PAPERS AND ORIGINALS

Digestive Disease: The Changing Scene*

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William Harvey published *De Motu Cordis* in 1628 and the *De Generatione Animalium* in 1651, two of the greatest books of observation and experiment ever written. During many of the active intervening years he was dissecting the abdomen, lecturing on digestion, and planning to write a treatise on nutrition. In his Lumleian lectures he constantly directed his listeners to the practical aspects of their profession, and in his work on the circulation he studied the fire-pump for inspiration rather than the writings of Galen and Hippocrates. This was regarded by many Fellows of the College as a "strange presumption" (Aubrey), and, as Bacon said, it seemed as if the College was "kept back by a kind of enchantment, from progress in the sciences, by reverence for antiquity," believing that experience without classical learning was useless. It is unlikely that these influences at Amen Corner can explain how Harvey seems to have accepted so fully the classical teaching on digestion and why he did not turn to practical experiments to test Galen's theory that food was concocted or cooked by heat in the stomach. Those parts of the body concerned with its nourishment, he wrote, "must possess the power of retaining food (for time is necessary for concoction), the power of digesting the concocted food, for which reason it boils it, and lastly the power of expelling the excrements."¹

Bad concoction led to corruption of the viscera and to death, indigestion being due to too little innate heat or to too much food which "overwhelmed and choked the heat and therefore accumulated many crude and raw humours."

Early Observations

Thomas Willis,² who gave us the first account of cardiospasm, which he treated by thrusting a rod of whalebone with a little button of sponge fixed to the top of it into the stomach, wrote of

food being "baked by too much heat" and the blood "burning forth and cruelly boiling up" in cases of "flux of the belly"—probably typhoid fever. Even though van Helmont in 1648 had observed the acid reaction of the gastric juice and thought that digestion was a process of fermentation it was still believed that some supernatural agent governed this process.

I have not found any record that Harvey questioned the concoction theory or that he tried any practical experiments such as de Réaumur, Spallanzani, and others carried out in the eighteenth century by introducing food into the stomach in perforated metal tubes and studying its state of digestion on withdrawal. Within 20 years of Harvey's death Regnier de Graaf in 1677 had attached small glass phials to the salivary and pancreatic ducts in a dog and studied the collected secretions using a technique very similar to Claude Bernard's and Pavlov's two centuries later and Starling's in the twentieth century.³

It is interesting that Harvey did not give time to experiments on digestion since it seems likely that digestive disorders were in his day by far the most important causes both of morbidity and of death. This must, of course, be remembered in relation to the fact that the expectation of life at birth was then only about 35 years, while it is today well over 70. Of 100 children born in London in 1600 only one would have been expected to live beyond 70.

What were the main digestive complaints of 300 years ago and how do they compare with today's? To ask this question is in accordance with the advice given by Christopher Wren to the physicians of the Royal Society in 1660 that they "should be desired to give us . . . histories of any new disease that shall happen . . . and changes in the old."

Harvey, Sydenham, and their contemporaries wrote much about hysteria and nervous disorders of the digestion. Sydenham, indeed, records that "of all chronic disease hysteria is the commonest," and Harvey repeatedly stressed the effects of the emotions on digestion. "The belly is the counterpart of the face," he wrote in a letter to the Bishop of Coventry and Lichfield, adding that in his practice of physic he had observed "more people die of grief of mind than of any other disease."⁴

Among the important *general* diseases of the time—plague, tuberculosis, smallpox, and malaria—many would have had predominantly digestive symptoms. Tuberculous enteritis must have been a common cause of chronic diarrhoea with wasting—then called diarrhoea colliquativa—and especially frequent in London because "we live," said Sydenham, "in a perpetual mist mixed with fumes from trade (sulphur) and coals which the sun is not powerful enough to penetrate."

* Abridged version of the Harveian Oration delivered at the Royal College of Physicians of London on 18 October 1972.

