PREVENTION

FOOD & DRUGS

Are there complementary beneficial effects for health ?

HEALTH

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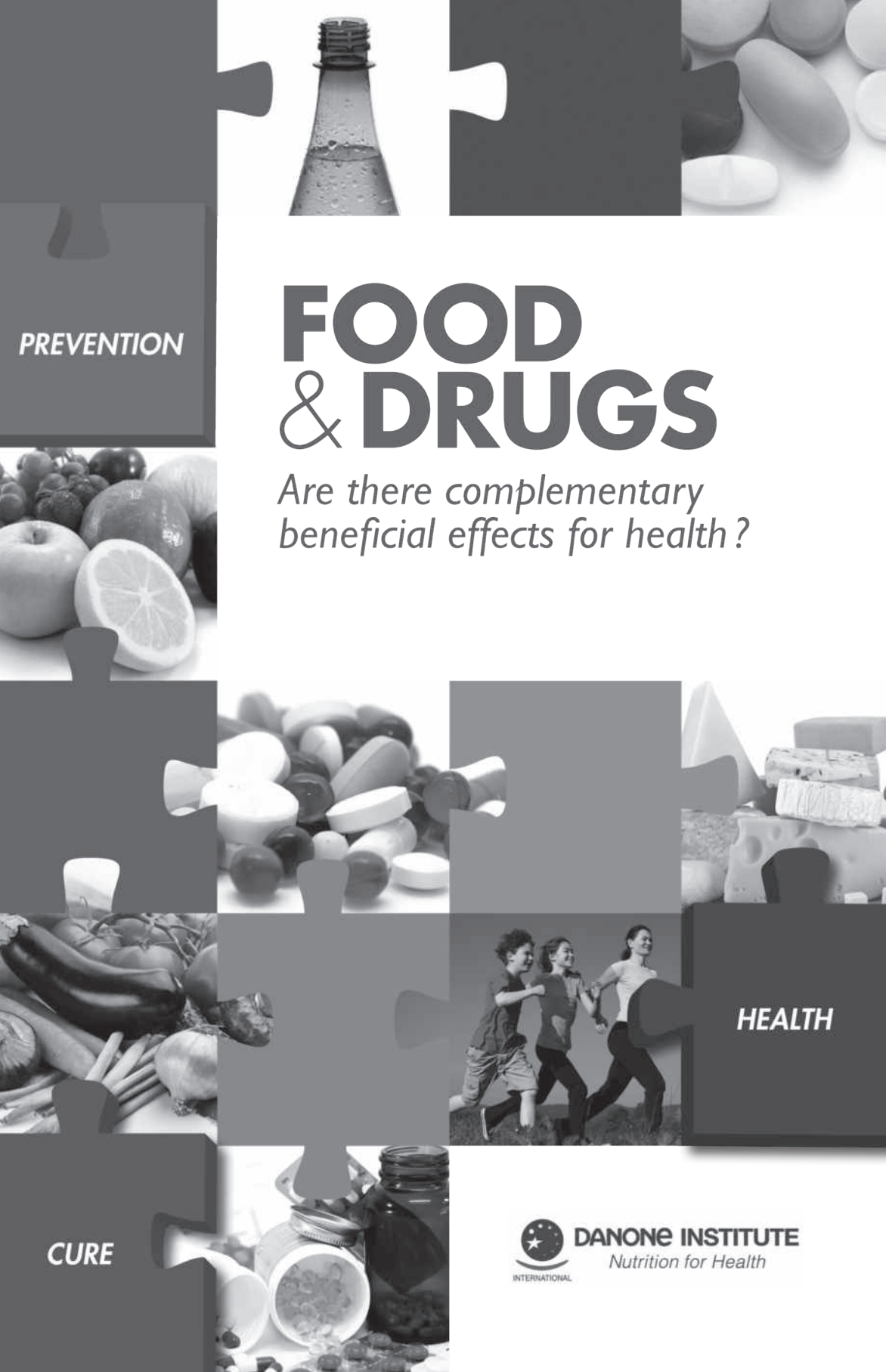

FOOD & DRUGS

Are there complementary beneficial effects for health ?

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Nutrition for Health

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Introduction to Food and Drugs for Health and for the Prevention and Treatment of Disease

by Peter J. Jones
and Dylan S. MacKay

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Food and drugs overlap considerably in definition and application, yet also possess several fundamental differences. Pharmacologically, drugs are defined as substances used to diagnose, mitigate, prevent, treat, or cure diseases. Foods are substances that provide taste, aroma, or nutritive value. The role of drugs in modern medicine is primarily for treatment, as prevention is unfortunately not at the core of modern medicine's tenet. In contrast, functional foods and food bioactives are defined as foods or components of food which have biological activity beyond their nutritional value. Functional foods and food bioactives are primarily incorporated into the diet as a preventative measure rather than a treatment of acute disease. Since drugs first originated from foods it is not surprising that the lines between the two are often thin. What distinguishes a food from a drug may not be as relevant as when it becomes a drug and what to do about the functional foods and food bioactives *in between*.

The connection between certain food items and good health was made early in human evolution. Evidence of the use of plants for medicinal purposes dates back to 3,000 BCE, when satchels of medicinal herbs were found near ice-men frozen in glaciers. Teas and aperitifs, made from steeping herbs in water or alcohol, are the remnants of early medicinal practices. Aperitifs are often still served after meals to aid in digestion and many types of tea are used as folk remedies for a variety of conditions. Some of the oldest texts on which modern Traditional Chinese Medicine is based are catalogues of herbs and minerals and their supposed effects on the body – the first pharmacopeias. Many of the ingredients used in Traditional Chinese Medicine originate from animals and plants and are often still used in food preparation. Foods that were thought to invigorate or extend life have always been highly valued and the knowledge of them passed on to future generations.

Functional Foods and Bioactives

The pharmaceutical drug finally separated from its attachment to natural products and botanical extracts at the point of discovery of synthetic chemistry. The development of computational drug design and other high throughput drug discovery techniques further removed drugs from their origins. Drugs are consistent and highly purified individual compounds which are now more often chemically synthesized than extracted from natural precursors.

However, more recently, functional foods and food bioactives have emerged and closed the gap between pharmaceuticals and foods allowing them to come full circle. Functional foods and food bioactives can often contain multiple biologically active components which can work synergistically or have potentiating effects on each other to promote health. The use of functional foods and food bioactives in the prevention of illness allows consumers to take an increased stake in their own health. Functional foods and food bioactives are perceived as more natural and safer than pharmaceutical interventions. This does not mean, however, that these foods cannot have potent biological effects.

Functional foods and food bioactives are being developed and tested to treat and prevent numerous diseases, plant peptides for their potential hypotensive effects, and fibre for its cholesterol-lowering capacity and ability to promote satiety. In addition, numerous food antioxidant sources are being investigated to reduce oxidative stress associated with diseases such as cardiovascular disease, diabetes, and obesity.

Plant sterols have been incorporated into vegetable oils and spreads to create functional foods which have been shown to effectively reduce LDL cholesterol levels by 6-15%. The main biological mechanism of plant sterols whereby they lower cholesterol levels is as a competitive inhibitor of cholesterol absorption in the gut. They compete with dietary and biliary cholesterol for incorporation in mixed micelles from which cholesterol is absorbed by enterocytes. When absorbed from the micelles by enterocytes, plant sterols are primarily excreted back into the enteric lumen by ATP binding cassette transporters ABCEG5 and ABCEG8, with very little plant sterol making it from the enterocytes into circulation, except in certain rare genetic disorders.

A common pharmaceutical intervention used to reduce cholesterol absorption in the gut is Ezetimibe™. Ezetimibe reduces cholesterol and plant sterol uptake by interacting with Niemann-Pick C1 Like 1 (NPC1L1) or aminopetidase N proteins in the small intestine. Since plant sterols and Ezetimibe both reduce cholesterol absorption, but use separate biological mechanisms, they could potentially have beneficial synergistic effects. A patient taking Ezetimibe with dyslipidemia could incorporate a functional margarine or cooking oil containing plant sterols into their diet and possibly reduce their cholesterol beyond what their current dose of Ezetimibe achieves. One human study so far, has looked at plant sterol and Ezetimibe supplementation. This study found the combination therapy of Ezetimibe and plant sterol to be the most effective treatment in lowering total cholesterol levels, but was not significantly different from Ezetimibe monotherapy.

Unlike the results of plant sterol/Ezetimibe trials, plant sterol/statins trials have shown additive effects on total and LDL cholesterol lowering. Statins work on the liver reducing endogenous cholesterol synthesis by inhibiting the enzyme HMG-CoA reductase. Plant sterols

and statins work independently to lower cholesterol by two separate mechanisms and exist as an excellent example of a functional food and a pharmaceutical which can be used in combination. Plant sterols can be used to allow for a lower dose of statin to be taken while maintaining the appropriate reduction in cholesterol required by a patient. A reduction in statin dose would save money and reduce potential side effects associated with statin therapy. Patient compliance would also likely improve on lower doses of statins, as perceived overmedication is a strongly associated with medication non-compliance.

The food bioactive Cholestin, manufactured by Pharmanex Inc. in the US, was an extract from red yeast rice (rice fermented with the red yeast *Monascus purpurus*) advertised as "supporting healthy cholesterol levels". The description of Cholestin's effect was deliberately vague because dietary supplements, which are regulated by the FDA in the US, cannot be "intended to diagnose, treat, cure or prevent any disease" lest they fall into the drug category, which receives far more vigorous scrutiny prior to approval. In 1998, the FDA declared Cholestin an unapproved drug. It was considered a copy of Merck's then patented statin, Mevacor. Cholestin and Mevacor contained the same active ingredient, lovastatin. The lovastatin in Mevacor is purified from the fungus aspergillus terreus, then made into a pill, where, as Cholestin, it contained 12 active ingredients that act together, according to its manufacturers. However, lovastatin, or lovastatin precursors, was by far the predominant active ingredient. The makers of Cholestin successfully appealed the FDA ruling in 1998, but the FDA's appeal was again granted in 2001. Cholestin is still available today, but the current formulation does not contain any red yeast rice extract. This product was a prime example of a food bioactive which had crossed over into a drug.

Distinctions between Foods and Drugs

What distinguishes a food from a drug in the marketplace today? In most cases the difference between a food and a drug is its intended use, which is dictated by how it is labelled. Using the current guidelines set by the FDA, all functional foods and food bioactives shown to treat or prevent a disease by peer-reviewed scientific evidence are drugs unless they are marketed without mentioning the health claims. In the US fish oils high in omega-3 fatty acids, which have been shown to effectively reduce plasma triglyceride, can be either defined as foods or drugs depending on the health benefits that are advertised with consumption. If the fish oil is sold with a claim that it can treat, prevent, or cure a disease it is a drug. If this claim is omitted that same fish oil is defined as a food. When a food product is found to be very effective in preventing or treating a disease, its maker may cannot advertise that information. This regulation is a strong deterrent to non-pharmaceutical health research and just one example of the many regulatory boundaries, which vary from country to country, that stand in the way of the widespread incorporation of functional food ingredients into common health practices.

Health claims based on the nutritive value of a food are generally allowed to varying degrees from country to country. Health claims which are not related to nutritive values but do not explicitly or implicitly mention a disease are also often allowed. In most cases, however, specifically mentioning a disease which a functional food or food bioactive prevents or treats causes that product to be treated as a drug.

Individual countries must be willing to suitably evaluate peer-reviewed scientific evidence and allow appropriate health claims based on these, which includes claims relating to the prevention of disease, while maintaining consumer safety as the number one objective. The health claims cannot be overly complex, so as to be easily understood by everyday consumers, while still being perceived as viable treatment options by health care professionals.

Regulations must also be put in place that punish and remove products which imply health claims in an attempt *to skirt the scientific consensus of a product's efficacy* – a move key to sustaining consumer confidence in health claims. Such regulations are vital if consumers are to be able to readily distinguish between evidence-based health claims and marketing gimmicks, such as healthy choice logos and healthy food product lines. Failure to ensure this distinction will lead to reduced consumer and health professional confidence in and reduced adoption of functional food items.

Countries must also clearly define when functional foods items become drugs and when they require prescriptions. As in the Cholestin example, functional food items which contain a pharmaceutical must be treated as such. In circumstances where a functional food bioactive is demonstrated to be efficacious, but is associated with some risk of overconsumption or negative health effects, then appropriate warnings about the health risks must be clearly labelled.

The name of products whose health claims are approved, together with the scientific evidence used to support the claims, must be circulated to physicians, especially family physicians, much like data on new drugs. Medical student nutrition and pharmacology courses should include these products, their mechanisms of action, and how to incorporate

them appropriately into treatment regimes. Similarly health care professionals must be made aware both of population sub-groups that may respond better to functional foods than other sub-groups and of combinations of functional foods and pharmaceuticals which can be beneficial and used to reduce the added costs and potential side effects of purely pharmaceutical treatments.

The most important fact about functional foods and food bioactives, as with many drugs, is that they must be incorporated into a healthy lifestyle. The importance of maintaining healthy diet and nutritional eating practices and physical activity must always be promoted. No functional food or pharmaceutical should be implemented or perceived to correct an otherwise unhealthy life.

The great chasm separating foods and drugs, fostered by pharmaceutical companies and synthetic chemistry, is disappearing. The possibilities for disease prevention and treatment of certain foods and food-borne bioactives, some of which have been known for centuries, are being elucidated by modern science and are filling in the continuum between foods and drugs. Adoption and use of these products will empower consumers to control their own health and enhance the profile of preventative measures in health care. For some individuals functional foods will be more appealing or more effective than pharmaceuticals, while for others drugs may remain the most effective and trusted course of action. The use of foods and drugs, alone or in combination, must, above all else, minimize side effects and improve the quality of life.

This handbook will further explore the boundaries between foods and drugs. Professor Pierre Bourlioux, from the Faculty of Pharmacy at the Université Paris-Sud (France), will begin by reviewing the history of foods and drugs. Dr. J.M. Antoine, the Scientific Director at the Danone International Institute in Palaiseau (France), will then discuss the history of disease with an emphasis on how definitions have evolved and how a diseased state is classified. Professor J.H. Cummings from the University of Dundee (UK), will examine diseases that are treated or prevented by dietary interventions, with special attention to the use of foods containing pre and probiotics in the treatment of gastrointestinal diseases. Dr. Kristofer Schipper (Professor emeritus, Ecole Pratique des Hautes Etudes, Paris, and Leiden University) will offer a comparative cultural perspective on food, drugs, and longevity with special reference to China. Dr. Daniel Brasseur, professor of nutrition at the Faculty of Medicine at the Université Libre de Bruxelles, will discuss the nutritional needs of individuals and how they change across environments, genetics, and age. The variability of food composition and nutritional recommendations will also be explored. Dr. Brasseur will then conclude by exploring the difference between food and drugs with special emphasis on their definitions and regulation. ■

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From Food to Drugs through the Ages

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Throughout time humans have used food both to nourish themselves and to treat disease. Greek mythology has it that the art of healing originated with the centaur Chiron, who studied medicinal herbs and plants. One of his pupils was the god of medicine Asclepius. He and his wife Epione handed down medicine to two of their sons – the healer Podalirius and the surgeon Machaon – and two of their daughters, Hygeia, the goddess of health, and Panacea, the goddess of healing, who collected herbs and plants to make her legendary potions.

