Gut, 1979, **20**, 329-347

Progress report

Peptic ulcer in India and Bangladesh

Historical background

Although gastric ulcer was known in the United Kingdom in the 19th century, duodenal ulcer did not become a clinical problem until the beginning of this century. It is not surprising therefore that earlier medical records in India do not mention duodenal ulcer and it is difficult to know whether it is truly a disease of this century[1,2] or that previously cases were missed because of lack of diagnostic awareness. In the famine years 1877-78 in Madras, Porter in a series of 381 necropsies reports only one gastric ulcer in an old woman, but in 1905 Niblock[3] was reporting operations for pyloric stenosis and said that cases had been seen since 1890. By 1924 Bradfield[4,5] was able to report 226 operations for one year for peptic ulcer in Madras. An apparent increase was occurring in Calcutta, where the prevalence of duodenal ulcer in 1000 necropsies in 1914[6] was 0·4% and in 1925 had risen to 0·9% in 1600 necropsies[7]. Other reports[8–14] confirm the rising recognition of duodenal ulcer in the south and in Bengal. Reports from the Punjab, however, commented on its rarity. White in 1892[15] reported his surprise at finding a perforated duodenal ulcer on necropsy and Hallilay in 1924[16] commented on the absence of peptic ulcer in Punjabi soldiers.

Present situation

Duodenal ulceration constitutes the major problem in the high incidence areas and consequently much more information is available about duodenal ulcer than gastric ulcer. As a result, this report concentrates on the occurrence of duodenal ulcer and mostly mentions gastric ulcer as it relates to duodenal ulceration. Prepyloric ulcers are uncommon and are included with duodenal ulcers. Concomitant duodenal and gastric ulcers are discussed separately.

Geographical distribution of duodenal ulcer

In a vast, developing country like India it is impossible to obtain exact figures of disease incidence. In determining the distribution of a given disease the picture has to be built up by assessing reports from a variety of sources such as the opinions of experienced workers, necropsy reports, the opinions or figures of radiologists, hospital admission, or operation figures. Weight has to be given to actual figures when available, as distinct from clinical impressions, bearing in mind the fallacies of selection in all hospital figures. However, when information from a certain area points consistently to a high incidence and from another area with equal facilities to a low incidence, it can be regarded as significant. By illustration, in 1973 a rural hospital of 700 beds at Kumudini near Dacca was having 70 positive barium meals a week

and 30 operations a week for duodenal ulcer, whereas a similar type of hospital at Ludhiana in the Punjab of 600 beds was operating on approximately 20 cases a year. Because of the difficulty in obtaining exact information, areas are described as having a high incidence when duodenal ulcer constitutes a major clinical problem and a low incidence where it is not regarded as a significant problem. When figures could be related to adult hospital admissions, an incidence of above 10 cases of duodenal ulcer per 1000 admissions is regarded as high, 1-10 per 1000 as moderate, and below 1 per 1000 as low.

Figure 1 is a composite map showing the distribution of duodenal ulcer built up from review of all the available information in the literature. The areas of high incidence[1-14,17-53] are in the south, up the West Coast as far as Bombay, all the way up the East Coast and inland into Andhra Pradesh, West Bengal, Bangladesh, Meghalaya, and into the plains of Assam and Kashmir. The areas of low incidence lie in the north, the Punjab, and adjacent areas of Rajasthan, Haryana, Uttar Pradesh, and Himachal Pradesh.

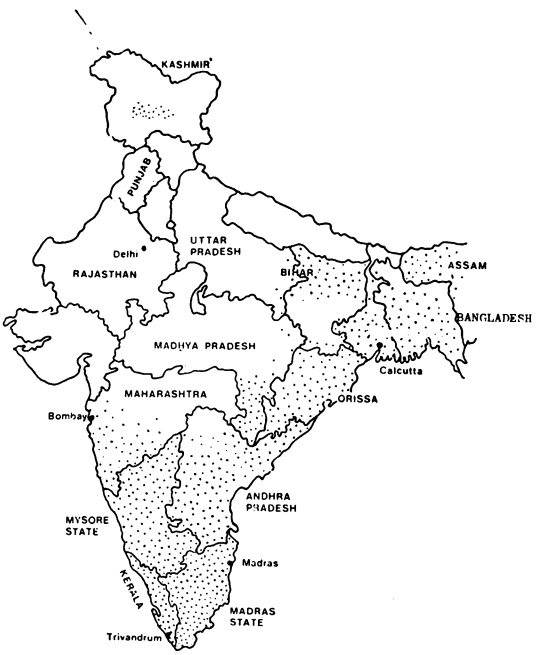

Fig. 1 *Distribution of duodenal ulcer in India. Composite map based on information from all available literature.*

Figure 2 is a map made up from information obtained by Mr Denis Burkitt and the author from questionnaires, correspondence, and personal visits to medical institutions in India and Bangladesh over a period of 20 years. All information has been carefully weighed in the light of the experience of the observer reporting, the availability of *x*-ray facilities and of surgical evidence, and all doubtful information has been excluded. (This is referred to later as the 'survey'.) The picture given is identical with that in the first map.

