptly tested against *Salm. enteritidis* H antigen, but no antibodies were detected. *Salm. wangata* (O—9, 12; H—z4, z23) was grown from his faeces, thus explaining his serological findings.

Nine of the 22 cases did not produce a positive Widal reaction according to the criteria stated above. Of these, however, three had a rising titre and two others were young children who, having had no T.A.B. inoculation, showed a raised H agglutinin titre. Only one case seemed to show no antibody response at all except to the Vi antigen, and that but weakly. All these patients were treated with antibiotics, five received ampicillin, three chloramphenicol, and one both these drugs. Effective treatment by destroying the organism and removing the antigenic stimulus may reduce the chances of observing a rising titre of antibodies in the course of the illness.

A white-cell count of over 10,000 cells/c.mm. virtually excludes typhoid fever, and there was a normal or low count in every case in the present series.

Clinical Features

The main clinical and laboratory features of the 22 patients admitted to St. Ann's or Rush Green Hospitals were in all respects common to what we should expect in typhoid, emphasizing the importance of fever, lethargy and mental apathy, the frequency of cough and sore throat, and the fact that diarrhoea (which occurred in only 10 patients) is by no means an essential

symptom of enteric fever. Respiratory symptoms were significant enough in the early stages in 10 patients to lead practitioners to diagnose tonsillitis or bronchitis. No fewer than 15 patients showed rose spots on admission to the infectious-disease units. Clinical evidence of myocarditis appeared in only four patients, but a further five showed electrocardiographic changes during the febrile stage. All E.C.G.s returned to normal during convalescence.

Of the nine cases with positive blood cultures the following two denied any symptoms.

A woman of 39, the wife of a known case. Investigation showed a rising Widal titre, and after admission to hospital she was found to be running a remittent fever up to 102° F. (38.9° C.), yet she denied all symptoms. Fever persisted for five days, falling to normal two days after starting treatment with ampicillin.

Her daughter, aged 11 years, had no symptoms, no fever, and no abnormal physical signs. Typhoid bacilli were recovered from stools as well as blood culture.

In 16 patients specific treatment consisted of one week's chloramphenicol in a dosage of 75 mg./kg./day followed by a second week in a dosage of 50 mg./kg./day. The remaining six patients were given ampicillin (3 g./day for an adult) for two weeks. Ampicillin was also used for the only patient who relapsed (with a cholecystitis) and for the only patient who produced a positive stool culture during his clearance tests. Six patients with marked toxæmia received prednisolone for from five to eight days. Four of these showed dramatic improvement within 36 hours, but the other two were slower to respond.

All 22 patients recovered without sequelae. Vi antibodies had disappeared from the blood of all cases by three months after discharge from hospital.

The remaining four patients contracted the infection in Harlow but were diagnosed and treated elsewhere. Two were a young couple normally resident in the town; when both fell ill they went to stay with friends in Hertfordshire in order to be nursed there. Their address could not be found for some time, but when they were finally traced and examined on the 31st day of illness *Salm. typhi* phage type A was isolated from the stools of the woman and she also had a suspicious Widal reaction. Her husband, who was less severely ill, had had T.A.B. inoculation in the Forces two years earlier. His stools were negative and the Widal test showed raised titres against *Salm. typhi* H, *Salm. paratyphi* AH and BH, and against Vi antigens.

Another patient, resident in Croydon, had consumed contaminated food in Harlow. Thirteen days later she complained of sickness, headache, and general malaise, but recovered after three days and returned to work. *Salm. typhi* was obtained from her stools 41 days after infection and she was treated as a convalescent carrier.

Finally, a man from Harlow, a chronic schizophrenic, was found to have typhoid fever while in a mental hospital in Colchester. Both his wife and son were confirmed cases, and at the time when they fell ill he too complained of headache, general malaise, and constipation. A week later he was admitted to the mental hospital, where he developed diarrhoea and lassitude. On the 25th day of disease *Salm. typhi* was grown from his stools and his Widal reaction showed high titres against *Salm. typhi* H, O, and Vi antigens.

