

the lens mount below the point of attachment of the sides (Fig. 4).

It follows that some kinds of spectacle frame could contribute to the cause of vehicle accidents that seem to be due to unawareness.

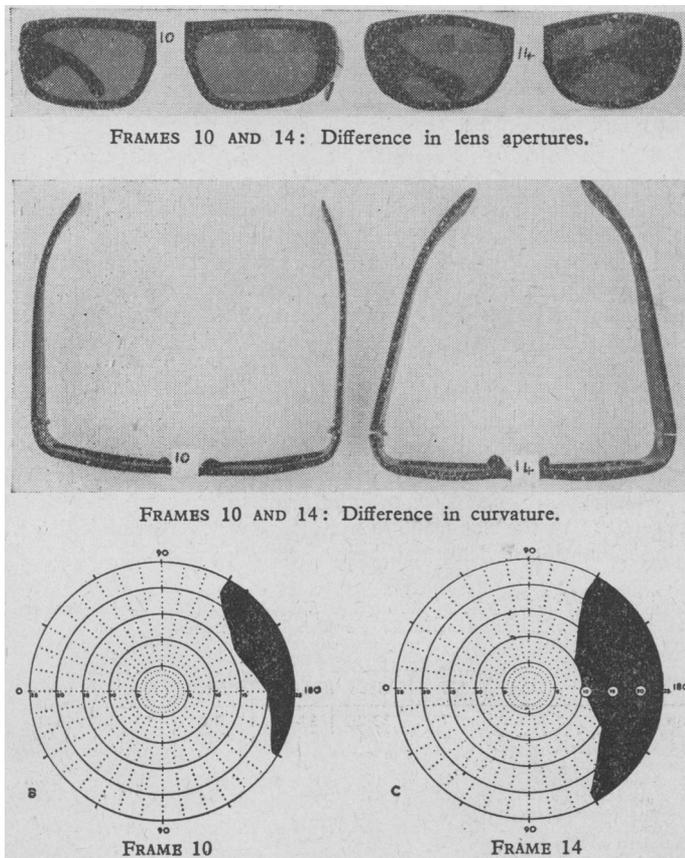


FIG. 3.—Differences in obstruction according to size of lens apertures and curvature of the front.



FIG. 4.—Relatively large area of obstruction.

Summary

Fourteen different kinds of spectacle frame were examined from the point of view of their obstruction when a driver looks backwards for information about traffic behind. A series of photographs were taken of three subjects wearing the spectacles and looking backwards over their right shoulder. Examination of these photographs shows that spectacle frames with wide shafts, thick lens mounts, and low attachment of the side-pieces can produce partial or total obstruction of the pupil and therefore of vision. This finding is confirmed by measurement of the field of view, a tangent screen being used. The investigation seems to reveal that certain kinds of ordinary and sun spectacle frames can, under certain circumstances, cause marked obstruction to vision and should not be worn by drivers.

Our thanks are due to Miss V. J. Neal for acting as a subject and Miss G. M. Villermet for technical assistance.

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Classical and El Tor Cholera: A Clinical Comparison*†

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Brit. med. j., 1966, 2, 447-449

A cholera pandemic caused by the *Vibrio cholerae* biotype El Tor (El Tor cholera) started in South-east Asia during 1961. This vibrio, when first isolated in 1906, was believed to be non-pathogenic (Gotschlich, 1906), and subsequently was thought to produce only a mild diarrhoeal disease. Recent experience has suggested no clinical difference between the diseases caused by classical *V. cholerae* (classical cholera) and *V. cholerae* biotype El Tor (deMoor, 1963). We are unaware of any simultaneous and comparative clinical studies confirming this speculation. Furthermore, the clinical similarity must be fully appreciated for purposes of effective treatment, just as any

bacteriological and epidemiological differences should be recognized for purposes of effective control (Mukerjee *et al.*, 1965).

Classical cholera has long been endemic in the Gangetic Delta, with frequent and severe epidemics. An El Tor vibrio was first isolated from a typical case of cholera in Calcutta on 1 April 1964 (Barua *et al.*, 1964; Mukerjee, 1964). Over the succeeding two months this biotype became established as the predominant pathogenic vibrio in the area. A unique opportunity was thus afforded to compare the diseases caused by these two organisms under identical conditions and without prior knowledge of the offending agent.