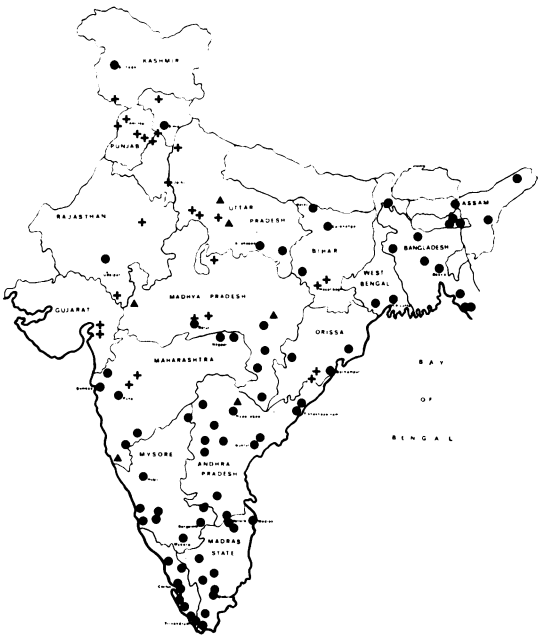

Fig. 2 *Distribution of duodenal ulcer in India as shown from personal inquiries made by D. P. Burkitt and the author.*
● *Common: major problem.*
▲ *Moderate number.*
✚ *Uncommon.*

The ratio between the incidence in the north and south has been variably given in the earlier literature as 15:1[10], 58:1[29], and 600:1[44].

Population surveys

Two of the published population surveys are from urban areas (Delhi[54–56] and Chandigarh[57]) in regions of low incidence, and these, as expected in an urban area, show a moderate incidence of duodenal ulcer (incidence 0·60% of a population of 10 009 of all ages and 0·69% of a population of 4331 respectively). (The problem of urban areas is discussed later.) There is also a report from a rural area near Chandigarh[58] which gives figures differing little from those in the town (incidence 0·81%). There are only two population surveys[59–61] from rural areas in the south (Vellore). Surprisingly, they report only a slightly higher incidence (1% and 1·18%, the population in the latter being 5542). Raghavan surveyed 5711 people in Bombay[37] and found 162 cases of duodenal ulcer (2·8%) and two of gastric ulcer.

The Indian Council of Medical Research starting in 1972 did a survey of 10 000 people in each of six urban areas (Delhi, Chandigarh, Srinagar, Kanpur, Goa, and Madras). All cases suspected of peptic ulceration were subjected to a barium meal and the films reviewed by an independent radiologist. The final figures have not been published yet, but the preliminary results agree with the pattern given.

Relationship to diet and climate

The areas of high incidence are ones of moderately high humidity and those of low incidence are of low humidity. This is reflected in the staple crops and diet. The areas of high incidence are nearly all rice eating and in most of the low incidence areas the principal staple food is wheat. There are intervening areas in Karnataka, Andhra Pradesh, and Maharashtra where millets form the staple diet, the main ones being cholam (*Sorghum vulgare*) and ragi (*Eleusine coracana*). Reports from cholam-eating areas in Karnataka (Hubli, Chikmagalur), Maharashtra (Miraj), and southern Andhra Pradesh (Jammalamadagu) indicate a high incidence of duodenal ulcer in these areas. Comments are made later on areas where ragi, or other millets, or pulses predominate, and where the incidence seems low.

Special areas

Figure 3 shows the location of certain interesting districts where there are high incidence areas adjacent to ones of low incidence.