These figures from Greek legend exemplify what has been a common practice through the ages – that of selecting particular products to improve health and/or medical conditions, with clear lines drawn between the male art of "curing" with medicine and the female art of "healing" through plants. The table below schematically "illustrates how human food habits have evolved over time. Early written documents and iconography suggest that the diet of Australopithecines comprised tubers, roots, fruits, insects, worms, and, probably, small animals. Early humans were already hunting and fishing, when Old Stone Age man began gathering wild cereals, collecting honey, and milking animals. The first attempts to conserve food can be traced back to protohistory, while the techniques of fermentation, salting, the use of oils and spices, smoking and curing developed over history. At the same time as they sought foods for nourishment, humans also widened their search for "special" foods that were good for their health and enhanced their performance. Following on from Chiron and his offspring, experiment and observation were handed down from generation to generation, resulting in long lists of foods and plants used specifically to manage health and treat disease.

Anthropologist and prehistorian Gilles Delluc writes: "We have been on this earth for 2.5 million years, since *homo habilis* inhabited Africa. We have hunted wild animals and eaten carrion. We have picked and gathered plants that we have farmed intensively. As omnivores, we are genetically programmed for this lifestyle." It appears that gathering plants for health purposes began just as long ago.

Australopi-thecines	Early Humans	Old Stone Age	Protohistory and History	Modern Times
Plants, tubers, roots, fruits	Plants, tubers, roots, fruits	Plants, tubers, roots, fruits	Plants, tubers, roots, fruits	Fruits, vegetables, low-fibre vegetables
Insects, worms	Insects, worms	Insects, worms	Honey	Sugar
Small animals	Scavenging, hunting	Hunting, fishing	Farming, hunting, fishing	Large-scale farming
		Wild cereals	Wild Cereals, farming	Cereals: bread, pasta
		Meat based products	Meat based products and dairy products	Meat, fish, dairy products
			Preservation	Processing

Prehistory

Excavations and analysis of prehistoric art provide valuable information on food, diet and medicinal practices, as well as religious practices.

Diet

The Miocene Epoch and Old Stone Age were vegetarian and insectivorous. Research shows that seven million years ago our ancestors ate plants, tubers, roots, and insects. In the Pliocene Epoch they progressed to meat – initially carrion then the flesh of animals they hunted. It became an important part of human diet in the Old Stone Age.

Changes in lifestyle in the New Stone Age brought swift changes in diets. People ate less meat as they gathered and grew crops, which accounted for a growing share of food intake. Stockbreeding allowed everyone to use milk, until then set aside for children. Furthermore, ceramic cooking utensils saw the emergence of a "*nouvelle cuisine*" – purees, mashes, and mush, as well as a rise in tooth decay, very rare until then. Archaeological digs have revealed varied diets that included hazelnuts, berries, sloes, and other seasonal fruits. Gathering, hunting and fishing remained important food sources, while sourdough bread is attested as early as 3600 BCE Winter stocks consisted of crops, dried fruit (especially apples), and the meat (perhaps smoked) of farm animals slaughtered in autumn.

With the Bronze Age new crops, vegetables, and grapes were grown. Crockery found in graves prove that beverage traditions developed during the second and mainly the first millennium BCE. Wine and oil amphorae of Western Mediterranean origin were discovered in Swiss archaeological sites.

Therapeutics: Instinct and Magic

Early humans quickly discovered that their environment could be dangerous or useful and acquired knowledge of certain practices. They distinguished between good and bad plants and animals: what was bad caused disease and pain. Disease was a foreign body that had to be eradicated by expelling evil or purifying the human body through sucking, purges, vomiting, bathing, etc. They grew plants such as valerian, camomile, milfoil and poppy, while their discovery of fire enabled them to brew potions with higher concentrations of active principles. They cured wounds by applying adrenalin-rich capsules with vessel-constrictive effects. Paleontological research also attests that they performed surgical operations like the extraction of foreign bodies and trepanation.

Archaeological Evidence

Paleopathological studies and medical prehistory techniques have made major strides in recent years through the study of pollens and coprolites, and the analysis of fossil DNA. It was meticulous investigation of the Cosquer cave on the coast of south-east France that brought to light the first evidence of mineral pharmacotherapy in the shape of large amounts of *moonmilk* (calcium carbonate), still used as medicine in Africa and China to stop bleeding and diarrhoea, weld bones, and encourage breastfeeding.

Another archaeological site, Pedra Furada in Brazil, revealed the presence, between 8,500 and 7,000 ago, of many medicinal plants

commonly used for indigestion, dysentery, respiratory problems, and pain.

Ötzi the Iceman is the name given to a mummified man discovered in 1991 in a glacier on the Austrian-Italian border. The body was about 5300 years old and is exceptionally well preserved. Around his neck was a necklace of perfectly clean, cut, perforated dried birch mushrooms, *pictoporus belalanus*, known to have laxative, antibacterial properties (still used in the Polish countryside) and could well have been used to treat his trichinosis.

Wild animals, too, are reported to look after themselves using therapeutic plants. In Tanzania chimpanzees have been observed eating the leaves of a small daisy-like plant at special times. They would first taste the leaves on the plant, then swallow them whole. Analysis revealed that the leaves were high in thiarubrine-A, a molecule that is extremely toxic for the worms that regularly infest chimpanzees' digestive tracts. Furthermore, female chimps ate three times more leaves than the males. Further research revealed molecules that stimulate the production of the so-called pregnancy hormone, progesterone. In sub-Saharan Africa humans chimpanzees living in proximity both use *vernonia amygdalina* against parasitic affections.

Medicine by Analogy

Medicine by analogy refers to the way in which the medicinal properties of a plant are inferred from its resemblance with parts of the human anatomy. Practised in ancient China – and certainly earlier in Europe – medicine by analogy reappeared during the Renaissance with the work of alchemists like Paracelsus, Porta, and Crollius. However, it yielded mixed results that often fell short of their claims and are difficult to verify, so inextricably linked were they with myth and magic.

Similarly, the taste of plants was thought to bear a relationship to its therapeutic properties. Most toxic plants, for example, tasted extremely bitter, which could denote that it was either beneficial or harmful. Bitter-tasting medicinal drugs aroused mixed feelings of fear and trust, feelings that hold sway even today. ■

From the Invention of Writing through Antiquity to the Middle Ages

With the invention of writing around 4200 BCE, history succeeded prehistory and it became possible to preserve knowledge for posterity.

Mesopotamia

It was in Nippur that the oldest Sumerian tablets were found (2100 BCE). They set out some of the therapeutic plants of the time: *e.g.* myrtle, myrrh, asafoetida, thyme, and willow bark, which was rich in salicylic acid and could lower fever, 4000 years before its derivative aspirin (10).

With writing knowledge of drugs progresses and was transmitted. Sumerian pharmacopoeia boasted some 250 plant-based medicines, while doctors used remedies known as *bultu*, "that which restores life". Their remedies were made from plants called *shammu*, an Akkadian term that also meant "remedy".

The valleys of the Tigris and Euphrates held hundreds of minerals, ranging from alum and sulphur, to salt and saltpetre, which went into the preparation of medicines sometimes included in wine or beer. A tablet dated between 721 and 703 BCE (on display at an exhibition in 2008 in the Louvre in Paris) offers an inventory of the plants of the vegetable garden of the kings of Babylon. It includes 67 plant species, the last of which are plants, trees, and shrubs used to make perfumes and medicines.

Egypt

Around 3000 BCE Egypt embarked on several millennia of a brilliant, prosperous civilization in which art and religion occupied pride of place. Doctors were generally priests, who held their art from the gods. Egyptians assigned the highest importance to the written word. Thot, god of Wisdom and patron of scribes, gave humans medical books. One of the most important medical papyruses is the Ebers papyrus that dates back to 1600-1500 BCE. Discovered at Luxor in the mid-1870s by Georg Ebers, it is the most comprehensive record of Ancient Egyptian medical knowledge. It mentions some 700 vegetable, animal and mineral drugs and their various pharmaceutical forms. They range from pomegranate root for worms, to diuretics like juniper, turpentine, scilla, from sedatives like cannabis, henbane, mandrake and the opium poppy to the stimulants absinthe and nutmeg; from figs and dates for liver complaints to the blue lotus, offering a mixture of foods and drugs.

Calcium carbonate was used as an antacid, salt and copper salts as disinfectants and astringents, and magnesia as a laxative. Honey was prescribed for disinfecting wounds, milk as an emollient and a sedative, while beef liver was used for eye complaints.

Moulds, known for their antibiotic properties, were prescribed, while medicine was administered in forms like ointments, eye-drops, inhalation, and potions.

Persia

Under Cyrus and Darius in the 6th century BCE, the Persian Empire expanded from India to the Mediterranean, becoming a crossroads of civilizations. Accordingly, the Persians used remedies from Mesopotamia, Egypt,

Greece and India. Lemon, rhubarb, cannabis, camphor, *asafoetida*, tragacanth, castor oil, and sesame were used. Persians believed in the curative virtues of waters containing the elixir of immortality, white haoma drawn from a mysterious tree, the *gaokerena*. Around it grew plants as numerous as the diseases they cures. Significantly, the term "paradise" originates from *pardes*, Persian for garden.

India

Ayurveda, the "science of longevity", was revealed by Brahma around 1300 BCE, setting out the direction of Indian science, which understood blood circulation, the transmission of bubonic plague and of malaria by mosquitoes. In the later Sushruta era in the 5th century CE, medical knowledge developed to encompass smallpox, diabetes, tuberculosis, hygiene and diet.

Phytotherapy plays a paramount role in Ayurvedic therapeutics. Ginger, for example, is used for flatulence, nausea, and blood circulation, tamarind as a laxative, lotus seeds for heart failure, and curcuma for menstrual pains. The *Charaka Samhita Sutra* mentions *rauwolfia serpentina* (or Indian snakeroot), prized as a cure for snake and insect bites and appeasement, and used today for its effect on hypotension and as a neuroleptic.

China

The Huangdi Neijing known as *Yellow Emperor's Inner Canon*, has been the basis for Chinese Medicine for over 2,000 years. Attributed to Huang Di, the Yellow Emperor (2697–2598 BCE), it comprises two 81-chapter books of questions put to Huangdi, the Yellow Emperor, by his ministers. The first book is the *Suwen (Basic Questions)*, the second is the *Lingshu (Spiritual Pivot)*. The highly influential *Suwen*, which lays the foundations of Chinese medicine, sets out the effects of the five flavours of food on health: "Water is yin and fire is yang; Yang makes breath and Yin flavours. / Thus, when food is too salty, / Stimulation thickens and coagulates And the complexion is altered. When food is too bitter / The skin fades And hair comes away; When food is too pungent, / Muscles contract / And nails desiccate. / When food is too **sour**, Flesh become callous /And lips become thin. / When food is too sweet, / Bones hurt / And hair falls out."

• *Chinese Therapeutics*

Tradition attributes to Shen Nung, who governed between 3000 and 2700 BCE – the *Great Herbarium* or *Pents'ao* in which he discusses recovery from diseases by minerals, animals, and especially plants.

Chinese doctors tested plants for their properties on various parts of the human body. Medicines were classified according to sympathies or antipathies. For example, mint was of a cold nature and was used to relieve diseases caused by hot elements. They used also the analogy principle. They argued that plants bore the "signature" of their powers. Orchids roots, example, were thought to resemble testicles and were recommended for virility disorders, while so-called "capillary stems" were used against hair loss.

Chinese empirical therapeutics also chooses medicines because of their similarity to the organ treated – another instance of the theory of signatures, or similarities. Yellow saffron is used for jaundice, kidney beans for kidney diseases, while products derived from animal or human organs can treat the same ailing organs in patients. Chinese pharmacopoeia is very rich. The *Pents'ao*, completed during the 16th century by Li Shih Chen, inventoried vegetable substances: saffron, bean, datura, rhubarb, rye, ginger, pepper, cinnamon, pomegranate, camphor, ginseng, mixing again foods, plants and drugs. Some Chinese drugs are of undeniable interest, *e.g.* rauwolfia, ephedra, xhaulmoogra.

Greece

Heir to the Middle East's earlier civilizations, Ancient Greece was celebrated for the art of healing, which can be divided into three periods.

Although the art of healing was magical and cures were attributed to gods and heroes, like Paeon and Hercules, plant-based medication played a key role, as *The Odyssey* recounts. Helen of Troy poured into Odysseus's glass "a substance which dissipates sadness, calms anger, and causes all evils to be forgotten". The substance was nepenthes, a mixture of plant-based drugs including opium, cannabis, datura, and helleborus. At around the same time that Homer is thought to have written the *The Odyssey* – 850 BCE – doctors as we know them today first appeared.

The latter half of the 5th century BCE was the century of Pericles, the statesman under whom Athens flourished as never before or since in the arts, literature and public well-being. It was a time known as the Golden Age.

The *asklepiades* – doctor priests who were the followers of Asclepius – drew on their experience to begin practising empirical medicine, free of religious and magical trappings. They practiced in *asklepeions* (medical sanctuaries). Doctors emerged who were self-employed or worked for the city. A tax, the *iatricon*, was set up to pay for the cost of medical treatment and doctors' fees. Public doctors treated their patients at home, or in a surgery (the *iatreion*) and, if necessary, referred them for hospital care. Medical schools, based on the earlier *asklepeions*, flourished. The most famous were in Rhodes, Cnide, and Cos.

It was during the Golden Age that Hippocrates (460-377 BCE) was born. He laid the foundations of ethical medicine and prognosis and treatment based on observation and reason. He believed that each disease had a natural cause; that it was due not to supernatural but to natural causes; and that a doctor had to restore balance between the body's humours for health to ensue.

• *Hippocrates and the Theory of the Humours*

Hippocrates held that balance between four fluids in the human body determined health. They were black bile, yellow bile, phlegm, and blood, and an excess or lack of any of them would cause imbalance and illness. Hippocrates' theory was akin to the Empedoclean notion of the four elements of fire, earth, air, and water. Black bile was mostly earth (cold and dry), yellow bile was fire (hot and dry), water was phlegm (cold and wet), while all four elements were present in blood. Hippocrates believed that cycle of the seasons was a factor in determining the humours. Blood governed in spring, bile in summer, black bile in autumn, and phlegm in winter. However, the humours in the body actually originated from ingested foods which had undergone cooking and ripening in the heart. Blood vessels transmitted the resulting humours to the body's organs. If ingested food did not fully cook or ripen, or humours did not reach their organs, they became unbalanced and disease resulted.