Common Causes of Death

Yearly *Bills of Mortality*—published from 1657 to 1758—give some idea of the main causes of death in the City of London, but, compiled from lists provided by “sworn searchers” who had to view the corpse and register their opinion on the cause of death, are of very little statistical value. “Griping in the guts” headed the list in 1676, being at times exceeded only by ague and fever, consumption, or convulsions, and must have been made up mainly by the acute dysenteries, infantile diarrhoea, typhoid, and salmonella infections. “Stopping of the stomach” was first recorded in 1636 and increased steadily till about 1660. Surfeit is another diagnosis often recorded. After about 1750 griping in the guts was replaced by “colic, gripes, and twisting of the guts,” and different suggestions have been made about what these various groupings meant, including rickets, chlorosis, and, more convincingly, strangulated hernia. “Gripes” were thought to be due to “undigested food,” especially if this was “cold and moist,” but must often have been caused by one or other of the many adulterations or impurities in the ordinary diet.

Long before William Harvey, Galen had written of the danger from contaminated cereals, drawing attention especially to the “wild grass” weed (*Lolium temulentum*) (possibly the tares of the parable in St. Matthew’s Gospel xiii, 24–30) which caused disorders of the juices of the stomach.⁵ Decaying of long-stored grain due to fungi or to “rust” in the growing corn may have been causing disease in the seventeenth century just as it did in the days of Ancient Egypt, of Ovid, and of Galen. Today we recognize the hazards of aflatoxin and ergot among the many natural contaminants which may be found in food, and in the early days of the settlers in North America a very widespread illness with gastrointestinal symptoms—called variously “the slows,” the trembles, the tires, the puking fever—is now known to have been due to drinking milk or eating beef from livestock which had fed on pastures where the weed white snakeroot was growing⁶—much reminiscent of venoocclusive disease of the liver due to alkaloids from *crotalaria* and *senecio* plants used for making native bush teas described in the West Indies by Stuart and Bras in 1957.⁷

Malaria must have frequently masqueraded as an intestinal disease, with diarrhoea, fever, and loss of weight. It still remains the world’s greatest threat to health. During the last war I learnt that abdominal symptoms, especially diarrhoea, could predominate, particularly in falciparum cases, and that the passage of blood and mucus was by no means rare; among early mistaken diagnoses were dysentery, gastritis, haematemesis, typhoid, and hepatitis.

Infection

Far and away the most important of the primary digestive diseases of Harvey’s day was, of course, infection, and the highest proportion of deaths in young children must have been due to enteritis. Even 200 years after Harvey’s death the mortality in children under 5 years of age was still more than 20 times greater than it is today, and it is a commentary on the present age that of 100 deaths in children aged between 5 and 14 years 36% are now due to accidents and violence and only 2% to enteritis.⁸

Sydenham wrote of summer cholera as a violent illness mainly limited to the month of August, when the temperature was about 60°F, and Pechey⁹ refers to this cholera morbus coming at the latter end of summer “as certainly as the swallows at the beginning of spring or the cuckoo at the heat of the following season.” This was, of course, acute enterocolitis and not true epidemic or Asiatic cholera, which is characteristically painless and without fever and did not reach Britain from the Ganges until 1831.

Although the idea that infection spread by contagion from the sick to the healthy had been put forward by Fracastoro in 1546 it was not until 300 years later that the role of the human carrier came to be properly understood. Even today in some

parts of Great Britain there are as many as 7% of healthy individuals carrying salmonella and in other parts an equally high proportion carrying sonne dysentery. In Harvey’s day it seems likely that the great majority of the public were carriers, either periodically or continuously, but most people must have developed a considerable immunity to their continued reinfections, an immunity which could have been easily upset, just as it is today when a visitor to a new area of the world falls a victim to some fresh local infection and suffers from an attack of traveller’s diarrhoea. There is good evidence that such immunity to intestinal infections is reduced by the ingestion of alcohol. In the seventeenth century water was, of course, highly contaminated but many drank very little of it, using either wine or ale or mead. A good deal of wine was then made in England and drunk in large amounts with a fairly high alcohol content. The account in Ward’s *Diary*, which is I believe almost all that we know of Shakespeare’s death, reads as follows¹⁰:

Shakespeare, Drayton and Ben Johnson had a merrie meeting and it seems drank too hard, for Shakespeare died of a feavour there contracted.