Epidemiological Investigations

Preliminary investigations were carried out on Whit Sunday and Monday, 2 and 3 June. All patients in hospital and their families at home were visited and carefully interrogated. Rectal swabs were taken of everybody who had had more than casual contact with the cases.

From the beginning it was obvious that we were faced with an explosive outbreak, of as yet unknown extent. Water and

milk were therefore immediately thought of as possible vehicles of infection, but both were soon ruled out. The whole population of the town is supplied by only two dairies, each covering a wide distribution area stretching beyond Harlow and even beyond the boundaries of the county. Contaminated milk would therefore have caused a very large number of cases throughout the town, while all the cases known at the time were localized within a limited area. Apart from these considerations, a check of the temperature records showed no breakdown in the pasteurization process of the milk. As to water, this is distributed by one company only through relatively new mains, so that any pollution would have affected the whole of Harlow. Routine samples taken in May by the Public Health Department and by the company were negative, and there was no record of any damage to water mains or sewers and no interruption of the water supply for any reason. Automatic chlorination records were checked and found satisfactory. Nevertheless, to exclude the possibility of localized damage to the mains, 40 samples of water were examined bacteriologically in the course of the next two days and pressure was tested at 161 points of the distribution system. All these tests were negative, and it was therefore concluded that food must be the source of infection. As soon as the shops reopened after Whitsun investigations were started in this direction. By that time seven confirmed cases were in hospital, and others, later diagnosed as typhoid fever, were being investigated.

The new town of Harlow has been built on the principle of self-contained neighbourhood areas, each with its own shopping centre. All the cases of typhoid fever except two occurred around the Stow shopping centre (see Map), and it was assumed that one of the 15 food shops there was responsible for the outbreak. Inquiries were made into the medical histories of persons employed in these shops and of those who had left within the preceding two months. All of them, as well as itinerant vendors, roundsmen, and delivery boys, were required to submit to rectal swabbing at a near-by clinic. At the same time, sewer swabs were placed in manholes serving the shopping centre. The first batch of these swabs was examined after 36 hours and subsequent ones after remaining *in situ* 7, 25, 30, and 35 days. Foodstuffs likely to carry salmonellae, such as fresh and synthetic cream, desiccated coconut, and egg products, were taken from the shops in The Stow and submitted to the public health laboratory for examination. With the exception of a sample of imported egg albumen, which yielded *Salm. infantis*, no pathogenic organisms were grown from them.

Despite the fact that the infected food must have been consumed early in May and almost a month had elapsed since, repeated and searching interrogations of the patients and their families proved most useful and revealing. Soon after the start of the investigation it became apparent that most of the affected households were customers of the same butcher's shop, and later it was ascertained that they all had eaten corned beef. However, because there are only three butchers in that shopping centre, it was necessary to be quite sure that it was not merely a coincidence that the victims had bought their corned beef in that particular shop. Therefore, while this clue was being pursued, the search for a carrier continued and all food-handlers who had already been swabbed were now submitted to Widal tests and faecal specimens were taken for culture. Altogether during the epidemiological investigation of the outbreak 403 rectal swabs, 361 faecal specimens, 167 blood samples, and 16 specimens of urine were examined. Included in these numbers are contacts of clinical cases who, as a matter of policy, had at least one Widal test, one rectal swab, and three faecal specimens each. With the exception of four cases involving close contacts of patients, all these examinations were negative. Case histories of the patients provided overwhelming circumstantial evidence to implicate the butcher's shop and the corned beef.

Twenty-one out of the 26 persons affected were quite sure that they had eaten corned beef purchased sliced from the same butcher's shop early in May. One stated that she had bought some cooked meat there but could not remember whether it was corned beef. One woman thought she had bought some brawn, but her husband, also a patient, could not remember having had any brawn but was quite certain that they had eaten corned beef. Another woman was in the habit of preparing corned-beef sandwiches for her husband, a milk roundsman, who contracted typhoid. Neither she nor her daughter had had any of this meat, but both became infected.

since of the three butchers in The Stow shopping centre, all selling sliced corned beef on the premises, it is the one with the smallest trade. The corned beef comes out of 6-lb. (2.7-kg.) tins manufactured in South America. The tins are opened when required and the meat is sliced and sold loose. According to the records in the butcher's shop, there was 3 lb. (1.36 kg.) of corned beef left unsold on Saturday, 4 May. During the week ended 11 May three new tins were opened, and of the contents of the last one only 2 lb. (0.9 kg.) was sold by closing-time on Saturday. If one assumes that on an average the same quantity of corned beef was sold every day during the week

Geographical distribution of the 25 cases resident in Harlow.