Hippocratic therapeutics is summarized by the formula: *contraria contrariis curantur*. In other words, cures should act in a way that is of an opposite nature to the complaint. An illness which brings on fever should be treated a drug that cools. Treatments like bleeding, diuretics (*e.g.* garlic, onion, leek, cucumber, and fennel), laxatives, and emetics restore balance by purging the illness.

However, Hippocrates also believed that "nature is the first doctor" and that, "food, whenever possible, has to remain the first medicine". In works like *On Diets, On Regimen in Acute Diseases*, and *On Airs, Waters, and Places*, he set out his recommendations that

man cannot live by food alone, but needs exercise, too, as they have contrary, balancing effects.

The *Hippocratic Corpus* is a pharmacopoeia of more than 230 drugs made from plants. They range from narcotics like belladonna and opium, purgatives like euphorbia and mercury, emetics like ginger and febrifuges like absinthe. Camomile, called *parthenion*, was deemed to have great powers and was even said to have cured a workman hurt during the construction of the Propylaea gateway to Athens of his injury.

All Ancient Greek medicine was concerned with the resources of the plant world: Diocles of Caristo wrote a herbalists' handbook, the *Rhizotomicon*, while later in the 4th century BCE Aristotle wrote treatises on medical botany. His disciple Theophrastus was the author of a *Historia plantarum*.

Rome

Roman medicine was initially influenced by Etruscan magic and divination before it was shaped by Greek thinking.

• *Diet According to Cornelius Celsus*

Aulus Cornelius Celsus (c. 25 BCE to 50 CE) was one of the greatest contributors to Roman medical thinking, though not a practitioner himself. His *Eight Books of Medicine* (*De medicina octo libri*) provide a comprehensive account of medical practices in Rome at the turn of the first centuries BCE and CE. Most dietary indications are to be found in Books I and II.

The remedies he describes include vinegar for stopping the flow of blood, cinnamon for sharpening the appetite, and horseradish and leeks for purging. For eye inflammations he proposes adding egg white to eyes drops. In Book II he states his belief that solid and liquid food impacts strongly on both health and disease and that it is his purpose to help both the sick and the healthy eat wisely.

Other influential Roman medical thinkers were Pliny the Elder and Scribonius Largus, though because medicine was considered a manual rather than noble art, its practitioners were chiefly Greeks. Archangatos, for example, officiated from premises that served as pharmacy, doctor's consultancy, and hospital. Asclepiades, another Greek doctor installed in Roma, followed Hippocrates in recommending gentle therapeutics like preparations containing bile and animal liver (vitamin A) for skin and eye infections. He was much influenced by the atomism of the philosophers Democritus and Epicurus. He believed living beings were aggregates of atoms separated by pores through which blood and humours passed. Any change in the size of the atoms caused imbalances and ill health.

The Roman Empire's eastward expansion into Asia Minor was to lead to changes in Roman medical thinking and practice.

• *Galen*

The most famous of all Roman doctors were probably Galen and Dioscorides, both natives of Asia Minor.

Claudius Galenus (131-201 CE), better known as Galen, crystallised Greek medical thinking. He had a brilliant career, working as personal physician to Roman emperor Marcus Aurelius. His ambition was to complete the work of Hippocrates, whose theory of humours he reworked. Unlike Hippocrates, he did not believe that humours originated in ingested food, but in the body itself, though he was of the opinion that different foods produced different humours. Furthermore, Galen thought that the ideal temperament was an equally balanced mix of four temperaments, each of which he associated with a humour: sanguine (blood), yellow bile (anger), black bile (melancholy), phlegm (phlegmatic).

Of Galen's enormous body of written work,

those most concerned with diet were: *The Passions and Errors of the Soul*, *Hygiene* (*De sanitate tuenda*), *On the Properties of Foodstuffs* (*De alimentorum facultatibus*). He believed that food and drink played a critical part in human health, together with physical and intellectual exercise. "Let us enjoy using the foods which are healthiest and easiest to provide as well as the most nourishing," he write sin *The Passions and Errors of the Soul*. Quoting Plato, he adds: "It is advisable to try, as far as possible, to turn away from evil and to embrace its opposite, thanks to food, to daily activities, and to the sciences."

Galen's work laid the foundations of medicine into the Middle Age, while his theory of the humours would not be challenged until the 19th century.

• *Dioscorides*

Dioscorides (c. 40-90 CE) is best known for his five-volume treatise, *De Materia Medica*, in which he exhaustively inventories 519 plants species, complete with instructions on their therapeutic preparation and applications. He describes, for example, the disinfectant properties of the male fern and the anti-inflammatory effects of yarrow, said to have been used to treat Achilles' wounded heel. Dioscorides also considers medicinal food sourced from animals and minerals. Importantly, he distinguishes between "food medicines" and "poison medicines", echoing the Hippocratic notion of healthy food as medicine: "Let your food be your medicine."

• *Gaul*

Gaul designates the land west of the Rhine and the Alps, and north of the Pyrenees (modern-day France, Belgium, Luxembourg, Netherlands, and western Germany). Gaul flourished between the 7th and 1st centuries BCE. The art of healing was practised by druids and their assistants, the Ovates, with the former acting as doctors and the latter as pharmacists. The holders of spiritual power in ancient Celtic civilizations, the druids had extensive knowledge of some 150 medicinal plants. Only they could gather the sacred mistletoe plant, for example, which could prevent and cure all kinds of illnesses and spells. They picked it with a golden sickle during the night of the sixth moon after the winter solstice.

Therapeutics made wide use of hot spring water and plants picked during the summer solstice before dawn. Mistletoe, for example, which grows in clusters on host trees, was reminiscent of tumours (see the theory of signatures). It does, in fact, contain proteins that can halt the division of cancer cells. The fruit of wild rose was an antidote to diarrhoea and gastritis, while its seeds were used for healing purposes. Red poppy improved digestion, burdock eased inflammation and infection, and henbane and primrose were used against neuralgia. Other widely used plants were verbena, salvia, clover, star anise, garlic, fennel, and absinthe.

Small eye-drop holders found near Toulouse and Reims in France testify to the pharmaceutical art of that time. Holders came in solid form, stamped with the manufacturer's seal, made from amber, yarrow, verbena, incense, myrrh, and ivy. To be used, the paste had to be mixed with milk or water, as instructed on the seal. The Gauls believed firmly in the therapeutic virtues of amber. Carried on a necklace it afforded protection against disease, which may explain the number of necklaces found in graves. ■

The Medieval Era East of the Mediterranean

When the Western Roman Empire fell in 476, it continued to the east in Byzantium, with Constantinople as its capital. Over the centuries, however, the Byzantine Empire evolved into a civilisation that was very difficult from its beginnings as the Roman Empire. Constantinople became a great centre of the arts and culture and remained so for a thousand years.

Byzantium

Between the 5th and 6th centuries, Byzantium was a repository of the ancient world's medical knowledge. It would, in turn, transmit that knowledge, together with its own, to the Arabs, to monasteries, and to the West.

In the 6th century, Alexandre de Tralles, doctor and brother of the architect of Saint Sophia, brought back from his travels various forms of therapeutic plants, *e.g.* opium, henbane, myrrh, that he described in his work *De arte medicinae* on internal disease and fevers. The Arabic physician, Mesue, proponent of crenotherapy and heliotherapy, recommended incense, castoreum, and saffron and opium and other forms of anaesthetic to treat pain.

Much later, in the 13th century, Nikolaos Myrepsos, an apothecary and myrrh distiller from Alexandria, published *Antidotarium Nicolaï*, a treatise on over 2,500 medicinal formulae and how they should be administered. The work would become the guide of Western apothecaries until the 17th century. It included, for example, instructions on the preparation of populeum ointment, a narcotic salve made from black poplar buds that was rubbed on the temples, pulse points, and the soles of the feet to soothe headaches and fevers, and bring on sleep.

The Arabic World

In the 7th century, a new religion, Islam, rose out of Arabia to the east of the Mediterranean sea. It was taught by Mahomet, born circa 570 in Mecca. The newly Islamised Arabic peoples, chiefly nomadic tribes, began their expansion.

From the 7th to the 16th centuries the Arabs transmitted ancient medical knowledge, while enriching it with their own discoveries. Under the Abbasid caliphs, Christians like Mesue the Elder or Serapion the Elder translated Greek and Latin medical works into Arabic, and Nestorian monks passed on the work of Hippocrates, Galen, and Dioscorides. They founded a medical school in Khoristan after the expulsion of the patriarch of Constantinople, Nestorius.

Damascus and Baghdad became important cultural and medical centres. They held the art of healing in high regard. Mahomet himself, who originated from the tribe of drug and perfume merchants, the Koraichites, left various comments in a work entitled *The Medicine of the Prophet*. "Pharmacy, the art of drugs and drink, is the noblest sciences of all with medicine," wrote Cohen El Attar in the 13th century. And, according to the *Handbook of the Dispensary*, the apothecary should "be a clean and religious man, fearing first God, then men. He has to weigh his words and especially his writings."

• *Diet and Therapeutics According to Rhazes*

Rhazes (c.864-923) was known as "the Arabic Galen" by medieval chroniclers. Abu Bakr Muhammad ibn Zakariyya al-Razi was born in Persia. The greatest doctor of his time, he reorganized the Baghdad hospital where he taught. He studied Hippocratic and Ayurvedic medicine and alchemy. Rhazes wrote more than 200 books including some 60 on medicine. The most famous was a medical encyclopaedia in 22 volumes, the *Kitab al-hawi* (*The Book Which Contains All*). It included medical knowledge from the 10th century and was translated into Latin in 1279 with the title *Continens*. His pronouncements on food include: "As long as you can treat yourself with food, do not consider medicines." "If the patient can be treated by diet, avoid medicines and combinations of medicines; if he can be treated by simple medicines, avoid combinations of several medicines." "Everything found in diet books has less value than the experience of a doctor who thinks and reasons." "Medicine is only easy for idiots, serious doctors always discover difficulties."

• *Diet and Therapeutics According to Avicenna*

Ibn Sina, known in the West as Avicenna (980-1037) is widely regarded as one of the most important physicians in history. He wrote numerous books, the best known of which is probably the *Canon of Medicine*, said to be over a million words long. It encompassed all existing medical knowledge, refined and codified into the science of medicine. Its influence on Medieval medical thinking was enormous and it was still in use in 17th century France. It provides extensive indications on diets, as does his *Poem of Medicine*, in which he writes, "If you would like to maintain a person's temper in good condition, give him suitable food." Avicenna himself provided much of the basis for later development of fundamental chemical processes such as filtration, distillation, sublimation, and calcination, so critical to the later development of pharmacy.

• *The Andalucian School*

Andalusia was a seat of thought, learning, and scientific discovery. Cordoba had become an important cultural and religious centre where the Judaic, Islamic, and Christian religions flourished.

The leading lights of the Andalucian school of medicine were the great surgeons Abulcasis, author of *Kitab al Tasrif* (*Inspired Treatise of Surgery*), Avenzoar (c. 1090-1162), and Avenzoar's pupil Averroes. A doctor and philosopher, Averroes was a towering figure, whose commentaries on Aristotle have earned him a lasting place in posterity. At the end of 10th century Arib Al Kurtubi wrote a treatise on obstetrics and aphrodisiac practices, particularly massage, while a century later Ibn-El-Baitar (1197-1248) wrote the *Djami El Marfridat*, an alphabetical compendium of food and medicines.

Another eminent figure was Ibn Maymun Said Maimonides, from an intellectual, rabbinical family, who was forced to flee Spain in the mid-12th century and became a doctor at the Egyptian court. His medical writings were in Arabic. They included the *Treatise of Poisons*, in which he warned against the overuse of antidotes, and his *Treatise on the Conservation of Health*, in which he argues that balance is the basis of health.

• *The Cairo School*

Cairo was also a hive of intellectual and scientific activity, with physician and polymath Ibn al-Nafis discovering pulmonary, capillary, and coronary circulation.

Therapeutics was based on hygiene and

medication, for which it drew on detailed knowledge of the pharmacopeia of the Ancients. Eighth-century physician Gabir ibh Harjyan used the theory of antagonisms, prescribing food remedies that were opposite in nature to the diseases they were designed to treat. For blood diseases he recommends cold, dry substances like vinegar and pomegranates; for pituitary gland complaints castoreum and asafoetida; for irritations, onion, roquette salad, and honey; for liver problems pumpkin and psyllium mucilage.

Arabic medicine introduced new "drugs" like coffee, camphor, areca nuts, tragacanth, arabic gum, manna, nutmeg, and amber. With the discovery of sugar cane, alcohol and vinegar, doctors create new formulations, adding juleps, syrup, sugar preserves, and elixirs, and oxymel.

In the 12th century there was a surge of interest among Arab doctors and scientists in chemistry. Indeed words like chemistry, alkaline, alcohol, alum, benzoin and borax all derive from the Arabic. At the same time the craft of pharmacist became separate from that of doctor. Public pharmacies and hospitals were opened. ■

The Medieval Era West of the Mediterranean

The Middle Age in Western Europe spans a thousand turbulent years of ebb, flow, creativity and interpenetration between the Latin, Byzantine, and Arabic civilisations.

The Middle Ages can broadly be divided into three periods.

- 5th to 10th centuries, a troubled time, marked in the 9th century by the Carolingian renaissance, which saw the rise of the arts, science and medicine. The first hospitals were built and the medical school of Salerno founded.
- 11th to mid-14th century saw the awakening of Europe, enriched by knowledge acquired through the Crusades and pilgrimages. By 1250 Europe's population had risen to 70 million from 40 million in 1000. Trade increased between East and West, while universities were built and flourished in Italy and France and Salerno waned. The first apothecary shops appeared. Botany and medicine were still closely intertwined. The University of Montpellier in France became a great centre for the study of botany, marking the beginnings of the separation between food and medicine.
- 1350-1450, the rise of experimental science.

The Salerno Medical School

Situated to the south of Naples in Italy, the Salerno School of Medicine transmitted the medical knowledge of the Greek doctors of antiquity and enriched Arabic research carried out in Baghdad. The principal work to emerge from Salerno, written around 1060, was *Flos medicinæ vel regimen sanitatis Salernitanum* (*Medicine According to the Health Diet of the Salerno School*). It set out rules for a healthy lifestyle and eating "to preserve health".

Platearius, a doctor and teacher at the school, opposed the tradition of complex medical formulae – sometimes of more than 10 plants – inherited from the Arabic medical tradition. Between 1130 and 1160 he wrote *The Book of the Simple Medicines*, a catalogue of medicinal plants and their therapeutic effects. Much amended and translated over the years, the most complete version inventoried 425 plants and 61 products of mineral or animal origin. (Current French pharmacy uses only 390 plants.)