In spite of all our modern measures against infection there are still over 4 million working days lost each year in Great Britain on account of acute diarrhoeas, mostly infective, the incidence of these cases having more than doubled between 1957 and 1967.^{11 12} Among the short-lasting illnesses of doctors and dentists “colitis” and “diarrhoea” come highest of the gastrointestinal disorders.

Acute Abdomen

Some of the fine clinical accounts of the acute abdomen of Harvey’s time read suspiciously like acute appendicitis, though the first records of this disease do not go back further than about 1759. After the late nineteenth century it rose to be one of the most important causes of death in children and adolescents in Great Britain, but its mortality has been steadily declining for many years now, and its incidence fell remarkably in Western Europe during the war years 1940–3.

What Harvey probably saw more often as an acute abdomen was that surgical emergency which is now quite rare in England but still exceedingly common in some parts of the world, such as Uganda—namely, volvulus. In London it is doubtful if sigmoid volvulus accounts for more than 2–3% of all cases of intestinal obstruction, whereas in parts of Africa it is responsible for not less than 10–20%,^{13 14} and is said to be as high as 30% in some parts of Asia.¹⁵

These notable differences may well be due to the change from the coarse, rough cereals eaten in seventeenth century England and twentieth century Africa, with their laxative effect on the bowel, to the more constipating type of diet in meat-eating countries with their more refined cereals. In spite of an intense concern with clysters and purgatives it is doubtful if constipation was at all a serious problem in Harvey’s day, but overaction of the colon associated with a high-residue diet causing distension may well have played a part in the incidence of “stoppage of the guts”—from volvulus, then called *miserere mei*.

Miscellaneous Maladies

WORMS

Worm infestation, while thought to be almost universal, was regarded as a most important cause of a multitude of digestive symptoms. Riverius wrote¹⁶: “Worms prick and pull the guts and obstruct them so they may be said to be the cause of disease,” and they figure largely in the old London *Bills of Mortality*. Harvey thought that worms bred in the caecum—a part of the intestine for which he could suggest no special purpose, acting as a token like the nipple and named caecum “because it is

obscure in its function." He notes¹: "Worms in all the guts; nothing so common as worms," and it is likely that he must have seen cases of intestinal obstruction due to massive worm infestation and even peritonitis due to perforation, now almost unknown in Great Britain though still not uncommon in parts of Africa.

SCURVY

In 1669 scurvy was described by Pechey as "the most reigning disease in this Kingdom," and Gideon Harvey wrote¹⁷: "it oft exerciseth its fury on the guts by causing insufferable gripes." It was called "tear-belly" (*scheurbuych*) by the Dutch, a name which goes back to Hippocrates, who spoke of "the belly puffed, with loss of blood by stool and tearing of the guts." One of the most unhappy characteristics of the disease was, of course, ulceration of the gums with falling out of the teeth and "stinking breath," which must have been a major cause of digestive symptoms.

Scurvy was especially common in London, particularly in the autumn, being attributed either to the air or to faulty diet with too much salt, especially in beer brewed from London's saline water; a main cause was, of course, the fact that wealthy people seldom ate green vegetables and that children were rarely allowed to eat either vegetables or fruit for fear of acquiring worms.

CHLOROSIS

Chlorosis—the "love-sickness"—was much talked of as a digestive disease but in fact it is doubtful if it often gave rise to abdominal symptoms of any significance. Essentially an anaemia of dietary origin it appears to have arisen for the first time about 1550, to have reached a peak about 1880, and to have disappeared completely 20 or 30 years later.

GOUT

Sydenham and most physicians of his day looked on gout as primarily a digestive disease, weakness and faintness of the stomach with gripes "as if from wind" being predominant symptoms and mainly affecting great eaters, the costive, and those much addicted to wine. Though classed as a distemper of the liver and spleen gout was also thought of as an affliction of the mind, as Sydenham—himself a severe sufferer like Harvey—emphasized in his well-known aphorism, "Gout rarely attacks fools—those who choose may except the present writer."