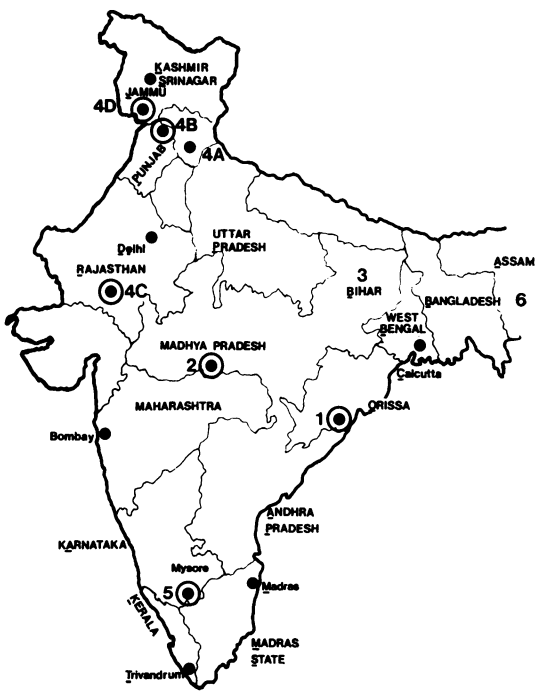

Fig. 3 *Areas of special interest with contrasting groups of high and low incidence of duodenal ulcer. Special areas. (1) Udaiyagiri. (2) Padhar. (3) Bihar. (4) A: Simla and Kangra Hills. B: Hoshiarpur. C: Aravalli Range (Udaipur). D: Jammu. (5) Mysore. (6) Assam.*

UDAIYAGIRI (KOND HILLS, ORISSA)

For many years the Mission Hospital at Udaiyagiri, situated in the Kond Hills and mainly serving the Kond tribes, was a main surgical centre for

Orissa, with frequent operations for duodenal ulcer[62]. In 1963 a marked discrepancy between the number of cases of peptic ulcer in the Oriyas coming from the plains (756 operations in 12 years) and the local Konds (43 in 12 years) from the hills (2 500 feet) was reported. Since then, the plains people have been going to the more accessible newly established medical schools at Bhubaneswara and Berhampur, and these in turn now report a high incidence of surgery for peptic ulcer. Despite other surgery continuing at Udaiyagiri, which is now attended by the Kond people only, almost none is being done for peptic ulcer[63] (personal communication). The diet on the plains is rice, whereas that of the Konds is made up of pulses, especially kulotho (horse gram) and kandula (Bengal gram), and millets (ragi and kahari), supplemented by mango seeds, sweet potatoes, leafy green vegetables, mahula flowers, and barks, roots, and fruit from the jungle as available.

PADHAR (SOUTHERN MADHYA PRADESH)—GOND TRIBES

Duodenal ulcer is a major problem to the east of Nagpur in the 'rice bowl' of Madhya Pradesh, but it is rare in the purely wheat-eating areas to the north of the State.

There is a large hospital at Padhar, west of Nagpur, in a rural area among the Gond tribes[64]. Very little duodenal ulcer is seen in the tribespeople, whereas it occurs frequently in the other villagers. The latter have a mixed diet of wheat and rice, whereas the staple diet of the Gonds is made up of maize, sorghum, and millets (sava, kodo, and kutki) which they make into hard *rotis* (unleavened bread), supplemented in season by pulses, beans, and green-leaved vegetables.

BIHAR

Admissions for duodenal ulcer are reported as frequent in the Ganges valley and in the rice-eating areas of northern Bihar—for example, Raxaul, where it formed 10% of the surgery (120 operations a year[65] (personal communication)) and where 750 kg of sodium bicarbonate and magnesium trisilicate are consumed a year—but are said to be uncommon in the drier hilly areas of the south (Hazaribagh), where more millets and pulses are grown. In Ranchi, however, where rice is the staple food, 160 operations (in 5612 surgical admissions) were for duodenal ulcer in 1977.

RAJASTHAN, PUNJAB, HIMACHAL PRADESH, KASHMIR

Although duodenal ulcer is uncommon in the wheat-growing plains of the Punjab, it has been reported as common in the hilly areas around Hoshiarpur [52,53] and also in Himachal Pradesh in the Kangra Hills[66] (personal communication) and around Simla. These are moister rice-eating areas. Likewise in Rajasthan in the Aravalli range of hills near Udaipur duodenal ulcer was frequent enough in the past for a surgeon (Dr B. N. Sharma)[67] to run 'gastrectomy camps'. The staple diet in these hills is a maize gruel, unlike the wheat diet elsewhere to the north of the state. Duodenal ulcer, while common in the rice-eating areas around Srinagar in Kashmir, is reported as uncommon in the hilly areas around Jammu (wheat-eating).

MYSORE

A survey of the rural male duodenal ulcer patients coming to the Holdsworth Hospital in Mysore City[46] showed that proportionately more come from the

rice-eating wetlands to the north than from the dry areas to the south where the millets ragi and cholam are the staple diet (ratio 3·25:1).

PUNJABI SWEEPERS IN ASSAM

A survey of 4000 Punjabi railway sweepers in Assam adhering to their traditional unrefined wheat diet showed no cases of duodenal ulcer[33], whereas the incidence in rice eaters was high (3·5% of 12 766 admissions to railway hospitals[31]).