Around 1100, alcohol was distilled in Salerno. It came in two forms: *aqua ardens*, 60°, and *aqua vitae*, 90°. The new solvent was used largely for the preparations of remedies and of perfumes.

Other works produced at Salerno include *Qui pro quo* and the *Antidotarium*, both probably written by Niccolo Salernitano, the school's director, around 1150. They were the first pharmacopoeias of the modern type, spelling the composition and properties of the preparations intended for practical intentions. Under the heading "Spongia Soporifera", the first modern type of anaesthetic, the narcotics to be used as anaesthetic are listed (opium, mandrake, hemlock, blackberry, lettuce, ivy), while fennel juice in the nostril is prescribed for reviving and restoring the patient. Salernitano's work was used as the *Apothecaries' Codex* in the reign of Saint Louis.

Monastic Medicine

Monks practised the art of healing between the 5th and 12th centuries, particularly under Charlemagne. In 544 Cassiodorus, a Benedictine scholar, wrote *Institutiones divinarum* et humanorum in which he urges monks to "learn the properties of simple and compound remedies". Monks both treated patients and acted as apothecaries. With the Crusades, epidemics, and the development of pilgrimages, the number of hospitals created by the episcopates and certain orders multiplied.

Food was an integral part of patient care, and was changed to vary diet. The pharmacopoeia of the time comprised six classes of plant remedies to treat certain kinds of illness: plants for fevers, women, wounds, bleeding, stomach complaints, and venom. The belief in signatures, whereby a plant's similarity to a disease or body part denoted its therapeutic properties, was widespread. The leaves of St. John's wort with small eye-like holes was used for eye infections, while tubers of the colchicum suggest gouty fingers.

The archives of the abbey of St. Gall in Switzerland give an idea of the layout of monasteries. There would be an infirmary located to the east where the sun rose, a vegetable garden, an orchard, and a herb garden, where between 16 and 20 medicinal plants were grown to judge from the St. Gall plan. There would also be an *armarium pigmentorum*, a store room managed by an apothecary, while the library would contain works on botany and pharmacopoeias. Monks both cared for their patients and made up their medicine. In the 12th century, however, various edicts prohibited the clergy from practising as pharmacists and doctors.

Diets in the Middle Ages

Little is know of early medieval diets outside what was eaten in monasteries. Ordinary people in the High Middle Ages, however, ate cereals, leguminous plants, pulses, root vegetables, dry and cooked fruit, and occasionally meat, while bread and mashes were staple fare. Salaries were often paid in bread form. Dairy products were intended for export, though butter was widely used in cooking and calorie-rich cheese was a favourite food of harvesters.

The diets of the upper classes and their taste for meat are widely documented, while the lower middle classes ate meat only on special occasions. Nevertheless records for food for workman building Basel Cathedral in the turbulent year of 1438 show that meat accounted for 54% of expenditure and fish for 27%, while cereals were not even mentioned. Equally, archaeological digs in old latrines in Switzerland and Austria in affluent city districts found traces of meat, fruit, and vegetables, though not of cereals. In the Swiss district of Laufon, however, excavation on the site of a house that had burned down in the 13th century unearthed carbonised traces of a wide range of cereals. Skeletons exhumed from a cemetery in Nanikon, also in Switzerland, showed evidence of lack of iron and rickets.

Health Diets in the 13th Century

From the 13th century, numerous manuals known by the self-explanatory term "health diets" were written. They were often, in fact, commentaries or elaborations on the *Flos medicinæ vel regimen sanitatis Salernitanum*.

The *Tacuinum Sanitatis* was originally a handbook written in Arabic by Ibn Butlan of Baghdad in 1068. Translated into Latin 200 years later, it adheres closely to Hippocratic teachings, describing the nutritional value of fruit, vegetables, cereals, meat, fish, and dairy produce. It also advises on lifestyles and exercise. This is how it describes curd:

"Nature: cold and wet… Utility: good for stomach flatulence. Disadvantages: weighs on the stomach. Remedy: sugar and salt. Effects: phlegmatic blood. Is appropriate for hot complexions, for young people, in summer, in southern regions."

Aldobrandino of Sienna was a little known 13th-century Italian doctor, who, in 1256, wrote in French *Le Régime du corps* (The Diet of the Body). It was a treatise on how to stay healthy by eating the right food, particularly by eating food that matched the eater's temperament, *e.g.* hot food for hot temperaments. It was the first dietary book in French.

Bartolomeo Sacchi Platina (1421-1481) was best known as a historian. Around 1470, however, he wrote *De honesta voluptate* and valitudine (On Honest Pleasure and Healthy Food), in which he set out his knowledge of and ideas on food, and healthy food and diets.

Jean Bruyérin-Champier (born in 1497) was a French doctor from Lyon who wrote an encyclopaedia on food *Re cibaria* in Latin in 1560. It proffers dietary recommendations like "those who have a fragile stomach, patients and old men, should always avoid raw food, and eat a little cooked salad." Bruyérin-Champier does not mince his words on some matters: "It is veritably scandalous that man does not know which foods he truly needs."

The Commerce of Medicines

After the crusades Naples, Florence, and in particularly Venice, which lay at the crossroads of East and West, became the hubs of the trade in medicines. Traders opened *fondachi* (from *fondok*, Arabic for shop) where they sold cinnamon, ginger, sandalwood, saffron, myrrh, etc. In France Marseilles and Montpellier were the centres of the spice, while Portugal, Spain and Holland become important in the wake of the discovery of America and the maritime route to India.

Following the 12-century ban on clergy exercising the medical profession, monks quit their ministries and became doctors and apothecaries – now increasingly secular professions – and merchants. Dispensaries and shops now opened in France and in Italy. In Paris in 1200 the district around the Petit Pont bridge near the Hotel Dieu hospital was home to many dispensaries. Apothecary shops opened on to the street with their wares on display in jars and painted pots. Apothecaries, holding the scales in their hands, would measure out spices and prepare remedies.

In the 12th century the first apothecaries' guild was established in the city of Arles in southern France. More followed in other French cities, while royal edicts regulated the pharmacist's trade in Paris.

In 1260 the great physician and alchemist Arnaud of Villeneuve emulated the Salerno school and introduced into French medicine the alcohol distillate first used at Salerno. It became a remedy sold exclusively by apothecaries against various ills: pains, infected wounds and bites. Endowed with power of rejuvenation, it took the name of aqua vitae, or water of life, one of the two declared aims of alchemy.

It is also argued that distillation led to the rediscovery of essential oils, 2000 years after the Ancient Egyptians. A 12th-century treatise first mentions the distillation serpentine to make surgical spirit, absolute alcohol, and, with a second distillation, methylated spirits. Alchemists made use of distillation to make essential oils and experimented with edible natural substances, such as fennel, nutmeg and cloves. They finally obtained the "three primal elements" to replace the four elements of Aristotle:

- Mercury (air and water), obtained by distillation. It was not the chemical but an oil which gave food its flavour.

• Sulphur (fire), from sublimation. It was a substance that provided moisture and sweet taste.
• Salt (earth), from crystallisation. It determined taste and consistency and was common to the two other normally antagonistic elements.
The separation between food and medicine had begun.

The First Universities

As European ports opened up to the trade of medicinal products, the first universities came into being in the West. Professors from Baghdad where the caliphs had founded a university spread around the Mediterranean rim, turning religious hospices into teaching hospitals. When Baghdad was sacked by the Mongols in 1200, exiled professors and pupils helped found Europe's first universities in Bologna, (1088), Salerno (1140), Padua (1222), Paris (1220), and Montpellier (1272), where the most famous surgeon of the 14th century, Guy of Chauliac, taught. ■

The Age of Reason

The 17th century was the century of reason and classical order. In the France of Louis XIV, the Palace of Versailles showcased the prevailing sense of rational order. Rationalism in therapeutics, however, had to contend with the power of inertia, tradition, prejudice, and mistrust of innovations.

Therapeutics and Medicine

Official medicine embodied by the Faculty of Medicine in Paris made wide, and often abusive, use of enema, purging, and bleeding – for both rich and poor. In one year Louis XIII received 215 enemas, 212 purges, and 47 bloodlettings. These medical practices and their practitioners were the butt of Molière's satirical comedies. Barber surgeons monopolised bleeding, while apothecaries prepared and administered clysters, with the royal apothecaries administering clysters as part of lavish ceremonies. Traditional vegetable remedies, like senna and rhubarb, were widely used for purging.

Hospital pharmacies were the religious privilege of "empirical", or "scientist", monks who competed with the apothecaries. The Capuchins friars Aignan and Rousseau, known as the Capuchins of the Louvre, created a soothing balm called *baume tranquille* containing opium and Queen of Hungary water made with rosemary aqua vitae, while the Oratorians prepared cornflower eye-drops, and the Discalced Carmelites from the Rue de Vaugirard in Paris make bee balm water.

Some empirical apothecaries treated only wealthy patients. One, Nicolas de Blégny, who had a shop on the left bank of the Seine, was famous for his concoction for wounds, arquebuse water, a compound of 14 plants. Another apothecary commercialised powder of sympathy for which he claimed magical powers, while the Capuchin monks of the Louvre produced emerald water, an alcoholic tincture of aromatic plants with purgative properties.

Cures sourced from animals, vegetables, and minerals were all used. From vegetables came products that purged, softened the skin, and opened the appetite, usually in the form of teas and waters, like flax, mallow, and Queen of Hungary waters.

Minerals gave rise to gem therapy, whereby the action of the "volatile parts" of precious stones may cure ailments. Gold was used in powder form or taken as a broth made from boiled chicken stuffed with gold coins.

Of the many fantastical remedies drawn from the animal kingdom, like viper, stag tears, wood lice, small worms, mice, only leeches and cantharid beetles had any future.

New Drugs

Drugs and spices like vanilla, coffee, tea and chocolate, discovered in the 16th century, now came into use.

Coffee was introduced to Paris in 1669 on a visit from Mahomet IV's ambassador, Suleiman Aga Mustapha Raca. Known for its laxative, digestive, diuretic and stimulant properties, it was also used for dropsy, gravel, gout, hypochondria, scurvy, migraine, and lung diseases. It quickly grew fashionable. In 1672 the first coffee shop opened. Coffee did have its detractors, however. The Princess Palatine compared its smell to the breath of the Archbishop of Paris!

Tea from China made its Paris debut in 1636. The Faculty of Medicine, particularly its most senior member, Guy Patin, was initially hostile,

calling it an "an impertinent innovation". Doctor Nicolas de Blégny, however, wrote a work on the power of coffee, tea, and chocolate to prevent and cure illness, stating that the best known effect of tea was to stimulate wakefulness.

Chocolate, discovered by the Spaniards in Mexico, was introduced to France by Queen Marie-Thérèse. The naturalist surgeon Exmelin, who believed chocolate was good for stomach complaints, described his own experience of cocoa: "I cured myself once of rather vehement dysentery with only raw cocoa beans." The Aztecs brewed a beverage from cocoa-beans, water, pepper, and spices called "chocolate" (from the Nahuatl word, xocolatl), which became very fashionable throughout Europe.

However the New World drugs that brought the greatest strides in therapeutics were ipecac roots and the cinchona bark.

Ipecac root was introduced to Europe by Legras in 1672 and was widely used as an emetic and expectorant to cure dysentery and fever. When Helvetius, chamberlain to the queen's household, used ipecac on the dauphin, curing him of dysentery, Louis XIV rewarded him by granting him sole rights to marketing the root.

Cinchona bark was imported into Europe from Peru, where it was used against malaria. Jesuit priests introduced it to Europe through Italy and Spain as a treatment for malaria, which was rife in Europe. Oliver Cromwell died of malaria, while Louis XIV was cured by Cambridge apothecary Talbot, who administered him powdered cinchona bark. The Paris Faculty of Medicine officially endorsed its therapeutic value.

The First Chemical Remedies

It was in the 17th century that therapeutics began to incorporate the findings of the sciences of alchemy and chemistry. Louis XIV facilitates this development by putting an end to the bitter controversy over antimony. He allowed antimony to be registered in the *Paris Codex of Pharmacopoeia* after it had cured him. Paracelus believed it was the ultimate purgative drug, while the Paris Faculty of Medicine successfully advised the Paris Parliament to outlaw it twice. It was not fully rehabilitated until 1666.

The Royal Garden of Medicinal Plants

In 1626 King Louis XIII ordered the establishment of the Royal Garden of Medicinal Plants, despite opposition from the Faculty of Medicine and apothecaries who feared it would rival their own gardens. (The apothecaries' garden was founded in 1578 beside the House of Christian Charity.) Native and imported plants grew there as did the vocations of future scientists like Buffon and Jussieu, who attended the free lectures on botany and anatomy.

Specialities and Pharmacopoeias

Although therapeutics grew more scientific, it remained a field shrouded in mystery. Secret remedies, known as "specialities" were very much in vogue among patients, despite the royal edicts prohibiting them. They included an elixir of well-being called theriaca; orvietan, an antidote to poison; *terra sigillata*, absorbent clay stamped with a seal of authenticity; Carmelite bee balm; etc.

Nevertheless scientific pharmacopoeia was on the march. Official pharmacopoeias were published. The Paris Codex appeared in 1638, followed 10 years later by the Toulouse Codex.

Nicolas Leméry, Louis XIV'S apothecary», wrote a *Traité universel des drogues simples* (Universal Treatise of Simple Drugs), which Morelot reworked and enhanced considerably as the new dictionary of Leméry's simple and compound drugs. ■

The Enlightenment

The century of the Enlightenment was also the century of the Encyclopaedia with Diderot and d'Alembert, scientists like Réaumur, Volta, Galvani, Fahrenheit, Franklin, Watt and Coulomb, inventors like the Montgolfier brothers, and the flying apothecary and inventor of the first gas mask, Pilatre de Rosier, and the natural histories of Buffon and Lacépède.

Botany becomes a Science

Botany now grew into a veritable science with Linné who gave each plant a double Latin name – the first one specifying its species, the second its individual name.

Explorers discovered new plants and trees, like the cahuchu tree, which produces a resin from which rubber would be made. Joseph de Jussieu discovered the cinchona, ipecac, and coca trees, which he sent back to France. Antoine de Jussieu and Declieux established coffee plantations in the West Indies, while Pierre Poivre went to Louis XV and Buffon with his project for an annex of the Royal Garden devoted to exotic plants in Mauritius and Reunion Island.

After the United States of America declared independence, botanist André Michaux introduced European plants to America. There he also discovered the healing properties of American plants: polygala for bronchial diseases, podophyllum rhizome and casara for purging, *gelsemium sempervirens* against neuralgia, the respiratory stimulant lobelia and the veintonic witch hazel.