Tranquility of mind and bodily exercise were two essentials in treatment. For exercise, Sydenham recommended riding on horseback as much the best, but surprisingly enough added: "When this cannot be done driving in a carriage comes to the same thing." This becomes understandable if a journey in a modern car is compared with one in a seventeenth century coach lacking springs of any sort and on roads which were little more than rough cart tracks with enormous pot-holes. Evelyn and others tell of the sheer muscular exhaustion caused by trying to keep seated during such a drive and also how frequently a passenger might be thrown out on the road, having no modern seat belt to keep him in.

Among 74 of my own cases of gout which I recently reviewed only five had significant digestive symptoms, and I doubt very much whether all the "gouty dyspepsias," constipations, colics, and vomiting attacks of Harvey's day were, in fact, really due to gout, which may often have been blamed as a cause of colic when the true culprit, in fact, was lead. The "terrible griping and pain of the belly" which might affect whole families must then often have been due to lead adulteration from water collected into lead cisterns from lead roofs or from adulterated wine. The Romans suffered badly from lead colic because they stored their wine in earthenware containers which had a high lead content, but it was Sir George Baker, nine times president of our College between 1785 and 1795 and a Harveian orator, whose classic

paper on the endemial colic of Devonshire, published in 1767, first made clear the dangers of lead in cider and of adding lead to wine to prevent it going sour. He described the remarkable case of a man who had 21 children, all of whom as well as both parents were affected by disorders of the stomach and bowel due to lead. But it was the surgeon John Hunter who showed that the "dry belly-ache of the West Indies" was due to adulteration by lead added as a preservative to rum. Today there may be still some rare hazards due to the use of lead-glaze pottery, and the amount of lead emitted into the air from lead added to petrol has more than doubled in the past 20 years.

Jaundice

In the seventeenth century Jaundice must have been common, the majority of cases being due to relapsing fever, "the yellow plague." It was unlikely to have been due to viral hepatitis unless the death rate then was totally different from today's. Harvey's frequent references to jaundice are more likely to refer to different types of biliary obstruction than to hepatitis, but Weil's disease must have been frequent since rats were in every building and plague was an ever-present threat. Typhus was, of course, a much greater danger and also a cause of jaundice, following famine almost as night the day, so that it came to be called "famine fever". Cirrhosis of the liver must have been common too, with much alcohol being drunk, but it is difficult to assess its prevalence then compared with the alarming position at the present time. In France cirrhosis ranks fourth of all causes of death between the ages of 25 and 64, and among white males in the U.S.A. fifth. The incidence is rising in many European countries but fortunately in the United Kingdom it seems to be stationary, with a figure less than one-tenth that of France and about one-quarter that of the U.S.A.¹⁸

Gall stones had been described by Gentile de Foligno as early as 1341, and Harvey wrote: "stones are often found in the gall-bladder, just as they are also in the bile-duct," and indeed some descriptions of gall stones in his day suggest that they occurred more often in the liver or the bile ducts than in the gall bladder.

Today about 10% of all people in Great Britain over the age of 45 have gall stones and at least 20% of women over the age of 70 probably do so. Although many of these stones are asymptomatic there is some evidence that their prevalence is increasing. In the U.S.A. not less than 16 million people have stones and over half a million people each year have their gall bladders removed. In Sweden reports indicate a threefold rise in the number of gall bladders removed between the 1940s and 1950s, and in the Bristol area Holland and Heaton¹⁹ showed a steady rise in the number of cholecystectomies carried out between 1933 and 1970. This rise was noted especially among younger patients and seems to represent a true increase in the incidence of gall stones and not just a rise due to improved diagnosis or greater readiness to undergo operation. It is difficult to judge how prevalent gall stones were in Harvey's day if allowance is made for age adjustment, but the ratio between gall-bladder stones and bile-duct stones may well have been different from that of today. These differences have important ethnic and probably dietetic causes. In the Hong Kong Chinese population, for example, most stones are of low cholesterol content and are formed in the bile ducts, whereas in the U.S.A. and in Great Britain most of the stones are found in the gall bladder and contain more than 70% of cholesterol. Japan occupies a midway position, but as its dietary pattern is becoming more Westernized so the frequencies of gall bladder and bile duct stones are changing.²⁰

In many parts of Africa the ratio of cholesterol to pigment stones is similar to that of Hong Kong—and there also the diet is of low calorie value with a low fat intake. High-calorie diets lead to a higher concentration of cholesterol in the bile, the prevalence of gall stones in obese women being statistically related to their calorie intake.