Type of ulcer—clinical characteristics and complications

In the rural areas of high incidence all the earlier reports are consistent in describing characteristics which differ from those of duodenal ulcer in the West.

SEX RATIO

The average sex ratio (male:female) in 27 case series[4,5,8–10,13,24–26,30–33,36–40,42,44,46,50,51,65,68–72] in the literature from high incidence areas is 16·6:1 (range 7·2-35). This is supported by the figures in the personal survey which give an average of 16·75:1 in 33 reports. In the United Kingdom the corresponding ratio has steadily fallen over recent years—in 1938 it was 4·5:1 and now it is approximately 1·9:1.

DUODENAL TO GASTRIC ULCER RATIO

The average ratio duodenal ulcer:gastric ulcer in 25 reports[4,5,8–10,24–26,30,32,36,37,39,40,42,44,46,51,64,68–70,72–74] from the literature in high incidence areas is 12·4:1 and in 31 reports in the personal survey is 32:1. (In the United Kingdom the corresponding ratio was approximately 3-4:1 in 1950 and has fallen to 2-3:1.) The ratio in some of the areas where duodenal ulcer is a dominant surgical problem is much higher—for example, 100:1 (Raxaul in North Bihar and Tilda in the rice bowl of Madhya Pradesh) and 68:1 (Kumudini in Bangladesh). If such very high figures are excluded from the personal survey, the ratio falls to 19:1.

PEAK AGE

All the reports agree on a peak age of cases of 30 to 40 years, about 10 years younger than in the West.

COMPLICATIONS

All the earlier reports[4,5,8–10,23–25,27,28,38,40,46,50,51,68,75] (personal communication), [76,77] and most recent reports from high incidence areas describe pyloric stenosis as the most frequent complication and comment on the rarity of perforation or haemorrhage. Pyloric stenosis often occurs soon after the onset of symptoms, which suggests that the frequency is not just due to lack of medical treatment over a long period of time. There are several reports[27,28,38,42,44,46,75,76] of a fibrous, tumour-like inflammatory mass around the duodenal bulb.

The figures for pyloric stenosis vary from 24% to 86% in cases coming to surgery and naturally depend on other local criteria for selection of cases for operation.

Perforation and haemorrhage in most rural areas are rare, but exceptions

are appearing. Malhotra reported a high incidence of haemorrhage (30·5% of cases) in railway workers in Assam. A change seems to be taking place in some other areas. Recent reports from Raxaul[65] (Bihar), from Vellore[69] and Madras[77], from Trivandrum and from Mysore City say that perforation and, to a lesser extent, haemorrhage are becoming more common, although pyloric stenosis remains the more frequent complication. (The survey of railway workers in South India by Malhotra[32] shows an incidence of haemorrhage (12·1%) and perforation (6·8%) very similar to that in the West, although pyloric stenosis (20%) still predominates.) Perforation has always been a feature in Bangladesh, particularly during Ramadan when people go for long intervals without food, but stenosis occurs even more frequently.

In addition to the above complications, post-bulbar ulceration[78,79] and stenosis, and choledochoduodenal fistulae[51,80,81] are commoner than in Western countries.

Economic status

All reports from rural areas state that duodenal ulcer is found predominantly in the lower income groups of manual workers. In the next paragraph it is postulated that a different type of ulcer is appearing in urbanised areas, possibly due to their more Westernised way of living and the pace of life. One would expect these changes to affect especially the more sophisticated, and reports from Delhi and Bombay show that duodenal ulcer is occurring more frequently in the skilled and semi-skilled workers and those with responsible posts. Most reports from Madras, however, show that the lower income groups are still principally affected, but the survey by Malhotra[32] of railway workers reports no difference between the social classes.

Urban areas

The 'stenosing' type of ulcer is a feature of duodenal ulcer in the rural areas of high incidence in other developing countries[47–49,82] and it seems that different aetiological factors are at work in these areas from those in Western countries. It might be expected, however, that where the style of living in developing countries approaches that of the West, then the characteristics of duodenal ulcer will also veer to those of the 'Western ulcer'. This seems to be occurring in West Africa and in Johannesburg and Durban in South Africa [28,83–85] and also in Calcutta, Bombay[36,37], and possibly Delhi in India, where perforation and haemorrhage are more common than stenosis. Interestingly, the stenosing type of ulcer still predominates in Madras[51,77], although perforation also is not uncommon. Madras appears to have the highest incidence of any town in India. In 1975 at the Madras General Hospital 2125 out of 13 000 operations were for peptic ulcer and pyloric stenosis was the most frequent complication. It is possible that the pace and competition of city life lead to a more acute ulcer resulting in a higher rate of perforation and haemorrhage. The proportion of admission rate for perforation in Bombay has always been high (25% of peptic ulcer admissions). According to Raghavan's report in 1962[36], 246 admissions were for perforation, 53 for stenosis, and 47 for haemorrhage. Three medical colleges in Calcutta visited by the author in 1976 said that in the city perforation was their commonest complication, whereas in rural hospitals in north and west

Bengal pyloric stenosis predominated. Inquiries suggested that this was a real difference and not due to problems of poor transportation in the rural areas.