Lavoisier and Organic Chemistry

Organic substances remained a mystery until the work of Lavoisier revealed the role of oxygen in the combustion of organic matter. He discovered that it released carbon dioxide and water, and therefore contained carbon and hydrogen. He also discovered the composition of air and water and the nature of breathing.

A far-sighted and a generous administrator, he improved the health of prison and hospital inmates and established an insurance fund for the poor. Beheaded by the French Revolution, he was told by his executioners that the Republic did not need a scientist.

The Birth of the Pharmaceutical Industry

In 1775, the French Academy of Sciences offered a reward to any researcher who could find an economic way of producing sodium carbonate, necessary for the manufacture of soap, glass and paper. In 1791, Leblanc established a factory that soon became profitable. The company was confiscated by the revolutionary government in 1794, then restored to its owner by Napoleon in 1801. Nevertheless, the deeply discouraged Leblanc committed suicide five years later. On 29 December 1788 the *Journal de Paris* ran an advert on the factory of the Count of Artois, which produced bleach from acids and rock salt. Thereupon the chemist Claude-Louis Berthollet claimed that he was the inventor of bleach.

By the end of the 18th century a chemical industry was beginning to take shape opening the way for a pharmaceutical industry.

The First Pharmaceutical Regulations

Despite the efforts of Louis XV and Louis XVI to prohibit or, at least, regulate secret remedies, apothecaries continued to prepare their so-called "specialities". Finally, in 1810, new legislation permitted any remedy, old or new, only if it was bought by the State after approval by a commission.

The teaching of pharmacy became more formally organised. Pharmacy courses were put in place in the French provinces and in Paris, where classes were held in the Royal and Apothecaries' Gardens. Courses were lengthy, with students finally being examined by doctors and master apothecaries. In their final exams they had to recognize plants and specify their therapeutic effects. Despite opposition from the Faculty of Medicine, Louis XVI gave pharmacists the right to teach at the Pharmacy College, which brought together privileged and master apothecaries. Under the Consulate in year XI of the Revolutionary Calendar (1802), Bonaparte promulgated a law that reorganized French pharmacy, created pharmacy schools, and regulated the manufacture of medicines, the sale of poisons, and the inspection of dispensaries. ■

Modern Times

In the 19th century the achievements of science in all fields – pure and applied sciences, medicine, and pharmacy – exceeded those of all previous centuries. The botanist and zoologist Lamarck published his theory of evolution and in 1802 coined the term "biology". The botanist monk Mendel founded the science of genetics and formulated the laws of heredity, while Mendeleyev first set out the periodic table of elements.

Experimental Revolution in Medicine

Advances in medicine and pharmacy were particularly spectacular in France in the 19th century, with the likes of Bichat, Corvisart, Bunch, Dieulafoy, Potain, and Charcot. Laennec invented the stethoscope and wrote the classic treatise, *De l'Auscultation médiate* (On Indirect Auscultation). His rival, Broussais, advocated bleeding and made leech treatment fashionable. The reputation of French medicine reached its peak.

Experimental physiology was founded by Claude Bernard and his teacher, the pioneering François Magendie, who carried out the first cardiac catheterization in 1844. Magendie loathed theories and systems, saying that when he was experimenting he had only eyes and ears, and no brain. His experimental work on animals to observe the effect of vegetable-based drugs on animals marked the beginning of modern pharmacology. He conducted experiments on the effect of morphine and strychnine on dogs, establishing that absorption was a simple physical and chemical bodily process.

Magendie's pupil Claude Bernard made a powerful impact with his work on the pancreas gland and, even more famously, on the liver. In his first lecture at the Collège de France, where he stood in for Magendie, he declared: "The scientific medicine I should teach you does not yet exist." By 1865 it did exist, however. It was in that year that he published *An Introduction to the Study of Experimental Medicine*, a work whose impact was comparable to Descartes' Discourse on Method in the 17th century. Bernard gave medicine the impetus to become a genuine science.

Plants Reveal their Secrets

• *Alkaloids and glycosides*

Alkaloids and glycosides – the active elements in plants' therapeutic effects – were extracted. This development made dosing more consistent and effective. Opium was now prescribed in pill form for sleeping disorders, fevers, and pains, and as a sedative and cure for diarrhoea in a camphorated tincture.

In 1806 Sterturner discovered morphine. In 1832 came codeine that Robiquet found to have analgesic, antitussive properties. In 1832 Merck discovered papaverine, a spasmolytic and vasodilator.

Pelletier and Caventou isolated strychnine and brucine in nux vomica, veratrine in helleborus, and quinine in quinquina, while Magendie and Pelletier separated emetine from the ipecac root and Runge and Caventou caffeine from coffee (1820).

The identification of active principles in plants once used in sorcery demystified their effects. Such plants included deadly nightshade,

mandrake and henbane. As early as 1809 Vauquelin had grasped that atropine was the active element in deadly nightshade and in 1833, Mein, Geiger and Hessé isolated it. Atropine eased spasms, slowed bowel movements, accelerated the heart beat, and dried up secretions. Geiger and Hesse also isolated hyoscyamine, the active ingredient in henbane, while in 1859 Niemann extracted cocaine from *erythroxylon coca* as a stimulant and local anaesthetic.

Vulpian and Claude Bernard studied the effects of curare obtained from various species of strychnos, while further discoveries of active principles yielded solutions to diseases that had been inexplicable in the 18th century. In 1875, for example, Tanret isolated ergotinine in rye pin, a fungal parasite that infected rye. Chemists also identified additional alkaloids, like ergotamine and ergotonine, from which they prepared hydrogenated derivatives, such as dihydroergotamine, which were as effective as their natural forebears for hypertension, migraine, and neuro-vegetative imbalances.

In 1869, chemist and pharmacist Nativelle isolated digitoxin, the active ingredient of *Digitalis purpurea*. Its effectiveness in treating heart failure would only be averred in 1930 for its properties of slowing and strengthening the heart and making the heartbeat more regular.

Earlier Stenhouse had, in 1851, extracted sparteine from scotch broom. Thirty-five years later Houdé discovered its cardioactive properties.

• *Cardiology*

Although the extraction of active principles improved the effectiveness of the treatments, in particular regarding dosage, the analytical methods at that time could not detect impurities due to raw material or solvent residues. Chemistry now sought to copy nature, while synthesizing active molecules, particularly for heart treatment.

En 1867, the Scottish physician Brunton discovered that amyl nitrite, isolated by Balard in 1844, could be effective against pains caused by angina pectoris. In 1879, the English doctor William Murrell discovered nitroglycerin, which had similar therapeutic applications (which Alfred Nobel mixed with gunpowder to produce dynamite). Thus, while vegetables had provided spartein and digitalin to treat cardiac complaints, synthetic chemistry yielded amyl nitrite and trinitrine.

• *The Aspirin Molecule*

The treatment of fever had always been a prime concern of medicine and during the century numerous scientists intensified the search. In 1849 Hofmann sought to transform a compound chemically, while Perkin made a similar attempt. During his work he extracted aniline from coal tar, but found it was too toxic. French pharmacist Leroux isolated salicylic acid, the active ingredient of the willow bark – used in Greece at the Hippocrates's time and by the Incas in America. In 1853, Gerhardt carried out the first acetylation of salicylic acid, so synthesizing aspirin. However, it was not until 40 years later, Hoffmann seeking medicine to cure the rheumatic pains of his father, obtained pure acetylsalicylic acid which he named "aspirin" – "A" for acetyl, "spir" for spiraea, and "in" to sound chemical. It was an immediate, fabulous success.

The analgesic properties of aspirin were discovered by chance. Eichengrün, a researcher from Bayer was distributing it to doctors to test its effectiveness in the treatment of rheumatisms. A dentist administered it to a patient suffering from dental pain in the place of antipyrin, of which he was short, and discovered the analgesic properties. The rest is history, with aspirin finding application in other fields like infections, immunology, endocrinology, etc. ■

The Relationship between Food and Drugs

Lemon and Scurvy

Hawkins in 1593, Lancaster in 1601, and Woodal in 1617 recommended the use of lemon against scurvy. But it was Lind who in 1747, in what could be considered the first published clinical trial, first experimented lemon on a group of 12 scorbutic sailors divided into six pairs. Despite results published in 1753, 42 years would elapse before the Admiralty introduce lemon on British ships, followed almost one century later on French vessels.

Our historical overview shows that since prehistory humans have used food not only to assuage hunger and provide energy, but also to soothe, and even cure, pain. Instinct and observation of the environment, particularly plants and animals, provided humans with clues as to ways to cure themselves. They came to associate the power of these natural cures with magic and religion – an association that would last for centuries.

The advent of writing, particularly the discovery of Sumerian tablets in 2100 BCE, brought the first precise, important data on the nature of the relationship between food and drugs. The discovery of a papyrus from 1600 BCE in Egypt revealed the use of "food vegetables" in medicinal form with food vectors like beer, wine, and honey. A tablet from 700 BCE describes the vegetable garden of the kings of Babylon with its 67 species of different plants, in addition to trees and shrubs intended for the preparation of perfume and medicine.

The Relationship between Food and Drugs from Antiquity to the Middle Ages

The emergence of medicinal diets in China and the Ayurvedic diet in India advising physical exercise – ideas echoed by Hippocrates in 500 years BCE – marked a turning point in ways of thinking about food and healthcare. Again in China, though not exclusively, there was a growing interest and effort in drawing up exact descriptions of plants and their properties.

The Greeks divided medicine into three categories: diet, pharmaceutical, and surgical medicine, while in Rome in the 1st century CE Cornelius Celsus wrote in the prologue of his *Treatise on Medicine*: "As the successors of Hippocrates we divide medicine into three branches: one with food, the second with medicines, and the third with the help of hands."

Pharmacy deals with remedies and diet with food, while many plants have both uses, blurring distinctions between food and drugs. Cornelius Celsus's *Treatise on Medicine* again provides evidence of the shift in thinking about the food and drug concept. "After performing remedies by removing harmful principles, it is advisable to look to substances which nourish, namely solid and liquid food, of which the influence is not less great on health than on disease. It is consequently my duty to make their various properties known, first so that people in good health may profit, and second to inform patients who need our care about the kind of food they may use, without being required to name all substances which compose them."

Hippocrates echoes Cornelius Celsus's sentiments in blunter terms ("Let food be your

medicine"), while Dioscorides speaks of "food medicines" and "poisonous medicines". Galen's ideas on the standard diet set the tone for 1,000 years. In 169, during his first stay in Rome, he started his treatise on keeping health, which he would later supplement with a treatise on food properties, *De alimentorum facultatibus*.

By the end of Antiquity, diet had been incorporated into new medical thinking with its three categories: natural things (physiology), things against nature (pathology), and unnatural things (external factors), *i.e.* air; food and drink; repletion and clearance; movement and rest; sleeplessness and sleep; afflictions of the soul.

Galen's thinking still prevailed in the Middle Ages in monastic rules, diet timetables, and versified diets. The most famous is the *Health Diet of the Salerno School*, published in 1066, which remained popular into the 19th century and ran into 240 editions. This Salerno was in fact a collection of rules for staying healthy by living close to nature. It also played down the importance of disease, with maxims like: "If you cannot find a physician here are three excellent ones: joy, peace, and moderate meals" and "Can man die while sage flowers in his garden?"

After the Arabs took Alexandria in 642, Galen's recommendations became part of the dietary thinking of such great Arabic doctors and writers as Rhazes, Avicenna, and Ibn Butlan, who wrote *Tacuinum Sanitatis*.

For medieval historian Carmelia Opsomer, dietary knowledge in the Middle Ages was governed by very structured practices in keeping with manuscripts like the *Book of Simple Medicines* and *Tacuinum Sanitatis* which set out recommendations very precisely. Both works date from the end of the Middle Ages and offer the advantage of summarizing traditions that grew over 1 500 years.

At the end of the Middle Ages, dietary and herbalist knowledge, practices, and writings on plants turned into medical encyclopaedias describing everything relating to health. The *Tacuinum Sanitatis* of Grenada, for example, contains a whole section on medicinal botany.

In the ensuing centuries, studies considered food for its healthcare properties. One such study was the *Le Trésor de la santé* (The Health Treasure), published by an anonymous French doctor in 1607. It supplies evidence that food was seen as having a dual function at the time of King Henri IV of France. The extract below shows how, in addition to recipes, it also contained descriptions of foods' dietary value.

"If fruit such as apples, pears, peaches are served at the end of meals, they should be covered with fennel, aniseed, caraway, coriander, and dill which are able to fight flatulence and the coldness of these fruits. They are hot, dry seeds of the third degree, helping digestion. But each one has some individual virtue.

"Fennel and aniseed help to keep good eyesight. Coriander and dill are contrary if too much is used. Fennel and coriander are slow to digest. Caraway, aniseed, and dill help the stomach and facilitate digestion. Caraway and coriander according to Avicenna have the principal virtue of preventing fumes from rising to the brain. Coriander and dill cause sleep." ■

Food and Drugs become separate

In 1100 the discovery of distillation was the first stage in the break-down of the drug-food continuum into two separate parts that would gradually come to be viewed individually.

The second stage came at the turn of the 17th and 18th centuries, as the rise of science and rationalism led to pharmaceutical publications that differentiated medicine (although it still used foodstuffs) from food. This shift was formalised in 1777, when apothecaries in France were officially separated from spice merchants by a royal decree creating the Pharmacy College.

From this time food and drugs grew steadily apart. The separation was compounded by the emergence of synthetic chemistry, viewed as products that were free from the impurities in raw materials and more efficacious, and by the rise of the pharmaceutical industry. The result is the science has come to consider drugs in isolation, while dietetics has regained importance in the guise of the subject of nutrition, a speciality taught in medical schools. ■

Conclusion

There has been a historical continuum between food and drugs since prehistory to the present day. Most foods have been used to provide energy, but some were identified as having a special role in improving health and curing diseases. Importantly, the notion of "healthy food" appears very early, which leads to the idea that the food-drug continuum evolved in four steps:

1. In the beginning there was no difference between food eaten for nourishment and food eaten to cure diseases.

2. The notion of "healthy food" emerged. In other words, some foods had come to be regarded as not good for the health.

3. Special foods were used to treat disease conditions. They were in fact used as drugs and were grown in separate gardens from other vegetables and plants grown for food.

4. Finally, progress over the centuries culminated in the ability to extract active ingredients from foods. This generated a new science around drugs that were separate from food. Diseases were cured by drugs only, and the most frequent dietary prescription from physicians in the event of serious diseases was to fasting.

To put it in a nutshell: patients need drugs to manage disease and food to meet their bodily requirements. Medicine and nutrition complement each other. Or, as Hippocrates wrote: "Whenever you can, let your food be your medicine."

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Diseases: History, Classification and Definition

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Abstract

Even before there was such a thing as physicians, the endogenous or exogenous origin of disease had long been the subject of fierce debate.