Peptic Ulceration

It seems likely that gastric ulcers have commonly occurred in Western Europe for many centuries, but the first full description was Cruveilhier's (1791-1874), whose name was, of course, attached to the disease (*maladie de Cruveilhier*). He noted that the stomach was frequently the site of simple chronic ulcers, and though he went on to say "the first part of the duodenum appears more particularly to be predisposed to chronic ulceration" most writers of about 100 years ago seem sure that chronic duodenal ulcer was rare.

In this century duodenal ulcer has become recognized as one of the most important diseases of our time, its prevalence in Great Britain as judged by postmortem studies being some 15% for men and 8% for women for all ages between 30 and 59. Its recent history dates mainly from the 1914-18 war, when the availability of good barium-meal examinations became general. Clinically it therefore has an established history of only about 60 years. One of my predecessors as Harveian orator, Sir Arthur Hurst, 35 years ago stated²¹ that before 1907 duodenal ulcers had never been clinically diagnosed in London apart from an occasional lucky guess in cases of perforation or melaena, and with his characteristic generosity and enthusiasm he spoke of Moynihan's discovery of the clinical picture of duodenal ulcer as being "as much a piece of original scientific research as the discovery of a new element or a new star, and as equally deserving of recognition."

The other outstanding advance to which Hurst drew attention was the flexible gastroscope invented by Schindler in 1932. Since then we have advanced to the present-day fibre-optic duodenoscope, which has enabled us to confirm that the actual presence of an ulcer has surprisingly little relation to duodenal symptoms. It is likely that duodenal dyspepsia has existed as it does today for a very long time, and I now begin to doubt whether duodenal ulcer is, as I used to believe, in fact a new disease but rather that the ulcer may be a newly recognized manifestation grafted on to an old long-existing duodenal "syndrome."

The incidence of duodenal ulcer rose steadily during the first half of this century until the past 5 to 10 years and now seems to be beginning to decline, though this is not so in the case of children. This is borne out not only by figures for duodenal ulcer sickness among doctors and dentists²² but also by a fall of 30% in days lost from work by men between 1955 and 1965 from duodenal ulcer.²³

The supposed effects of modern life in causing "stress" and the evils of urban existence have been much blamed as the cause of duodenal ulcer, which is, indeed, often spoken of as a disease of civilization. This, I believe, is only very partially correct, and twin studies have shown²⁴ that an almost equal mixture of genetic and environmental factors are concerned. In general the higher the standard of life as regards physical conditions the higher the incidence of psychosomatic illness and of anxiety dyspepsia, and today more prescriptions are being written in Great Britain each year for psychotropic drugs than for any other group of medicines, at a cost of over £18m. Harvey was, of course, well acquainted with the effect of insecurity and fears of the supernatural on digestion, similar to the feelings of alarm and guilt which oppress the village dweller in rural Africa today, where the "silence" of the forest can be more threatening than the roar of the traffic in suburban England. To overcome such insecurity and lack of self-assurance many seventeenth century patients found consolation in their religious beliefs, and their hymn-singing may have been the counterpart of today's tranquillizing pill.