Changes are also seen in the incidence of gastric ulcer. Sen in 1945[74] reported a somewhat higher incidence of gastric ulcer in Bombay than elsewhere in India. Raghavan from Bombay (1962)[36] reported a ratio of DU:GU = 6·4:1 and Antia[72] a ratio of 8·7:1. Rao in 1936[39] found a similar ratio of 6:1 in Vizag. A levelling out of the DU:GU ratio towards Western figures is also reported from Vellore (1971)[69], which may reflect social changes in the community.

Indian communities in other countries

South Indian Asians seem to retain their predisposition to duodenal ulceration when living in other countries—Malaysia, Fiji, South Africa[86–90]—which suggests that climatic factors are not responsible for their susceptibility.

Religions: Hindus v. Moslems

Hindus are mostly vegetarian and Moslems are non-vegetarian. Chatterjee *et al.*[73] reported 10 times as many duodenal ulcers in Hindus as Moslems in West Bengal. Dogra's earlier figures[8–10] suggested a preponderance in Moslems in Mysore, but this was not substantiated by later work[45,46]. He did not find any preponderance among Moslems in Madras or Travancore. Raghavan[36,37] from Bombay reported a higher incidence in Hindus, but Antia *et al.*[72] found no difference between religious groups. In general, in any given area there seems to be no difference in incidence between the two religious groups.

Gastric ulcer

PREPYLORIC ULCERS

These have been included with duodenal ulcers (see above).

CONCOMITANT GASTRIC AND DUODENAL ULCERS

These are reported in nine series from the larger surgical centres with a mean incidence of 2·6%[8,25,26,32,46,68,101]. They are not always accompanied by pyloric stenosis, although this is present in a large number (57% in one series[46]).

GASTRIC ULCERS

(other than prepyloric or concomitant gastric and duodenal ulcers)

Gastric ulcer in most areas is so relatively uncommon that little information is available. In the published literature the ratio of duodenal to gastric ulcer differs little between high incidence areas (12·4:1 in 21 reports (see above)) and low incidence areas (20:1 in six reports—five of these were urban[18,22,39,54,57,58]) suggesting that factors which predispose to one probably predispose to the other. The picture is confusing, however, because in the personal survey the ratio is much lower in the low incidence areas (1·6:1 in five reports) than in the high (30:1 in 31 reports). Raghavan[91] reports that, whereas the admission rate for duodenal ulcer at the K.E.M. Hospital, Bombay, between 1931 and 1956 rose steadily to 6·8 per thousand admissions, the admission rate for gastric ulcer remained stationary at 1·5 per

thousand. (Since 1956 with the introduction of vagotomy and drainage procedures the admission rate for duodenal ulcer has steadily increased.) There is little information about possible aetiological factors in gastric ulceration in India. The available information with regard to the aetiology of duodenal ulceration will now be reviewed.

Possible aetiological factors in duodenal ulceration

A. POSTULATED FACTORS WHICH ARE CONTROVERSIAL OR NOT SUPPORTED BY THE EVIDENCE AVAILABLE

Acid secretion[36–38,46,77,92–102]

Most reports give values of mean basal and maximal outputs and of nocturnal secretion that are lower in the West for both controls and duodenal ulcer patients, but these do not always take into consideration differences in body weight. The duodenal ulcer patients show higher means for all three than the controls, but the figures cover a wide range with many in the range of normosecretors and a few hyposecretors. The mean figures for six comparable series[37,51,95,96,99,101] are 21·1 mmol HCl for maximal acid output for duodenal ulcer patients and 12·6 mmol for controls. Desai [103,104] reports that subjects under 60 kg require more than 0·04 mg/kg histamine subcutaneously for maximal output and suggests 0·074 mg/kg. Subjects under 50 kg also showed a correlation between acid output and weight. If allowance is made for weight and adequate dosage of histamine the values for maximal acid output are comparable with those in the West.

Basu *et al.*[105] also suggest that 8 μg/kg/h pentagastrin intravenously and not 6 μg/kg/h is required for maximal acid output, but this is disputed by other workers, including Desai[106]. Jalan *et al.*[107] in Calcutta have shown a high output of acid in response to small doses of insulin. They suggest that this is an adjustment to a low fat, high carbohydrate, low calorie diet and may be a factor in duodenal ulceration.