Disease is, in fact, dual in nature. It has two components: a pathogenic factor (infectious or not), and the innate or adaptive reaction of the host, which may cause undesirable consequences.

When does the body's response exceed what is considered normal, whether from a physiological or statistical perspective? What constitutes an abnormal consequence? Both questions are matters of debate and definition that vary with social changes, scientific understanding, shifting norms, and many other factors.

Curing a disease requires a drug to be taken to treat the pathogenic factor and control any harmful consequences. Nutrition plays a critical role in managing the host's response. Furthermore, only adequate supplies of nutrients can correct dysfunctions that arise from nutritional deficits. Such disorders may be classified as diseases, but they cannot be treated by drugs.

A proper diet will ensure that the body's physiological functions operate efficiently. Such functions include the systems of defence (innate and acquired immunity) and repair that allow people to survive most diseases present in their environment. Drugs are, however, necessary to treat the pathogenic factor. Food and drugs: dual tools against the dual nature of disease.

According to Greek mythology, humankind originally lived in a disease-free golden age until Prometheus robbed fire from the gods and handed it over to humans. The theft brought both great benefit and great woe.

The benefit was a dietary revolution. Humans were now able to cook their food, which prompted new dietary patterns and led to modern food habits. Societal behaviour, too, changed as certain members of human communities learned to master fire and cook safer, more enjoyable food while the others were out hunting or working in the fields.

Woe came when Zeus, the owner of fire, hatched an Olympian plot to avenge the theft. He created a woman, Pandora, and asked her to take a box as a gift to Prometheus' brother. Cunningly, he forbade her to open it. Pandora, however, was unable to resist the temptation. She opened the box, and out swarmed evils previously unknown to humankind. They overran the world. One of them was Disease. Thus, according to Greek mythology, diseases are clearly external forces that attack humans. They do not come from humans, but humans have to contend with them.

Interestingly, another figure from Greek mythology, the centaur Chiron, famed as a skilled physician and surgeon, also learned botany and the secret of healing plants. He discovered medicine in local food and used music to help the body fight disease. Chiron thus introduced the second component of disease: the reaction of the host.

Another famous Greek, Hippocrates, developed a different hypothesis. He thought that Nature *(physis)*, which included the human body, was equilibrium and harmony. Accordingly, he called the science of this harmony "physiology", while the equilibrium it sought denoted oscillations around a mean value. Exogenous factors could affect that equilibrium, driving oscillations too far from the centre, so requiring a special effort from the body to restore the usual balance. Disease, then, for Hippocrates, was the body making efforts to recover its equilibrium. It therefore originated in the human body. Accordingly, the prime objective of therapeutics was to help the body restore its equilibrium, not to suppress exogenous factors.

Hippocrates' theory is alive and well accepted today. The word "malady" (and the French *maladie*) come from the *Latin male habitus*, which means "in a bad state, functioning badly" – in other words, disequilibrium may be emotional or molecular and so accessible to modern tools. If equilibrium is taken as bodily functions fluctuating around a central point, then disequilibrium consists of stronger, abnormal fluctuations. The implication is that a continuum runs from health to disease, which in turns prompts the question: Where does normality end and abnormality begin?

Endogenists vs. Exogenists

Disputes as to whether disease was endogenous or exogenous in origin were very lively up to two centuries ago. French physician François Joseph Victor Broussais (1772-1838), father of the "irritation theory", argued that endogenous disequilibrium was the starting point of all disease.

Although the 1832 cholera epidemic killed off that theory, it spared Broussais, who would die a few years later from an endogenous disease, rectal cancer. His legacy was the concept that the normal and the pathological were fundamentally the same and lay along a continuum where their variations were only quantitative in nature.

Another endogenist was German physician and polymath Rudolf Ludwig Karl Virchow (1821-1902), the father of pathology, who urged his students to think microscopically and look at cells from where, he argued, all diseases originated. His work, *The Handbook of Special Pathology and Therapeutics*, which described leukaemia, setting out his brilliant contention, which would later give rise to the art of autopsy. Interestingly, however, he made the same mistake as Broussais and was unable to consider the other microscopic origin of diseases: germs. This led to his famous dispute with the obstetrician Semmelweis over the latter's practice of washing his hands with antiseptic – a simple practice that drastically reduced deaths from the puerperal fever that killed so many mothers after delivery.

The great French philosopher Auguste Comte (1798-1857) was convinced by Broussais' theory and came to argue that there could be no disease without tissue damage – a contention echoed by Marie François Xavier Bichat (1771-1802), the father of histology and pathology, who hypothesised that diseases attacked tissues rather than organs.

Claude Bernard (1813-1878), who pioneered physiology, was another advocate of the endogenous origin of disease. His famous work on the pancreas led him to consider the failure of an organ, the pancreas, as the cause of a disease, *diabetes mellitus*. He first articulated the concept of "homeostasis", whereby "the constancy of the internal milieu conditions free, independent life". He was looking for a constant cause of disease. But his focus was on organs, not on exogenous factors.

On the other side the great dispute were the "exogenists" – Koch, Pasteur, and Cohn, who looked for the origin of disease outside the human body.

Heinrich Hermann Robert Koch (1843-1910), one of the founders of microbiology, was awarded the Nobel Prize for his work on tuberculosis. He isolated the pathogen, the tubercle bacillus (subsequently named after him), and identified the characteristic damage it caused and the reaction of the host. He also discovered other pathogens, like *Bacillus anthracis* and *Vibrio cholera*. He postulated that a microorganism (or germ) was responsible for a disease, but that to prove that it was the cause, it was necessary to demonstrate that it could:

- be found in all cases of disease,
- be isolated, produced, and maintained in a pure culture,
- could reproduce the disease,
- be retrieved from an inoculated animal and cultured again.

Koch's postulates were supported simultaneously by Louis Pasteur, who demonstrated that some diseases could be cured by killing their pathogens, and by Ferdinand Cohn (1828-1898), who undertook the classification of bacteria in

four groups – sphaerobacteria, microbacteria, desobacteria and spirobacteria.

Auguste Comte's position that there could be no disease without tissue damage opened the door to a consensus between exogenists and endogenists, who could agree that a sick person suffered from a "disease" generated by an exogenous pathogenic factor, triggering an endogenous reaction and ending in a disease.
Notwithstanding the integrative Aristotelian view whereby the opposite approach is also a science, opposites are still opposites. Medicine should be able to use one single approach to explore both sides of the etiological coin. Clinical and biological signs stem from two intricate phenomena. One relates to the effects induced directly by the pathogenic factor (*e.g.* destroying epithelial cells, invading neutrophils, necrosis), and the other is the body's reaction as it seeks to cope with the invaders (inflammation, fibrosis, increased blood flow, etc.). For example, a knife wound is the cut made by the knife, which might lead to an oedema on the rim of the wound as the body reacts to it with a local inflammatory cascade and coagulation to stop the bleeding.
In fact, the body reacts in a limited number of ways that are very often not specific enough to identify, characterize, or even suggest, the cause of a disease. Using Koch's postulate, physicians can, however, establish and recognize a cause if the same reaction to a given pathogenic factor occurs with a specific pattern and is reproducible. However, identifying the pathogenic factor very often serves an informative purpose, helping to decipher different diseases within similar syndromic reactions.
Pathogenic factors cannot be ignored despite Broussais' theory. Their identification has led to the classification of disease – a medical science named "nosology". In fact, many diseases are specific entities characterized by the pathogenic factors triggering them, by their clinical and biological signals, and by the way they evolve and are treated.
A pathogen-induced disease is easy to identify, because there is a qualitative difference between disease status and the former healthy status without that particular pathogen. Infective, toxic, and physico-chemical agents can all be disease-inducing exogenous factors. Numerous diseases have been classified by the pathogens causing them – the names of Yersin and Bordet spring to mind. The recent example of AIDS is instructive. It was named to describe the dysfunction of the immune system, but was recognized as a disease only when a specific retrovirus was identified by Montagnier and Barré-Sinoussi as pathogenic factor.

However, "pathogenic" factors are so called because they induce either a specific type of damage to the host tissues or organs (analysed by anatomopathologists), or a specific reaction in the host. Otherwise "the silence of the organs", to paraphrase Leriche, denotes health. Pathogen-induced diseases can be identified if the damage or the host's reaction is systematic, noticeable, and reproducible, as Koch astutely postulated after observing specific lesions induced by a specific microorganism. In fact physicians collate clusters of signs (syndromes) and make progress towards treatment when they identify a syndrome which has a specific cause/reaction.
Among the first infections ever noticed were fevers which occurred with set regularity – malignant tertian and quartan fevers. They were classified as a specific disease long before the malaria-causing parasite *plasmodium falciparum* had been identified. Now, however, its presence in a blood droplet is the decisive diagnostic criterion, while the body's reaction is considered a non-essential factor. Disease, from this perspective, is extrinsic.
Interestingly, the body's reaction of the organism is still used to monitor the efficacy of treatment and restoration of health is determined by the end of the endogenous reaction. Disease is thus considered from the point of view of the reaction of the organism. It is intrinsic. ■

The Health and Disease Continuum

Claude Bernard's celebrated work on the glycogenic function of the liver led him to postulate that there was a continuum between health and disease.

The body gradually lost its capacity to regulate blood sugar, so leading to a diabetic condition, but with no clear limits delineating when blood sugar was rising above fasting values and when it was crossing the diabetes line.

In reality, however, there is a physiological threshold that can be used as the border between normality and the disease of diabetes. *Diabeto* in Greek means "I go through", in reference to the passage of glucose through the kidney when glycaemia is above 1.8 g/l. Glycosuria, or "sticky urine" – the presence of sugar in the urine – is the oldest sign of diabetes. Bernard was well aware of glycosuria, but was not willing to accept that there was a threshold separating normality from disease. He argued that there were non-detectable traces of sugar in urine in the normal state in order to confirm his concept of a continuum between health and disease.

There are numerous functions and biological parameters with different basal values in different subjects, and boundaries between normal, borderline, and pathological states are usually arbitrary. When does a cell become a cancer cell? When does loss of bone density become osteoporosis? When is blood pressure or secretion of the thyroid hormone too high? Where is the end of normality along the continuum recorded in a population?

"Normality" can be understood in two different ways. Either it is the common physiological state, functioning as usual, or it is used with a statistical meaning.

Physiological Normality

Physiological normality is when every organ functions similarly in every subject in basal conditions, fulfilling its physiological role, *e.g.* 60 heartbeats per minute and a bodily temperature of 37°C in the morning at rest. Every function is also able to adapt to the daily usual changes, so that, when climbing the stairs, an individual's pulse rate, respiratory rate, and expiratory air flow increase.

A kidney that is not able to clear blood creatinine and a heart that cannot adjust bloodflow to cope with its daily work load do not work normally. They cannot cope with the usual tasks of everyday life. What, though, is a "normal task" if not an arbitrary threshold? A "normal" task for a young person may become a major, abnormal challenge for someone who is older (although the waning in physiological strength is also, in itself, normal.) Similarly, some tasks require higher capacity than others: woodcutters need stronger hearts and muscles to carry out the normal tasks of their daily round than office clerks do for theirs. Which prompts the question: Who are the normal representatives of a population? Olympic athletes, young male students, or office workers?

Statistical Normality

Normality can also be a matter of statistics. For the sake of simplicity, let us consider that variations in human health are governed by Gaussian, or normal, distribution, whereby a majority of individuals are – statistically – clustered around a mean value, *i.e.* normality. It is generally accepted that those who fall

within two standard deviations from the mean are "normal". The farther someone is from the mean, the more likely he, or she, is to be "abnormal". This statistical inference is routinely used to draw the boundaries of biological analysis in hospitals, using the huge amounts of available data and a cut-off threshold.

Nevertheless, from a species perspective it is desirable that a group of normal people should have as a wide a range of extreme geno-/phenotypes as possible to ensure that some of its members have a high probability of surviving in unexpected conditions and prolonging the species in new conditions. Such subjects, distributed at the extremes of the "normal" group, may become the mean value in a new environment. In the jungle, for example, the human species may survive by selecting pygmies, who are small enough to hide in the undergrowth. In grassland, the species may need tall Masai people, who can see over the grass. From our European perspective, pygmies are abnormally small and the Masai abnormally tall. But both are adapted to their environment.

In a given environment a borderline condition can become an advantage. Some top cyclists have very slow heartbeats at rest that enable them to win races – a capability denied to those whose heartbeat is normal. Similarly, highly trained athletes develop polycythemia, which enhances the flow of oxygen during intense effort. Such effort becomes for them the "norm" and the huge number of blood cells that super-athletes produce is adapted to that norm. At rest, however, there is a very real risk that polycythemia will cause their blood to clot. Are they abnormal athletes? Or is it abnormal for them to rest? Or then again, do their bodies achieve too high a level of specialization that puts them at risk in standard conditions of life?

Statistics can be used to establish a limit on blood values measured at the same time in fasting basal conditions. But most functions are not steady and oscillate around a set point, a pattern explored by the science of chronobiology. Body temperature rises in the morning when we wake up, reaching a zenith of around 37.5° in the afternoon, dropping as bedtime approaches, and descending to a nadir of 36.5° at around 5 a.m. The average temperature is 37°, but it can change, decreasing in winter and increasing in summer to adjust to local conditions and reduce the energetic expenditure due to homoeothermy. Explorer Jean-Louis Etienne exploited these temperature patterns when he trained for his solo expedition to the North Pole. In industrial, air-conditioned societies, however, body temperature changes are less necessary or pronounced.

Many other physiological functions and responses – hormones, immune responses, digestive enzyme secretions, wakefulness and sleep, and body weight – follow circadian rhythms and seasonal cycles. They are controlled by *Zeitgebers*, or synchronizers, receiving information from the external and internal environment and giving the tempo. There is no easy way to check whether the changes are well adapted to the changes in the environment, or whether they are within a physiologically normal response.

Some organs have their own in-built "pacemakers", like the heart and the stomach. But they do not always oscillate symmetrically around a mean value. Certain functions can, in fact, be very asymmetrical, like appetite and sleepiness, or non sinusoidal, like breathing, where inspiration is much shorter than expiration. Normal physiology is in reality a mixture of different rhythms and interferences, characterized by very irregular oscillations that defy precise description. Although it is possible to predict and describe overall patterns and shapes, details vary infinitely. Each minute is

different from the previous one, just as the individual waves breaking on the sea shore are unpredictable even though the point which the tide will reach every day can be predicted with precision – important information for sailors seeking to anchor.

Monitoring physiological variability can be used to explore the intensity of stress: when the level of stress increases, the variability of the heartbeat decreases. Conversely, if the pulse is too regular, the result can be a disease like ventricular tachycardia or auricular fibrillation with a fast stable rate unsuitable to daily life. A pacemaker's rhythm may be very stable, but is totally ill-adapted to daily life. The loss of variability becomes an illness.