Colon

Preoccupation with the behaviour of the bowel linked with ceremonies for its ritual cleansing as a means of purifying both body and soul was probably a characteristic of neolithic man and

is certainly not missing from the present-day scene in Great Britain. Overenthusiasm for the use of purges and clysters at the time of William Harvey and in the eighteenth century can be alarmingly matched by the more dangerous enthusiasm for colectomy advocated for a variety of conditions such as constipation and visceroptosis in England within the past 60 years. Today the gastroenterologist's concern with the colon is much related to symptoms which he attributes to the variously named syndrome of "irritable" or "spastic" colon. In my own private practice I find that I have made this diagnosis in the past 20 years in 525 patients, compared with 305 cases of diverticular disease and 295 cases of non-specific diarrhoea mostly due to infection. It is certainly a common condition and is said to account for up to 70% of all patients presenting with digestive complaints in North America. It is, I believe, almost wholly of nervous origin and I am doubtful if more than a few cases are caused by any specific food factor.

What has become of increasing interest in recent years is the possible relation of the irritable colon to the fibre content of the diet and to the development of diverticula. I have no accurate personal knowledge of how often patients with a long history of irritable colon and anxiety symptoms develop diverticular disease, nor what exact proportion of cases of diverticular disease have a history of previous constipation or a low roughage diet. In my cases I find I have made the diagnosis of spastic colon in just over 20% of cases of diverticular disease before barium-enema examination has shown the presence of diverticula.

In a recent small series of 36 of my own proved cases 15 gave a history of more than 10 years of bowel symptoms before being referred to me, but in a large series of patients attending the Royal Victoria Hospital, Belfast, Parks²⁵ found that half had had symptoms for only one month before being seen at hospital. Parks and Connell,²⁶ from motility studies of the colon, are doubtful whether the irritable colon is a precursor of colonic diverticula, but whatever the precise relationship may be it seems certain that diverticular disease today is the most frequent organic disorder of the colon occurring in Britain and in many Western nations and is increasing in prevalence, though accurate knowledge of its true prevalence dates only from about the past 50 years.

As has been noted by Burkitt,²⁷ Painter,²⁸ and others, the geographical distribution of diverticular disease is of the greatest interest. My own observations in Nigeria confirm the view that it is extremely rare in that part of Africa. A recent survey of 7,910 barium-enema examinations carried out in north-east Scotland²⁹ among patients attending hospital with abdominal symptoms compared with a roughly similar series reported³¹ from University College Hospital, Ibadan, showed a proportion in Scotland of about 1 in 5 and in Nigeria of about 1 in 1,000. Other extreme differences in incidence of diverticular disease have been listed by Painter and Burkitt, who have suggested that it is lack of fibre in the diet which is the essential cause. This is based on the view, for which much evidence exists, that when the contents of the colon lack bulk the bowel muscle contracts on a virtually empty lumen, so that segmental rings of contraction produce areas of high pressure between them, producing bulges or diverticula. Whatever the exact mechanism may be my own experience has fully convinced me that the change from the old low-residue diet, which was so often unhelpful in treatment, to the present-day high-residue diet, most ably advocated by Painter, marks a notable advance in the relief of symptoms.

The roughage in our food consists of crude fibre made up of cellulose, hemicellulose, pectins, and lignin, but of the cellulose ingested in a normal European diet less than 1% is recoverable unchanged in the faeces.³² Though it may be a most important factor it is I think doubtful if the purely mechanical action of "roughage" making a large-size stool is the only one which affects the transit time of foods through the gut or the number of bowel actions occurring daily. Indeed some foods which add to stool bulk by having a high lignin content are, in fact, constipating.

Cellulose-splitting organisms are present in human faeces and also various strains of cellulose-splitting fungi, mainly of the *Aspergillus* group, both of which may well be as important as regards the frequency of bowel evacuations as merely the non-absorbed food residue itself. It may, in fact, be the chemical stimuli arising from destruction of hemicellulose and cellulose by the bacteria in the gut which produces the laxative effect of high-roughage diets. Certainly the action of bacteria in fermenting cellulose to form carbon dioxide is one of the main factors causing excessive production of flatus with consequent colic stimulation, and among other substances produced by bacterial action on cellulose the lower volatile fatty acids have some purgative effect, while some residues have a high water-retaining property.