Nundy[108], measuring acid output from the stomach and alkali output from the duodenum simultaneously, reports an imbalance[109,110] in which there is an excess of acid over alkali in duodenal ulcer subjects.

Malhotra, using test meals of alcohol, reports hyperchlorhydria occurring in 70% of duodenal ulcer patients in Assam and in only 10% of those in Madras.

Pepsin

A higher output in duodenal ulcer patients than in controls is reported in one study[102] under basal conditions and in response to antral stimulation (sodium bicarbonate, or peptone, or alcohol), to insulin hypoglycaemia, and to maximal histamine stimulation. The difference was significant for basal output and after insulin and histamine. Two studies[112,113] from Bombay show a greater pepsin output in duodenal ulcer patients than in control subjects after subcutaneous histamine and also after maximal stimulation with histamine or pentagastrin. This increase in duodenal ulcer subjects is supported by another report on uropepsin output[111]. Pimparkar, however, showed similar pepsin concentration in duodenal ulcer patients and controls in response to various foods and spices[116].

Spices

Several writers[8–10,27,28,30–33,37,42,44–49,71] have commented that there is no relationship between the consumption of spices and the distribution of duodenal ulcer in India. Spices and condiments are consumed in the lower incidence areas of the Punjab and Rajasthan as well as in the higher areas of the South[30].

In Africa, although hot peppers and spices feature in the diet of the high incidence areas of southern Nigeria and the highlands of Ethiopia, they are absent from the very high incidence areas of the Nile-Zaire watershed. In other developing countries, also, no correlation has been found between the consumption of spices and the incidence of duodenal ulcer[82].

In India, Pathak[114] showed that spices caused only a slight increase in acid output and a big increase in mucus. Pimparkar *et al.*[115,116] had similar findings and found no difference in response between duodenal ulcer patients and controls. Nundy[108] (personal communication), however, using the intragastric titration method with 0·3 N sodium bicarbonate of Fordtran and Walsh[117] as a means of measuring acid output, has shown that red peppers in a solid meal produce an acid output in excess of maximal acid output in both duodenal ulcer patients and controls. This may be due to the fact that, because the pH is maintained at 5·5, the normal physiological cut-off mechanism of the antrum in response to acid does not occur. It is interesting to note also that Solanke[118] in Nigeria and Johnson[119] in Ethiopia found that, while red peppers had little effect on acid output in normal subjects, they produced an acid output equivalent to that following maximal stimulation in duodenal ulcer patients. Chillis have also been shown to increase the DNA content of gastric aspirate[120,121].

Malnutrition

McCarrison's earlier experiments with rats[122–125] suggested a link between duodenal ulcer and malnutrition in the South, with its relatively poor diet as compared with the Punjab. Dogra[126], and later Orr and Roa[71], were unable to repeat the results in subsequent experiments[36,37,39,42,45–49,71,82,127–130]. Geographically in India and elsewhere there is no conclusive evidence to suggest that the incidence of duodenal ulcer is linked with protein, vitamin A or B intake, or general malnutrition.

Infrequent meals

Long intervals between meals are mentioned as possible factors in two population surveys from Dehli and Vellore[54–56,60,61], but infrequent meals occur equally frequently in high and low incidence areas both in India and other developing countries[45–49,82].

Smoking

The population surveys from Chandigarh[57] and Delhi[54–56] report an increased number of smokers among duodenal ulcer patients, but no other evidence suggests any link with smoking[37,45–49,60,61]. Malhotra[32] points out that the consumption of tobacco is higher in the low incidence area of the Punjab than in the South.

Tea, coffee, and alcohol consumption

A high tea, coffee, and alcohol consumption is mentioned as common in

duodenal ulcer patients in one survey from Vellore[60,61], and alcohol in two others, from Bombay and Delhi[129], but apart from these reports no other link has been suggested[37,46–49]. With the use of both conventional gastric aspiration and intragastric titration with 0·3 N sodium bicarbonate black tea[131] has been shown to produce an acid output equal to 89% of that obtained by maximal histamine stimulation in duodenal ulcer patients and controls. The response is reduced to 57% if milk and sugar are added.

Blood groups

There is a natural increase in group B in the Indian population[32,34,36,51,132]. Allowing for this, most reports show no difference in the distribution of blood groups between duodenal ulcer patients and the normal population. One report only, from Mysore[46], records a significantly higher number of duodenal ulcer patients in group O at the expense of group B.