In this case cross-contamination in the kitchen is a possibility. Finally, a little boy, a symptomless excreter, picked up *Salmonella typhi* from a neighbour's child with whom he played and who was later confirmed as a clinical case. In six households some members disliked corned beef and had not eaten any; they remained well.

The case of a boy of 12 years is particularly interesting because, apart from the woman in Croydon mentioned earlier, he is the only patient living outside the localized area of the outbreak and his family never buy at the particular butcher's shop. He and another boy helped the milkman referred to earlier with his rounds; each worked during alternate weeks. His turn was during the week ending 11 May, and on at least one occasion he had a corned-beef sandwich from the milkman. He fell ill on 22 May, five days after the milkman. The other boy, who was also given sandwiches by his employer, but at a different time, did not sicken.

The implicated butcher's shop belongs to an organization which has many shops and stores in London and the Home Counties. The cleanliness of this shop is satisfactory. The staff consists of two butchers, one of whom is in charge, and a 15-year-old apprentice who contracted typhoid fever. The two butchers have been with the same shop many years, the apprentice only since 16 April. A fourth person employed temporarily had left before the outbreak. A grocer's shop belonging to the same organization is next door. It has a separate entrance but in the back communicates with the butcher's shop, and clothes lockers and toilets are common to both.

The fact that members from most of the affected households had shopped at the suspected shop is in itself very significant,

in question, then the contents of a newly opened tin were sold over a period of three days, though it could possibly be longer if trade was slack during that part of the week.

There is evidence pointing to 9 and 10 May as being two of the dates when the contaminated meat consumed by eight patients was bought. Their onset of symptoms was between 17 and 26 May, giving an incubation period of 9 to 18 days. In five persons the date of onset was 15 May, and it must therefore be assumed that either they bought and consumed the infected food up to three days before 10 May or their incubation period was particularly short.

Other investigations also pointed to the week ending 11 May as the time of infection, and in the case of seven patients it was possible to pinpoint the date when the contaminated meat was purchased. A woman and her husband bought corned beef at the implicated shop regularly every Friday. Both fell ill—one on 18 May the other on 19 May. A relative, living in Croydon, stayed with them in Harlow on 11 and 12 May. On the first day of her stay they all had corned-beef sandwiches and she fell ill on 23 May. In this case corned beef was purchased on Friday, 10 May. In another incident, father, mother, and a little boy fell ill on 17, 21, and 25 May respectively. The woman was not a customer of the implicated butcher's but shopped there on one occasion only when she took her child to hospital to see an E.N.T. consultant. The date of the visit was checked with the hospital and found to be Friday, 10 May.

Finally, a case which came to light early in July is of great clinical and epidemiological interest. It concerns a woman of 47 who suffered from an eczematous eruption at the beginning of May. This spread considerably and after unsuccessful

treatment by the family practitioner she was admitted to hospital on 21 May and discharged on 6 June, the rash having cleared. Starting from her first day of stay in hospital she had bouts of high temperature, particularly in the evenings, with shiverings and headaches. When discharged home she was lethargic, had anorexia, and felt generally ill. On 16 June she again started running a high temperature and complained of shivering followed by profuse sweating. She was readmitted to hospital on 3 July, when *Salm. typhi* was isolated from her faeces. A shopping diary found in the woman's home showed that corned beef was purchased from the particular butcher's shop on 9 May. From the examination of this woman's temperature chart and clinical notes it is quite certain that in addition to her eczema she was suffering from typhoid fever during her first stay in hospital and that the date of onset was around 21 May. She then had a relapse 10 days after discharge.

Discussion

Having established the shop as the place of infection and corned beef as the vehicle, it is now necessary to consider how this food became contaminated. Exhaustive search did not reveal a carrier, although at first this appeared to be the most likely possibility.