Material and Methods

The present observations were made during a study designed to evaluate, under controlled conditions, the effect of small

* This investigation was supported by United States Public Health Service Research Grant No. TW00141-05 from the National Institutes of Health.

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dosages of tetracycline in the treatment of cholera (Wallace *et al.*, 1965). Further clinical observations concerning non-vibrio cholera-like disease occurring simultaneously were also made (Carpenter *et al.*, 1965a, 1965b).

Only male patients over 10 years of age, admitted during the period of April through June 1964 to Calcutta's Infectious Diseases Hospital, having a history of water diarrhoea and in a hypotensive state (systolic blood-pressure below 80 mm. Hg), were included in the study. No patient received antibiotic therapy before admission. All patients were randomly assigned to a control or treatment group, and therapy was the same in both groups except for the administration of tetracycline to the latter. The control group received no antibiotics (Table I). After initial rehydration and correction of acidosis, vomiting did not occur, and therefore did not interfere with oral therapy.

TABLE I.—Distribution of Patients in Various Tetracycline Therapy Regimens

	Classical	El Tor
Control (untreated with tetracycline) ..	5	6
500 mg. orally every 6 hours for 4 doses (2 g.) ..	5	7
250 " " " 6 " " 8 " (2 ") ..	1	13
250 " " " 6 " " 4 " (1 ") ..	4	5
500 " intravenously 12-hourly for 2 doses (1 g.) ..	2	3
Total patients	17	34

On admission all patients were placed on cholera cots. Blood was drawn from the femoral artery for immediate determination of whole blood pH, plasma bicarbonate, and plasma specific gravity. Sodium, chloride, potassium, calcium, and plasma protein with albumin/globulin ratio determinations were later performed according to standard techniques. An intravenous infusion of a single standard electrolyte replacement solution (Serofusol¹) was initiated through an 18-gauge needle and all patients were rapidly rehydrated. The patients were maintained in a state of physiological hydration with Serofusol during the course of diarrhoea. Potassium losses were replaced by oral fluids. Plasma specific gravity determinations were performed after rehydration and at least daily thereafter to confirm a clinical impression of adequate hydration.

On each patient's admission a stool specimen was obtained with a sterile rectal catheter and daily thereafter by either catheter or rectal swab. All specimens were streaked immediately on bile-salt agar and either gelatin-taurocholate-tellurite agar or meat-extract agar. Six-hour enrichment cultures from alkaline peptone-water were also streaked on the same media. Isolations were verified by sugar fermentation and by slide agglutination, both group and specific Ogawa and Inaba antisera being used. *V. cholerae* biotype El Tor was characterized by resistance to lysis with Mukerjee's phage type IV, by resistance to polymyxin B (50-unit discs), by being haem-agglutinin-positive, and by forming a pellicle in broth at 18 hours. Haemolysis tests were negative when performed by classical tube and plate techniques. Haemolysis by the El Tor vibrios could, however, uniformly be demonstrated on sheep-blood agar incubated anaerobically and in tubes of brain and heart infusion broth with glycerin (Barua and Mukherjee, 1964). All patients were kept in the study ward for at least seven days and until three consecutive daily stool cultures for vibrio were negative. All quantitatively sufficient stool specimens were frozen, and electrolyte determinations were subsequently performed.

Results

Of 195 hypotensive patients with acute diarrhoeal disease admitted and followed up during these observations only 63 were positive for *V. cholerae*. No bacterial pathogens were

isolated from the majority of the remaining 132 patients with a cholera-like syndrome. Non-cholera vibrios were isolated from 10 patients, *Providencia* from 4, *Salmonella enteritidis* from 3, *Shigella dysenteriae* from 1, *Shigella flexneri* from 1, and a single patient had both *Sh. flexneri* and *Providencia*. Of the 63 patients bacteriologically positive for *V. cholerae* 17 had classical *V. cholerae*, 34 had *V. cholerae* biotype El Tor, and 12 did not have adequate studies for more definitive identification. All 34 of the *V. cholerae* biotype El Tor were of Ogawa serotype. Fifteen of the classical strains were Inaba and 2 were Ogawa serotype.

The patients were comparable in regional background, in occupation, and in having a generally substandard diet. The admission histories and vital signs are summarized in Table II. There is no statistically significant difference by the "t" test for any characteristic between those having classical and those with El Tor cholera. The various treatment groups were compared and also showed no significant difference. The past medical histories were not remarkable. A family history was pertinent in one instance when the father of a patient with El Tor cholera had similar symptoms on the same day. History of vaccination against cholera was identical in both groups: 11 (65%) of the classical and 22 (65%) of the El Tor patients had apparently never been vaccinated. There was a history of vaccination (one to six months prior to onset of disease) in two (12%) of the classical and five (15%) of the El Tor patients. The remaining patients had been vaccinated prior to 1964.