Colonic Carcinoma

Carcinoma of the colon causes more deaths in Great Britain than any other cancer of the digestive tract and in 1969 killed over 15,000 people in England and Wales alone. In contrast to these alarming figures carcinoma of the colon as well as ulcerative colitis and large-bowel polyps are rare in Africa and uncommon in Japan, though common among Japanese who have emigrated to Hawaii, its incidence in general running parallel to the pattern of Western civilization and to the incidence of arteriosclerotic heart disease. Colonic cancer in contrast to carcinoma of the stomach is more often seen among the lower socioeconomic classes and is more likely to be found among the obese and the well-fed who eat a high-fat and high-protein diet.

Birkett³³ concludes that the more "natural" the foodstuffs eaten the less frequent is cancer of the bowel, but it may prove that differences in the bacteria and fungi in the bowel are of more importance in this connexion than are differences in the quantity of roughage in the diet. Hill *et al.*^{34 35} showed that the composition of the gut flora depends particularly on the amount of fat in the diet and that the ratio of anaerobic to aerobic organisms is much higher in people living in a Western diet than in those living on a low-fat and largely vegetarian diet. Anaerobic bacteria can produce substances carcinogenic to animals both by degrading bile acids to form deoxycholic acid and by increasing the rate of nitrosamine formation from nitrates and amines, as may arise, for example, from the traditional method of curing fish and meat by adding nitrates or nitrites. In high-fat eaters there is likely to be a greater chance of production of bile degradation, since there will be a greater amount of biliary steroids put into the gut in these people.

Surfeit and Obesity

In Harvey's day foods for all but the very well-off were bulky, had low-calorie value, and were highly spiced or much salted both to preserve and to disguise the taste of often partly rotten meat. Meals were eaten with the fingers and, with a hungry population, often swallowed very fast with little or no mastication. Teeth and gums were likely to have been sore from scurvy, though dental caries was unusual.

We can thus readily understand how a "surfeit" was common, though gluttony was looked on as one of the seven deadly sins. Though acute digestive disorders from a surfeit are not common today, chronic digestive disorders from steady overconsumption of concentrated foods and drinks are common and often associated with what is now one of the most important disorders of the Western world—obesity.

In Tudor times and until the eighteenth century fatness was rather admired, and Harvey affirmed that "fat promotes health." Before the nineteenth century obesity was relatively rare, just as in most African villages today it is unusual to see a fat person and most exceptional for any of the villagers to suffer from gall stones. Our diet today contains such a high proportion of very palatable, easily available, and relatively cheap carbohydrate foods—much of it in the form of refined sugar—that in England probably not less than 50% of the population of both sexes over

the age of 40 are overweight. We are uncertain how big a part obesity plays directly in digestive disease but there is good evidence that it is concerned with hiatus hernia, though probably not with diverticular disease³⁶; together with lack of physical exercise it is certainly concerned in the development of arterial disease and thus of ischaemic disorders of the alimentary tract ("abdominal angina") and with cholelithiasis.

Conclusion

With the population in Great Britain steadily acquiring more wealth and more leisure, and with more high-calorie processed foods and more potent drugs becoming available to them, some of the changes in the pattern of digestive diseases that I have mentioned may perhaps increase. Though there must have been great hazards from impure food and uncontrolled medicaments in Harvey's time we can hardly afford to be complacent about these problems today, using as we are some 20,000 or more accepted food additives as preservatives, sweeteners, colouring agents, or flavourings.³⁷ In the developing areas of the world—which in some medical respects resemble seventeenth century England—these hazards are greatest, and as Dr. Ogunlesi, professor of medicine at Ibadan, Nigeria, wrote to me, "With the increase in education and the impact of modern advertising there is a steadily increasing intake of patent medicines for almost every complaint"—a danger perhaps comparable to that posed by the speculative herbal mixtures of Harvey's day.

Since Harvey's death social changes and advancing science have so altered the pattern of digestive diseases that conditions such as malaria, scurvy, tuberculosis, and many infections have almost disappeared from our country. Increasing knowledge with more financial outlay and more skilled work by engineers, technicians, and social workers may perhaps bring us an equal control of such major digestive diseases as schistosomiasis, hydatid disease, Chaga's disease, amoebiasis, and, perhaps even more important, of protein-calorie malnutrition. But with all our potential power to achieve these successes and to control our environment there still does not seem to be a comparable change in our ability to control our own aggression, and that digestive calm which follows serenity of mind does not yet seem to have arrived.