Encephalograms reveal a similar pattern: normal brain activity is beyond precise description, even though a regular overall picture of alpha, beta, and delta waves can be observed. Significantly, epilepsy shows as regular, well ordered bursts of spikes.

If I drop a glass once I am clumsy, but when it becomes a habit and I drop every single one I pick up it is time to look for a neurological disorder. Does my dropping glasses become noticeable because I do it regularly? If so, then regularly doing something abnormal may be a disease, as physicians can describe what is reproducible. Or is my dropping glasses abnormal because it is not adapted to the stress and strain of daily life? The difference between health and disease lies in the impact on everyday life. ■

Disease or Functional Variation

Let us consider a current debate on health and disease: obesity. When is it a disease and when is it merely a variation in the adipocytes' function of storing fat?

From a statistical point of view people of excess weight are those who are over two standard deviations from the mean weight of a given population. The current consensus in the West is that a people are of normal weight if their body mass index (BMI) is between 18.5 and 25. They become overweight with a BMI of between 26 and 30, obese up to 34, and extremely obese from 35 upwards. However, the average population in the US is gaining so much weight that the average weight there is rising, with boundaries increasing accordingly. The percentage of obese people may thus decrease, as weight classified as abnormal in 1985 becomes the norm!

If the end result is taken as the touchstone, then the optimal weight is that of those who live longest. But cultural perceptions of body weight vary. Being overweight can be considered a sign of health in Africa where AIDS is a devastating disease, aesthetically desirable for Botero when he selects models for his works, or as the incarnation of wealth and power. At the other extreme, fat is hardly the most fashionable body format on Californian beaches.

From a biological point of view, an increase in BMI can be considered as an abnormal pathological event. The parallel rises in all-cause mortality and body weight support that perspective. Rising BMI can also be seen as the body wisely adjusting to new environmental conditions by storing excess energy in specialized cells – adipocytes – in order to preserve the vascular system from fatty deposits, so preventing atherosclerosis, an earlier killer than obesity.

Finally it may be that the body feels it is necessary to increase its storage capacity, either because people no longer store food in their houses but have to store energy somewhere, namely in our fat mass, or because global warming is driving people to anticipate some long, uncertain winter food shortages. Famine is still a risk that the human race cannot forget.

Fat storage can be used as an example of how a "normality" marker can be determined. An interesting experiment is to starve a vole every other day. Voles eat a great deal and cannot stop easily. Fasting every other day causes them severe stress. During the first days of the experiment, there are biological signals of abnormal fasting conditions. Basic parameters are affected: the vole's body temperature drops, its basal metabolism slows, and it loses weight much more sharply than in usual daily variations. The vole's fatty tissue than begins to adapt, as it stores more fat and becomes "overweight" on feeding days.

This fat storage pattern can be considered abnormal compared to that of a wild vole able to eat every day. Yet it enables the laboratory vole to maintain a normal body temperature, metabolic rate, and level of activity when fasting, with its lowest weight regaining pre-experiment values, similar to that of a wild vole. How should this surplus weight be considered? As healthy adaptation, or as the beginning of obesity?

The second way to delineate obesity as a disease is to identify when organs cease to be silent as surplus weight exceeds the body's

ability to adapt to it:

- Either the body is unable to readjust to fasting conditions and cannot clear all its energy intake. The result is a metabolic syndrome with hyperglycaemia or hyperlipemia and an increase in inflammatory markers such as C-reactive protein.
- Or joints are not able to cope with the physical overload, or lung capacity is impaired with permanent hypoxia and hypercapnia.

Another interesting example of how a bodily function sheds light on the blurred dividing line between normality and pathology is the way the body controls its temperature. In everyday life the body's thermo-receptors are sensitive to a range of temperature between 36° and 38°. When fever sets in, another set of thermoreceptors that are sensitive to higher temperature tell the hypothalamus to regulate body temperature at a higher set point. Does that mean that fever is not an abnormal signal because there is a physiological system to take care of that "abnormal" situation?

The same question arises with the other repair systems, like the DNA repair system, anti-oxydative cascades, and noci receptors. Is it because there are repair systems that DNA damage is normal? Or is there a continuum with a common rate of repair in the usual healthy body and a borderline situation where the existing repair system reach the limits of its capacity? Using the model of excessive energy intake, it is possible to suggest different successive repair systems: increases in energy expenditure, increases in fat mass, then atherosclerosis. ■

Pathogens and Defence Systems

To return to the debate over the exogenous or endogenous nature of illness. Most symptoms that reveal an infection are signs of the host's response and not damage directly induced by the pathogen.

Diarrhoea, for example is due primarily to an increase in the host's digestive secretions, even if some toxins can also trigger that reaction. Abscesses speak of the reaction of white blood cells rather than of a multiplication of germs. Signs of inflammation – like fever, high CRP, and high sedimentation rates – are mechanisms to improve the local conditions for healing. In a way, there is no disease without a reaction of the host, and a pathogenic microorganism is pathogenic because it is recognized as such by the defence systems.

The body has two kinds of defence systems – innate and acquired immune systems.

The innate immune system is activated irrespective of the disease, marshalling immune cells to sites of inflammation and infection. It doubtless evolved over time to enable humans to survive in the environments they inhabited. The innate system also has a switch-off mechanism that is as important as its switch-on. Food allergy is an illustration: most people's immune systems learn not to react to the daily invasion of foreign food proteins in their bodies. Some, however, continue to react to specific proteins called food allergens. Leriche argues that stimuli to which the body has learnt not to react are not pathogens. The organs are silent and the body is healthy.

A more specific kind of immune system is the acquired immune system that remember specific invaders for certain lengths of time – though why the memory lasts longer for tetanus than for flu is a mystery.

These defence systems are part of our daily life, keeping gut flora within the gut lumen and preventing germs from entering some parts of the gut, namely crypts, so that parent cells continue to generate endlessly renewed epithelial cells.

It makes sense to consider that a disease is composed of a pathogen, or an abnormal function, and a reaction of the body's innate immune or repair systems, and the consequences of both. Accordingly, treatment of a disease will involve destroying the pathogen or compensating for the abnormal function, helping the immune or repair system, and managing the consequences of both.

Tuberculosis, for example, is induced by a mycobacterium tuberculosis that generates granulomas, destroys bone and induces hemopthysia (coughing up blood). Symptoms include fever, sweating, and loss of appetite, while consequences are weight loss, fatigue, pallor, lymph node reactions, and immune reactions specific to tuberculin. Treatment includes an antibiotic to kill the mycobacterium, proper nutrition to compensate for blood loss and higher protein turnover, and possible local action like pleural puncture, or orthopaedic correction.

Nutrition, for its part, is part of disease management rather than treatment. It provides what is necessary for the immune systems to function correctly. But is it possible to include food that actually strengthens the body's defence systems? ■

Nutrients as Cures

Some genetic defects require diets to be modified (*e.g.* low intakes of phenyl-alanine for phenyl-cetonuria), while certain nutrient deficits induce certain disorders (*e.g.* scurvy, rickets).

These are systematic and reproducible, so they can be detected by physicians, but not cured by anything other than nutrients. As they can be detected by physicians should they be considered as diseases, even though there are no drugs to cure them? Or are they nutritional disorders?

One of the first signs of vitamin A deficiency is night blindness and xerophtalmia. Its nutritional cure has been known for centuries and Hippocrates prescribed fresh ox liver to cure it. Vitamin A's role in the vision system was demonstrated by the 1967 Laureate of the Nobel Prize for Medicine, George Wald. It also plays a part in many other pathways like coenzyme Q, vitamins E and D, biosynthesis of squalene, synthesis of serum and muscle proteins, and cell membrane structure and function.

The earliest symptom of vitamin A deficiency is the failure to produce retinal due to the formation of rhodopsin, resulting in night blindness. This, is, however, fully reversible. The following stage is the structural change in the retina and xerosis (drying) of the conjunctiva, resulting in distortion and ulceration of the cornea, iris prolapse, and the loss of the lens. There is no treatment other than vitamin A, preferably taken orally for greater efficiency. These diseases can be cured only by adequate nutrition.

The link between vitamin D deficiency and rickets was also established a long time ago. As early as 1807 Bardley recommended cod liver oil as a source of vitamin D. It is an important factor in the gut's calcium absorption ability, bone mineralization, renal calcium reabsorption, and muscle strength. Parathyroid hormone (PTH) is effective in vitamin D related rickets. It has no impact on calcium absorption, but combines with vitamin D to act on bone and the kidneys. PTH induces responses very fast (in a matter of minutes), while vitamin D, which should be taken either as food or a supplement, takes hours.

Another important vitamin is vitamin K, important for synthesizing blood coagulation factors I, VII, IX, and X by acting on mRNA molecule synthesis. Vitamin E, too, has multiple impacts, with deficiency being expressed in the reproductive, muscular, nervous, and vascular systems in the form of reduced spermatogenesis and testes atrophy, foetus resorption, muscular dystrophy, and increased creatininuria.

Beriberi linked to vitamin B1 deficiency was described by Eijkman in 1890, while as early as 1884 Takaki demonstrated that dry milk and meat could cure beriberi in the Japanese navy. Again these diseases can be cured only by proper nutrition, not drugs.

Vitamin B12 therapy can cure megaloblastic anaemia. It requires an intrinsic factor secreted in the stomach, which disappears with aging and, sometimes, after surgery, when it must be administered parenterally, like a drug.

There was probably extensive knowledge of foods rich in vitamin C long before James Lind's study demonstrated the efficacy of lime

as an antidote to scurvy among British sailors in the mid-18th century. Interestingly, lime was considered neither a food nor a drug, but something in between that was administered under the supervision of the captain, not the cook or the surgeon. There is an yet undemonstrated theory that huge doses of vitamin C can prevent the common cold, but Coulehan has not been able to reproduce the result of his first study to that effect in 1974. The vitamin's small contribution to cold prevention was achieved through normal doses. Increasing them has not proved more efficient.

Pharmacological doses of biotin can be effective in rare hereditary disorders of the metabolism affecting propionyl CoA carboxylase and B-methylcrotonyl carboxylase. In fact, deficiencies in essential nutrients generate dysfunctions in specific pathways, systematically resulting in specific symptoms and diseases that can be cured and prevented only by adequate food intake providing the required nutrients. ■

Conclusion

Diseases are part and parcel of our lives. We survive because we are able to cope with most of them. There is no disease without a cause (pathogenic factor) and a reaction (innate or acquired) from the host: disease has a dual composition.

Some pathogenic factors may be exogenous or extrinsic (like infectious micro-organisms), some endogenous or intrinsic (*e.g.* the failure of Langerhans cells).

Some diseases, like infections, constitute a discontinuity in normal life with a clear-cut onset – the classic shivering in flu, for example. Others are dysfunctions, like renal clearance, where a continuum runs from normal physiological functioning to borderline and pathological conditions. Diseases may also be metabolic disorders due to inadequate nutrient intakes. It is important to bear in mind, however, that the boundaries between "normal", "borderline", and "disease" are often arbitrarily defined.

Management of a disease needs to incorporate:

- The cure of the cause of the disease – the pathogenic factor, whether infective or not. Drugs provide significant help in this respect. They can also act as a substitute for missing endogenous factors like insulin. Nutrition, for its part, is the only therapeutic solution to nutritionally induced disorders.

- The management of the host response: how immune and repair systems work. Nutrition helps prevent and manage diseases by ensuring that immune and repair systems function efficiently.

- The potentially acute and long-term harmful consequences of disease.

Foods should provide an adequate supply of nutrients in order for the body to function properly. Nutrient deficiencies induce specific disorders that can be cured only by restoring adequate levels of the deficient nutrient. The role of food is to provide nutrition and is a normal part of everyday life.

The purpose of drugs is to cure "abnormal" pathogenic factors and manage their harmful consequences. Human beings benefit from both – food on a daily basis, and drugs as infrequently as possible.

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Foods to treat and prevent Disease

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Abstract

Foods and diets are an essential part of the prevention and treatment of disease. This has been true historically, but is now more so with the development of functional foods designed specifically to modify physiological function and bring a benefit to health over and above that of providing energy and nutrients for growth and the maintenance of body function.

A question frequently asked by people visiting their doctor is whether they should change their diet. For many chronic diseases the answer is undoubtedly yes. Dietary advice is an essential part of the management of coronary heart disease and diabetes and international organisations such as FAO/WHO have agreed guidelines for diet and health that encompass not only cardiovascular disease but also obesity, cancer, diabetes and bone health.

Foods may also be used specifically to treat and prevent diseases such as some forms of acute diarrhoea and inflammatory bowel disease. Therapeutic diets are used routinely in hospitals for the management of renal and hepatic disease, whilst specific food intolerances call for carefully manufactured ingredients as in coeliac disease. Food can enhance function in healthy people leading to improved performance and strengthened immunity. A healthy diet is an essential part of a lifestyle approach to good health and a key strategy in the management of many diseases and the maintenance of optimal function.

Every large hospital has a department of dietetics. It is there because diet is an integral part of the management and prevention of many diseases. One of the most common questions patients ask their doctor, when given a diagnosis of diabetes, heart disease, high blood pressure, kidney failure, osteoporosis, peptic ulcer, or Crohn's disease, for example, is: "Do I need to change my diet?" Indeed, for the prevention of most of the chronic non-communicable diseases characteristic of industrial societies there are well-established, internationally recognised, dietary guidelines applicable at population or individual levels (WHO, 2003).

For some conditions, such as coeliac disease, diet is the only way of managing the condition, whilst for others, such as cardiovascular disease and diabetes, diet underpins a comprehensive approach to prevention and treatment that includes other aspects of lifestyle, prescription drugs, and surgery when needed. Of course, if you break a bone in an accident, develop an acute urinary, gut, or chest infection, or become severely depressed, diet is of little value until the acute episode is over and a programme of rehabilitation is undertaken. We should not, however, exclude diet from our thinking about any condition until we are sure of its cause.

The advent of "functional foods" (Diplock *et al.* 1999) has shown that specific foods can be used to prevent infection (MacFarland, 2006), improve function (Stellingwerff *et al.* 2007), and reduce risk factors for common diseases (Miettinen *et al.* 1995). A good diet, which comprises a selection of foods, is essential for health, while a bad diet can advance the onset and course of a disease. The lack of clarity and ongoing controversies in understanding this relationship is partly due to the sometimes arbitrary division we make between health and disease.

The Health and Disease Continuum

Pickering was probably the first formally to observe the continuum that exists in the many variables that characterise human physiology with his observations on blood pressure.