TABLE II.—Comparison of Admission History and Vital Signs Between Classical and El Tor Cholera Patients*

	Classical			El Tor		
	No.	Mean	Range	No.	Mean	Range
Age (years)	17	33.2	12-70	34	32.1	14-72
Monthly income (rupees) ..	14	72.4	0-114	30	86.5	0-200
Onset of diarrhoea (hours before admission) ..	17	17.5	5.3-45.2	33	15.2	3.5-49
Weight (kg)	10	41.0	23-49.7	24	42.0	24-45.9
Systolic blood-pressure (mm. Hg)	17	26.2	0-80	34	26.8	0-80
Respirations (per minute) ..	16	33.9	20-44	34	34.6	12-54
Perceptible pulse† (per minute)	10	133.2	84-180	22	139.8	96-200

* Pair-wise comparison reveals no significant difference by the "t" test.
† Seven classical and 12 El Tor patients had an imperceptible pulse upon admission and are not included.

All patients gave a history of watery diarrhoea upon admission. The onset of disease was an abrupt occurrence of diarrhoea in 14 (82%) of the classical patients and 30 (88%) of those with El Tor cholera. One classical patient's initial symptom was vomiting, and two had a sudden onset with simultaneous diarrhoea and vomiting; one El Tor patient also had an onset of simultaneous diarrhoea and vomiting, and three had a history of abdominal pain before any diarrhoea.

Sixteen (94%) of the classical-cholera patients had moderately severe cramps of the extremities, and one gave no history of cramps. Eight (24%) El Tor patients gave a negative history of cramps, two (6%) had very severe cramps, and the other 24 (71%) complained of moderately severe cramps. Of the classical patients 10 (59%) had no abdominal pain and 7 (41%) had moderate pain. Of the El Tor patients 21 (62%) had no abdominal pain and 13 (38%) had moderate pain. All patients had a history of vomiting at least twice before admission except three El Tor patients, who denied vomiting and nausea.

The admission arterial blood and plasma determinations before any therapy are summarized in Table III, and the differences are not generally significant by the "t" test. The differences in stool electrolyte values, upon admission and before treatment, likewise are not statistically significant (Table IV), though only three determinations upon stools from classical patients were made. More extensive stool electrolyte determinations from 25 classical patients have been performed and reported by one of us during the Calcutta epidemic in 1963

¹ Serofusol was supplied by Laboratories Vifor, Geneva, Switzerland. Each 1,000 ml. contained Na⁺ 140 mEq, Ca⁺⁺ 4 mEq, Mg⁺⁺ 1.5 mEq, Cl⁻ 100 mEq, lactate- 45.5 mEq, and glucose 15 g.

(Carpenter, 1964). The values are comparable to those reported here.

TABLE III.—Comparison of Admission Arterial Blood Studies Between Classical and El Tor Cholera*

	Classical			El Tor		
	No.	Mean	Range	No.	Mean	Range
Plasma specific gravity ..	17	1.0413	1.037-1.048	34	1.0405	1.031-1.048
Total protein (g. %)	11	10.6	7.3-13.2	25	10.6	6.1-15
pH ..	14	7.12	7.00-7.28	29	7.17	6.92-7.40
Sodium† ..	14	147.6	130-157	33	151.1	142-161
Potassium† ..	14	7.05	4.6-11	33	6.28	3.3-10.1
Calcium† ..	7	5.6	5.2-6.2	17	5.9	5.1-9.9
Chloride† ..	15	109.2	101-118	32	113.4	101-126
Bicarbonate†	17	9.5	1.1-20.1	33	10.8	2.2-24.7

* Pair-wise comparison reveals no significant differences at the 10% level by the "t" test for all comparisons except chloride, which was significant at the 5% but not the 2% level.

† Values in mEq/l. of plasma water.