Assistants in the suspected butcher's shop had two Widal tests, one rectal swab, two faecal specimens, and a urine test each. The apprentice who himself developed typhoid fever was a victim and not the cause of the outbreak. He was in the habit of picking up bits of corned beef left over on the slicing-board, and, when the shop manager was in a generous mood, was also allowed to have some corned beef for his morning tea break. He had not been outside Harlow and had no previous history of ill-health.

One man in the shop looked like a possible carrier. He was employed there temporarily from 24 March, and on 28 March was away ill. During the war he was a merchant seaman and while on the Gold Coast had a severe febrile illness of unknown nature. This man had two rectal swabs, two stool cultures, two Widal tests, two blood cultures, and two urine tests, and all were negative. So was a sewer swab which, unknown to the man, was placed in a manhole outside his house.

The staff of the adjoining grocery shop were most carefully investigated—all with negative results.

Even people who had the remotest connexion with the shop, such as decorators who worked there towards the third week in April, were subjected to examination.

Any unsold piece of corned beef is stored overnight in a refrigerated room, where it is kept on a separate shelf. Nevertheless, the possibility was considered that it might have somehow come in contact with raw meat. Various salmonellae which live in the gut of the animal are often found on carcasses, but *Salm. typhi* has never been found in raw meat. It was thought that perhaps the surface of the carcass became contaminated by the hands of a meat porter and that the bacteria were accidentally transferred to cooked meat. Every porter who had delivered carcasses during the last two weeks in April and the first 10 days in May was therefore traced and examined, but no carriers were found.

The contents of several tins of corned beef of the same batch as those sold during the week ending 11 May were bacteriologically examined, but no *Salm. typhi* was grown from them.

The conclusions that could be drawn from all these investigations were that (a) only one 6-lb. (2.7-kg.) tin of corned beef was involved, because there were only 26 cases of typhoid and *Salm. typhi* was not found in other tins of the same batch, and (b) the meat was already contaminated when the tin was opened.

Instances of canned food contaminated with various strains of *Salmonella* before the tins were unsealed have been reported (Wildman *et al.*, 1951; Report, 1956). Two outbreaks of

typhoid fever associated with tinned meat bear resemblance to the Harlow outbreak. One was in Crowthorne (Moore, 1950) the other in Pickering (Couper *et al.*, 1956). The mechanism of contamination in the latter incident was assumed to have been through the leakage of polluted cooling-water applied after heat-sterilization of the tins. Similar conclusions were arrived at earlier in a case of infected canned cream (Sandiford, 1954).

The tin implicated in the Harlow outbreak could not be found. At the time of the investigation it was lying buried together with scores of similar tins under many tons of refuse on the municipal tip. However, 10 unopened tins of the same batch were traced and submitted to expert examination. They were of the tapered-hole and braggad-cap variety with a locked soldered side and fully soldered slip-on ends. In two of them viable mesophilic aerobic and anaerobic spore-forming bacteria were found. This suggests post-sterilization contamination through seam leakage, because the organisms could not have survived the high temperature to which tins of corned beef are normally subjected. Moreover, the bacteria were found in that portion of the meat which was adjacent to the end-seam areas and not in the centre, where the product would have received the least heat. However, no evidence was found of seam damage in any of the tins when they were submitted to air pressure and fluorescent leak-detection tests. The failure to do so can be explained by the possibility of the microscopic channels becoming blocked either by tiny particles of food or by solder which had undergone corrosion.

One must assume, therefore, that there was seam leakage in the tin responsible for the Harlow outbreak and that the contamination of the product occurred either through cooling in polluted water or from a typhoid carrier who handled the tin when it was still wet after cooling.

Summary

An outbreak of typhoid fever due to *Salmonella typhi* phage type A is described. Twenty-one or possibly 23 of the 26 affected persons had eaten corned beef purchased sliced from one shop. The others became infected through close contact with confirmed cases. Very extensive investigations did not reveal a carrier in either this or any other shop within the localized area of the outbreak. There is strong circumstantial evidence that the vehicle of infection was corned beef from one 6-lb. (2.7-kg.) tin contaminated before it was opened.

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