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Changes of Blood Pressure, Renin, and Angiotensin after Bilateral Nephrectomy in Patients with Chronic Renal Failure

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Summary

Circulating levels of renin, angiotensin I, and angiotensin II were increased in six patients with chronic renal failure and hypertension uncontrolled by dialysis and hypotensive drugs. Lower and often normal levels were found in 10 patients whose blood pressure was controlled by dialysis treatment. For a variety of reasons all patients were subjected to bilateral nephrectomy. The logarithm of the decrease in plasma concentrations of renin and angiotensin II was significantly related to the fall of blood pressure after operation. Plasma renin concentration correlated significantly with blood angiotensin I concentration and with plasma angiotensin II in samples taken before and after nephrectomy. Renin, angiotensin I, and angiotensin II were measurable in samples of blood taken 48 hours or more after the operation.

Introduction

Blood pressure is often increased in patients with chronic renal failure. Two abnormal processes seem to be involved—sodium retention with increased cardiac output, and raised renin with increased peripheral resistance. Although both abnormalities are sometimes present together, sodium retention is the predominant feature in most patients. When this is so blood pressure can usually be controlled if the excess sodium is eliminated by regular dialysis treatment and dietary sodium

restriction. In the smaller group with raised renin removal of sodium usually fails to control blood pressure, renin increases further, and bilateral nephrectomy may be necessary to control severe hypertension (Toussaint *et al.*, 1966; Blumberg *et al.*, 1967; Onesti *et al.*, 1968; Brown *et al.*, 1969, 1971; Gleadle *et al.*, 1969; Safar *et al.*, 1970; Stokes *et al.*, 1970; Wilkinson *et al.*, 1970; Ledingham, 1971; Bianchi *et al.*, 1972; Lazarus *et al.*, 1972; Verniory *et al.*, 1972).

The object of the study described here was to assess the relation between changes of blood pressure and changes in circulating levels of renin, angiotensin I, and angiotensin II after bilateral nephrectomy in chronic renal failure.

Patients and Methods

Altogether, 16 patients were studied. All had end-stage chronic renal failure needing regular dialysis as maintenance treatment. Creatinine clearance was below 5 ml/min in each case. The interval between the onset of regular dialysis and bilateral nephrectomy varied greatly (see table). Except in cases with polycystic disease, the kidneys removed at operation were shrunken and often showed histological evidence of inflammatory and hypertensive change. The primary diagnoses listed in the table were, therefore, based on a combination of clinical and pathological observations.

Diastolic blood pressure taken in the lying position before dialysis was used to classify patients into the following groups.

Group 1.—In six patients it proved impossible to reduce average diastolic blood pressure below 110 mm Hg in the month

Clinical and Pathological Data in the 16 Patients Under Study

	Case No.	Age and Sex	Duration of Renal Dialysis Before Nephrectomy	Renal Lesion
Group 1	1	32M.	4 months	M.H.
	2	35M.	1 month	M.H.
	3	32M.	2 weeks	M.H.
	4	21M.	8 months	G.N.
	5	20M.	1 week	G.N.
	6	24F.	4 months	P.N.
Group 2	7	29M.	2 months	G.N.
	8	37M.	2 months	P.N.
	9	17F.	9 months	G.N.
	10	25M.	5 months	G.N.
	11	28F.	1 year	P.N.
	12	33M.	2 months	G.N.
Group 3	13	36M.	2 months	G.N.
	14	43M.	6 months	P.K.
	15	33F.	6 months	P.N.
	16	42F.	2 months	P.K.

Group 1 = uncontrolled hypertension, group 2 = controlled hypertension, and group 3 = normal blood pressure. M.H. = Malignant-phase hypertension. G.N. = Glomerulonephritis. P.N. = Pyelonephritis. P.K. = Polycystic kidney.

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