TABLE IV.—Comparison of Admission Stool Electrolyte Values Between Classical and El Tor Cholera Patients*

	Classical			El Tor		
	No.	Mean	Range	No.	Mean	Range
Sodium (mEq/l.)	3	125.1	124.1-125.8	16	135.0	105.4-153.3
Potassium (mEq/l.)	3	26.6	23.6-32.1	16	19.2	7.3-33.2
Calcium (mEq/l.)	3	9.8	0.5-1.0	14	0.8	0.2-1.5
Chloride (mEq/l.)	3	99.7	92-105	15	98.9	71.8-117

* Pair-wise comparison reveals no significant difference by the "t" test.

All patients had clinical evidence of severe dehydration with poor skin turgor, dry mucous membranes, sunken eyes, and flat neck veins. All patients except two (12%) classical and five (15%) El Tor were cyanotic.

A comparison between the disease course of the two control groups is seen in Table V. It is particularly interesting to note the total volume of diarrhoea, which averaged 13.2 litres for classical cholera and 18.6 l. for El Tor cholera. The variously treated groups were similarly compared, and those pairwise comparisons were not statistically significant. Illustrative of this similarity is the comparison between the 6 classical and 20 El Tor patients who each received 2 g. of tetracycline. The

classical patients had a total stool-volume which ranged from 1 to 17.4 l. and averaged 8.6 l. during the course of the disease. The El Tor patients ranged from 0.3 to 16.8 l. and averaged 5.6 l.

TABLE V.—Comparison of Disease Course During Hospitalization Between Classical and El Tor Cholera Patients Receiving No Antibiotic Therapy*

	Classical			El Tor		
	No.	Mean	Range	No.	Mean	Range
Duration of diarrhoea (hours) ..	5	102.9	67-149.3	6	86	42-127
Amount of diarrhoea (litres) ..	5	13.2	4.3-27.3	6	18.6	5.6-32
Total intravenous fluid (litres) ..	5	14.1	5-25	6	19.4	8-30.5

* Pair-wise comparison reveals no significant difference by the "t" test.

Conclusions and Summary

The above data confirm that there was no significant difference in the clinical and biochemical manifestations between the diseases caused by the classical *Vibrio cholerae* and by the *Vibrio cholerae* biotype El Tor occurring in the same population at the same time. The disease caused by either organism is identical and should be called cholera.

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Medical Memoranda

Peripheral Neuropathy due to Disulfiram

Brit. med. J., 1966, 2, 449-450

Tetraethylthiuram disulphide (disulfiram, Antabuse) has been used extensively for the control of chronic alcoholics since its introduction (Hald et al., 1948). Most workers agree that it interferes with the oxidation of alcohol by blocking hepatic oxidative enzymes, leading to the accumulation of acetaldehyde, which is responsible for the alcohol-disulfiram reaction (Goodman and Gilman, 1955). Minor side-effects of disulfiram are relatively common, including drowsiness, headache, memory impairment, decreased libido, gastro-intestinal symptoms, halitosis, and skin rashes (Martensen-Larsen, 1953). Agranulocytosis (Jacobson, 1952) and thrombocytopenic purpura (Leibetseder, 1952) have been reported, and large doses are goitrogenic in rats (Christensen and Wase, 1954).

Peripheral neuropathy and toxic psychoses may be caused by disulfiram. These complications are not uncommon in chronic alcoholics, and early recognition that they may be due to the drug is important, since the drug-induced cases respond well to its withdrawal. These two side-effects have not been widely reported in Great Britain. To draw attention to one of them

the following case of peripheral neuropathy arising during disulfiram therapy is recorded.

CASE HISTORY

A 39-year-old dentist was admitted to hospital in August 1965. He began drinking to steady his nerves during qualifying examinations 14 years before, and six years later was treated with electric convulsion therapy for paranoid depression. After this episode he began drinking heavily, and in the last five years consumed a bottle of whisky a day. One year before admission he was given disulfiram, for the first time, for two months, and one alcohol reaction was induced.

Seven months before admission he lapsed into another alcoholic bout and was again given disulfiram. At that time neurological examination and E.E.G. revealed nothing abnormal. After two moderate alcohol reactions he continued taking disulfiram, 1 g. daily, faithfully administered by his mother, for nearly seven months. The patient and his mother insisted that he took no alcohol during the whole period. In addition, he regularly took chlordiazepoxide (Librium) 30 mg. daily, and ethchlorvynol (Arvynol) 500 mg. and trichlorethyl phosphate (triclofos) 1 g. nocte.

Three weeks before admission he developed, within 48 hours, a severe peripheral neuropathy, with paralytic foot-drop, clumsy