Hookworm

The higher humidity of the high incidence areas[27,133–135] suggested the possibility that hookworm infestation may be a factor. Several surveys[136–139] have shown no association. Malhotra[32] points out that there is no hookworm in Assam where the ulcer incidence is high, and plenty of hookworm in the Gurdaspur District of the Punjab, where the ulcer incidence is low. He found only a 1% incidence of hookworm in duodenal ulcer patients among railway employees in South India.

Pantothenic acid

Raghavan *et al.*[140] in Bombay found no evidence of any dietary deficiency of pantothenic acid in 25 duodenal ulcer patients, but their blood levels were significantly low and the urinary output reduced, although not significantly.

B. POSSIBLE FACTORS WHICH FIT IN WITH DISTRIBUTION AND EVIDENCE AVAILABLE

Refined and unrefined staple carbohydrate food (Cleave's hypothesis)

The possible association of refined carbohydrate diets and sugar consumption with the incidence of peptic ulcer was postulated by Cleave[1,2] and is supported by a considerable amount of geographical and historical evidence. Cleave's hypothesis fits in well with the distribution of duodenal ulcer in India, the staple diet being refined polished rice in the high incidence areas (plus cassava in parts of the south) and unrefined wheat in many of the low incidence areas.

Cleave attaches importance to the extra buffer content of unrefined foods, which has been confirmed experimentally[141]. Lennard-Jones' experiments[142] suggest that these result in a lower acidity of the juices entering the duodenum, but this was not supported by another series of test meals (Tovey)[141] which suggested that the initial neutralising effect is more than offset by a later acid rebound. Nundy[108] in Delhi and Jalan *et al.*[143] in Calcutta using intragastric titration with 0·3 N sodium bicarbonate have shown that acid outputs are similar after a chappati meal (unrefined wheat) to those after a rice meal, although the intragastric buffer content is higher after the former. In Jalan's series the resulting pH readings are similar after either meal. Pimparkar and Donde[116] also found that a test meal of unrefined

pulses (Bengal gram, Black gram, Red gram, Green gram, or lentils) gives a significantly higher acid concentration than a test meal of cream of wheat. Grimes and Goddard[144], however, have shown that after a meal of white bread unbuffered liquid leaves the stomach more rapidly and in greater quantity than after a meal of wholemeal bread.

Jayaraj[145] has studied the protective effect of instilling food substances into the stomachs of pylorus-ligated rats and has shown that unrefined rice, wheat, and ragi which have a high buffer content are strongly protective against rumenal ulcers and that unrefined maize and cholam (*sorghum vulgare*) with a low buffer content offer no protection. Refined rice and cassava also gave no protection, but, surprisingly, refined wheat offered as much protection as unrefined.

Masticatory and non-masticatory diets (*Malhotra's hypothesis*)

Malhotra[30–33,146–149] suggests that the increased mastication required by the Punjabi diet of chappatis made of unrefined wheat results in a bigger volume of saliva with a higher bicarbonate and mucus content than that resulting from the sloppier rice diets. This results in a raising of intragastric pH and possibly a reduction in bile flow[150–152], as suggested by reduced faecal urobilinogen outputs. He postulates that, as a result of increased mastication, the first part of the duodenum is exposed to lower acid levels and is also less likely to be damaged by bile reflux, because of the reduced volume of bile.

This hypothesis also fits in with the low incidence reported earlier in the Gonds (Padhar) where the diet of rotis requires prolonged mastication[64].

Malhotra also postulates that the shorter chain fatty acids present in a Punjabi diet as compared with a South Indian rice diet cause less gall bladder contraction, allowing more time for concentration of bile and absorption of sodium bicarbonate in the gall bladder, so that a smaller volume of less alkaline bile enters the duodenum.

Protective factors (*Cheney's hypothesis*)

Cheney[153–155] and Singh *et al.*[156] described a protective factor present in a number of foods, which, when prefed to animals, protected them against experimental peptic ulceration obtained by a variety of methods. The factor was thermolabile and was present particularly in cabbage, egg yolk, and milk. The content in cabbage depended on the season and storage facilities. Further work on cabbage by Adami[157–159] identified it as being liposoluble and related to vitamin K. Eventually gefarnate (geranyl farnesyl acetate) was synthesised and shown to have a therapeutic activity slightly less than carbenoxolone in the healing of peptic ulcer[160,161]. Experiments similar to Cheney's[145,162] have been done on Indian foods. South Indian diet prefed for two weeks to rats before pyloric ligation gave no protection against rumenal ulcers, whereas Punjabi diet gave considerable protection. The factor involved has again been shown to be thermolabile. The protein content of the diet did not affect the number of ulcers. Experiments done on individual items of diet showed that unrefined wheat, rice, or maize (or wheat or rice bran) had no advantage over the refined products, all giving no protection. This suggests that any protective action probably lies in the supplements, rather than the staple carbohydrate food. Cabbage, ladies fingers, certain pulses—for example, horse gram—and soya bean are strongly protective. Whole cream milk is more protective than skimmed milk. Some

vegetables such as amaranthus and lettuce were not protective. Removing the pulses (Bengal gram 1·7%, Green gram 1·7%, Black gram 1·7%, lentil 0·5%) or removing the vegetables (amaranthus, potato, and ladies' fingers) from the Punjabi diet deprived it considerably of its protective effect, and removal of both led to a large number of pylorus-ligated rats dying from perforations.

With regard to two of the special areas of low incidence mentioned earlier, prefeeding experiments showed the kulotho (horse gram) of the Konds at Udaiyagiri to be strongly protective and also the millets (sava and kutki) eaten by the Gond tribes at Padhar.

Jayaraj has shown that the protective factor in horse gram, cabbage, and the millets sava and kutki is an ether-soluble lipid which is equally effective if given orally or by injection. He is currently doing extraction experiments on other protective food substances.

CLINICAL EVIDENCE

Punjabi v. South Indian diet

Malhotra[163] reports a series of 42 patients from Bombay, with healed duodenal ulcer, of whom 21 were converted to a 'masticatory' Punjabi diet and 21 continued on their previous rice diet. Over a period of five years only 14% of the first group relapsed, compared with 80% of the second group. (This difference is highly significant.)

Unrefined rice and other grains

Cleave[1,2] submits convincing evidence of the protective action of an issue of rice bran for one year in duodenal ulcer subjects in a PoW camp at Changi, Singapore, and also the protective effect of a diet of unrefined grains (Korea mixture) in the camps in Japan, as compared with polished rice in the PoW camps in Hongkong. A recent uncontrolled clinical trial suggesting that rice bran may be of value in producing remission of symptoms has been reported[164], but no further trials have been done. There is no evidence however in the personal survey of the geographical distribution in India to suggest that duodenal ulcer is less common in areas where lightly milled or home-pounded rice is used, or that there is any difference in the effect of parboiled as distinct from raw rice.

Conclusions and the way ahead

All three hypotheses—Cleave's, Malhotra's, and Cheney's—receive support from the geographical distribution of duodenal ulcer in India and it is possible that all three postulated factors have a part to play.

Attempts have been made, however, to apply these hypotheses to the differences in geographical distribution seen in other countries, and especially in Africa[47–49,82], but it has not been possible to fit all three at once into any of the other situations found.

There can be no doubt that many factors are responsible and that these may vary from country to country, but further study of the situation in India may provide many important clues to the future understanding of this crippling problem.

The Indian Council of Medical Research (ICMR) will be publishing the reports of their population surveys started in 1972. The practical difficulty of

conducting such surveys where radiographic (or endoscopic) confirmation of diagnosis is essential, means that they have to be conducted either in urban areas or adjacent to hospitals where such facilities are available; it is doubtful whether it would be practicable or possible with the facilities available to conduct rural surveys of equal value. Yet the situation in rural areas unaffected by the stresses of urban life is more likely to provide clues to possible dietary aetiological factors.

The most fruitful source of information at present, despite all the inherent problems of selection, will be from hospital figures, considering the whole spectrum of positive barium meals, endoscopy findings, surgery for peptic ulcer, and the occurrence of complications. The ICMR is currently gathering such information from several major (urban) centres, and an extension to other centres would be valuable.

More information is also needed about the proportion of admissions for gastric ulcer in high and low incidence areas of duodenal ulcer, to see whether it runs parallel with duodenal ulcer, in which case the same aetiological factors might be responsible for both types of ulcer. The other possibility is that the incidence of gastric ulcer is uniform in all areas and it is only the incidence of duodenal ulcer that is variable.

The work on possible protective factors in North Indian diets and other foods is being continued by Jayaraj at the Central Food Technological Research Institute, Mysore, together with the identification of the lipid isolated from the 'protective' foods. This may be a most valuable contribution.

It would be of great value also if further dietary experiments similar to Malhotra's in Bombay could be conducted to see whether changing the diet of duodenal ulcer patients from a South Indian to a North Indian diet affects the relapse rate, particularly with endoscopic control.

It would be valuable to have further confirmation of Malhotra's studies on the effect of mastication on intragastric pH using a pH intragastric electrode. His deductions from faecal urobilinogen outputs that bile flow is reduced with masticatory diets need confirmation by other experimental means.

Further information along the above lines may help greatly in the understanding of the causes of peptic ulcer and in particular duodenal ulcer, not only in India but throughout the world.

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