From his work in the general population he concluded that "there is no natural dividing line between those with high pressure and those without" (Hamilton *et al.* 1954) and that "the practice of making a sharp division between normal and pathologically high pressure is entirely arbitrary" (Pickering, 1955). Blood pressure is a risk factor for stroke and heart disease. With the development of drugs that can lower blood pressure it became necessary to decide at what level to intervene to reduce risk. This has been the subject of countless research studies with a blood pressure of around 135/85 (and under) being considered as carrying an acceptable risk. At a population level this is a reasonable approach, but for an individual the risk may be different, because of the many other factors that contribute to the occurrence of cardiovascular disease.

Other continuous variables are well known. They include the distribution of blood cholesterol levels of between 3.0 and 7.5 mmol/l in the general population (Stamler *et al.* 1986). Over this range and beyond there is a progressive increase in risk of coronary heart disease (Stamler *et al.* 1986; Jackson *et al.* 2005). Again, with the increasing availability of drugs that can lower cholesterol, there has come a call for risk to be quantified and for the designation of a cut-off point at which therapeutic intervention is recommended. Diet can also be used to modify blood cholesterol levels and, by implication, is part of a strategy to reduce risk of heart disease.

Less well known is the distribution of normal values for gastrointestinal functions such as bowel habit. Mean daily stool output has been shown to vary from 20 to 300 g/day in a healthy UK population (Cummings *et al.* 1992) and can be related to risk of bowel cancer when data from other countries are obtained. The risk is continuous, with no clear cut-off between low and high risk. However, because bowel habit in g/day is, unlike blood pressure, an impractical measurement in the population, there are no clear guidelines for "bowel health".

There are many other examples of the continuum that relates physiological functions to disease risk and diet to health risk. Examples include the relationship between body mass index (BMI) and mortality, bone mineral density and fracture, and alcohol intake and liver disease. ■

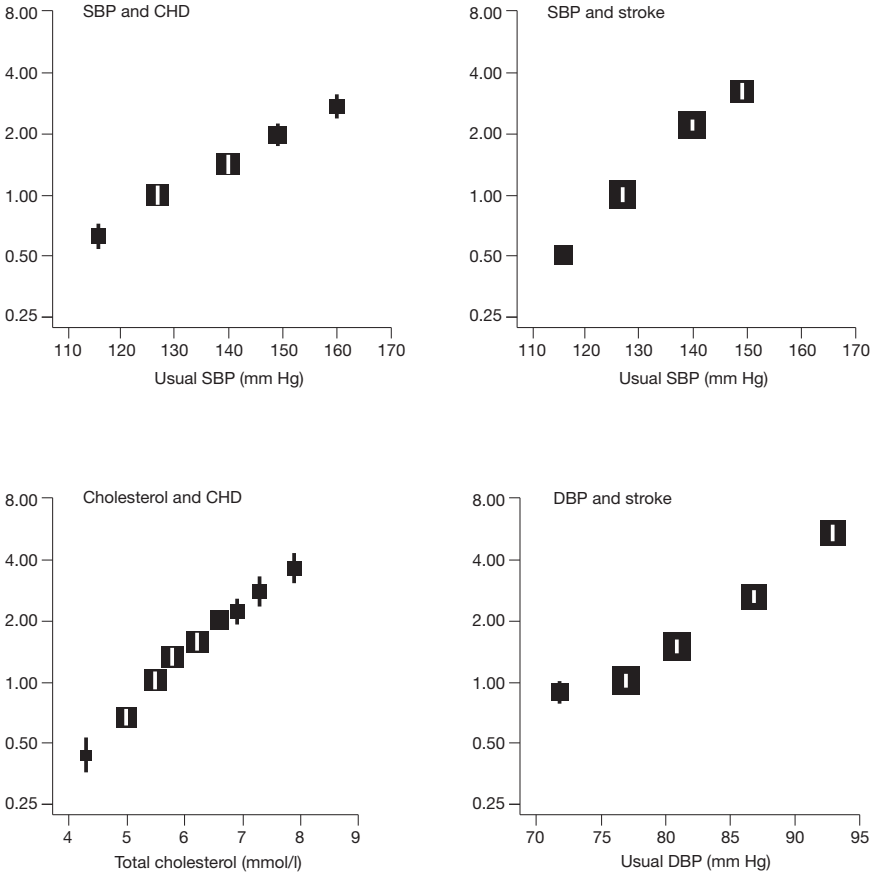

Figure 1.

Relative risk of coronary heart disease and stroke by blood pressure and cholesterol concentration (Jackson *et al.* 2005)

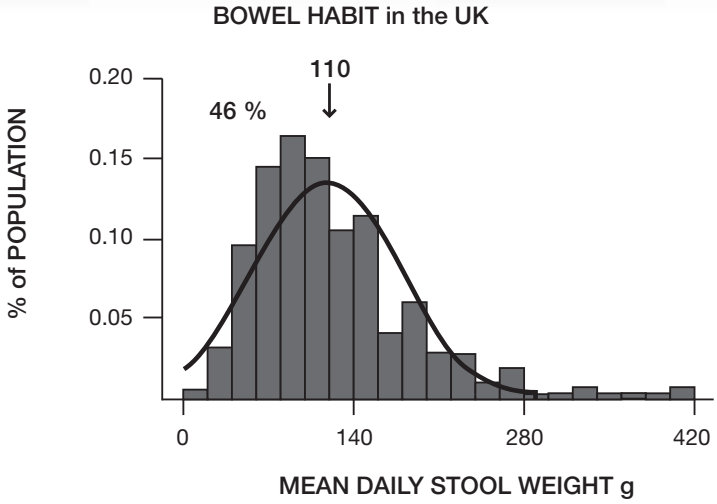

Figure 2.

Normal bowel habit – mean daily stool weight g/day – in a UK population (Cummings *et al.*1992)

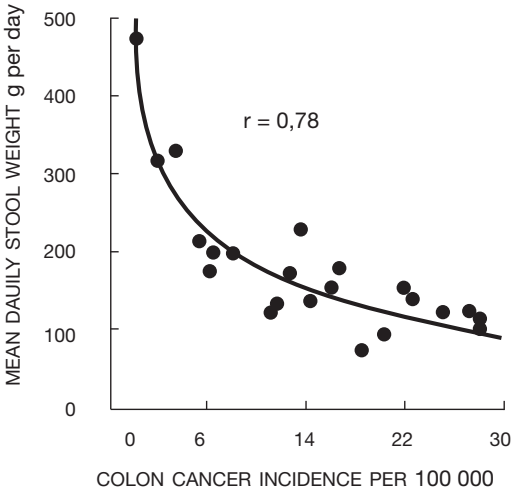

Figure 3.

Bowel habit and bowel cancer risk (Cummings *et al.* 1992)

Diet and Coronary Heart Disease

Coronary heart disease is the single most important cause of death in most industrialized societies and its prevalence is rising rapidly in populations in transition in developing countries.

Specific diets, foods, and nutrients are now well described in current textbooks as having a key role in both its prevention and treatment (Mann J., 2007; Geissler, 2005). In the 1950s Ancel Keys pioneered epidemiological studies showing clear increases in risks linked to blood cholesterol levels for diets that were high in saturated fat (Grande *et al.* 1965) and low in antioxidant vitamins and wholegrain foods. Risk is also been related to consumption of trans fatty acids, n-3 polyunsaturated fatty acids, alcohol, salt, coffee, and soya.

"The Mediterranean diet is a well known model of diet for primary and secondary prevention of major chronic diseases", stated a major medical journal recently (Sofi *et al.* 2008), adding that adherence to this diet "confers a significant protection for overall mortality, as well as cardiovascular disease". Specific nutrients, such as plant sterols found typically in soya, have been shown in multiple studies to reduce blood cholesterol and LDL-cholesterol (Miettinen *et al.* 1995). They are now incorporated into low fat spreads and dairy drinks with claims that they are "clinically proven to dramatically reduce cholesterol to help maintain a healthy heart". In the UK the Joint Health Claims Initiative (JHCI)[5] approved five generic health claims relating diet to cholesterol and heart health. The claims are still legally acceptable under UK law, although the new EC Health Claims Regulation (1924/2006) which is now binding in the UK will eventually supersede national bodies like JHCI.

Dietary modification is thus considered essential to the prevention of coronary heart disease in many countries, with some setting their own targets (*e.g.* US Department of Health and Human Services 2005), while the WHO draws up global targets (WHO, 2003).

Of course, other lifestyle changes are also needed, such as giving up smoking, taking more exercise, and maintaining normal weight. In many countries, however, smoking is now restricted to 25% of the population, so diet

[5] *www.jhci.org.uk*

assumes a far greater role in prevention. For high-risk individuals and secondary prevention effective drugs exist, *e.g.* statins that lower cholesterol and reduce the risk of heart disease. But a medical practitioner would be considered negligent if he or she were to prescribe them without dietary advice and an initial trial of dietary "therapy". The issue in diet and cardiovascular disease is not evidence, but persuading people that changing their diet and lifestyle is equally as important as relying on a handful of pills each day. The rapid rise in deaths from coronary heart disease in the 20th century has led to an equally rapid expansion in research in the field diet and disease prevention.

The observation that blood cholesterol was a major, measurable, risk factor and that dietary saturated fat contributed to its control was a turning point for our understanding of the role of diet in health, which now goes beyond the simple provision of nutrients for energy, growth, and the maintenance of function. Enquiry into this relationship has since spread into all aspects of health, and diet is now seen as a key lifestyle contributor to the cause, treatment and prevention of many diseases. ■

Approved claims

12/10/01	Generic health claim for reduced saturated fat and blood cholesterol
04/02/02	Generic health claim for wholegrain foods and heart health
27/07/02	Generic health claim for soya protein and blood cholesterol
06/05/04	Generic health claim for oats and blood cholesterol
11/02/05	Generic health claim for omega-3 PUFA and heart health

Table 1

Approved claims allowed on foods for prevention of heart disease as recommended by the UK Joint Health Claims Initiative (http://www.jhci.org.uk/)

Diet and Cancer

Whilst diet, quite correctly, cannot be considered useful in the treatment of cancer, it is thought to be fundamental to determining our risk of common cancers such as those of the colorectum, stomach, oesophagus, and prostate.

It may be a contributory factor to others. On its website the World Cancer Research Fund (WCRF)[5] lists ten "Expert Recommendations" for cancer prevention. The words "diet" or "food" appear in eight of them.

The WCRF's 2007 report, entitled *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective*, draws attention to convincing or probable evidence that the consumption of foods containing dietary fibre, garlic, milk and calcium lessen the risk of colorectal cancer. Similarly, non-starchy vegetables, fruit, and foods containing carotenoids decrease the risk of oropharyngeal cancer, while the same is true of food with vitamin C for oesophageal cancer, of non-starchy vegetables, fruit, and allium vegetables for gastric cancer, and of foods containing lycopene and selenium for prostate cancer. (Interestingly there are no well-established foods that reduce the risk of breast, ovarian, cervical, or endometrial cancer.)

The consumption of red and processed meat heightens the risk of colorectal cancer, while salty foods increase gastric cancer risk. The WCRF expects such evidence, at the convincing or probable level, to generate public health goals for cancer prevention. There is now a global consensus on the importance of diet in cancer prevention with WHO making specific recommendations like: "Have diet which includes at least 400g per day of total fruits and vegetables"; "Overall consumption of salt-preserved foods and salt should be moderate"; "Those who are not vegetarian are advised to moderate consumption of preserved meat."

The recognition of diet's role in cancer prevention is reflected in national guidelines. In 1998 the UK's Department of Health recommended that the population "increase intakes of a wide variety of fruits and vegetables… and non-starch polysaccharides (dietary fibre) from a variety of sources" and "consumption of red and processed meat should not rise".

A consensus thus exists on the importance of patterns of diet and of individual foods in both the prevention of and increase in the risk of various cancers. This, together with the evidence of coronary heart disease prevention, underlies the widespread acceptance by the general population that a good diet can be beneficial and allows national authorities to claim, in a very public way, that food and diet can prevent disease. ■

[5] *www.wcrf-uk.org/research_science/recommendations.lasso*

Diets and Foods that Treat Disease

Coeliac Disease

Coeliac disease is probably the best known and best documented condition for which diet is a treatment. It affects 1:100 of the population in most countries where data are available. Diet is not just *a* treatment. It is the *only* treatment. Effective in almost all cases where compliance is good, it "cures" – provided patients stick to the diet for life. The required diet is gluten-free, which in effect means avoiding foods containing wheat, barley, and rye. However, substantial advances in food technology over the years have allowed the production of essentially gluten-free foods containing wheat flour.

In the UK these foods are available in supermarkets, but can be prescribed by the patient's general practitioner and thus funded by the state. Those approved for use are listed in the *British National Formulary, Appendix 7 Borderline Substances* where, under "Foods which may be prescribed on FP10 or GP10 (Scotland)", the category "Gluten-sensitive enteropathies" lists 25 manufacturers whose products have been approved. In some cases (*e.g.* Juvela) a company may secure approval for as many as 27 different products. The foods are mostly breads, rolls, pasta, biscuits, and pastry, but include ingredients such as flour, cake mixes, and xanthan gum (*British National Formulary*, 2008). Thus the situation exists whereby a food can be prescribed by a doctor to treat a particular condition, which it will "cure". These foods do not have to undergo clinical trials to demonstrate their efficacy.

Not only are specific foods a treatment for coeliac disease, but the pathogenesis of the interaction between gluten and health has been clearly worked out. The pathology of coeliac disease is that of a T-cell mediated autoimmune disorder, triggered by specific proteins found in wheat, barley, and rye. Gut damage is confined principally to the duodenum and upper jejunum where there is complete loss of villi and hypertrophy of the mucosa with infiltration of the lamina propria by inflammatory cells. This results in the so-called "flat mucosa" characteristic of the condition. A key feature is migration of lymphocytes to the surface epithelium (McGough and Cummings, 2005).

Among the events leading to these pathological changes two factors are essential: genetic susceptibility and gluten in the diet. There is a strong genetic component to coeliac disease. Concordance in monozygotic twins is 75-90% and 10-20% in dizygotic twins. In first-degree relatives the prevalence is 10% and 2% in second-degree relatives. Almost all coeliac patients (95%) are HLA-DQ2 or DQ8 haplotypes on chromosome 7. Concordance amongst HLA-identical siblings is about 30%. Other candidate genes may also be involved (Fasano *et al.* 2003; van Heel *et al.* 2007).

Gluten is a water-soluble protein found in wheat and consists of an alcohol soluble fraction gliadin and an insoluble fraction glutenin. The gliadin fraction can be further subdivided into α, β, γ and Ω fractions, all of which are toxic in coeliac disease, although the α fraction is thought to be the most active. These alcohol-soluble proteins are known as "prolamins". In wheat they are called "gliadin", in barley "hordein", rye "secalin", and oats "avenin", although most coeliacs can tolerate oats. A 33-mer peptide, rich in proline and glutamin, has been isolated from gliadin and is thought to contain the toxic

sequence. After pancreatic enzymes digest wheat proteins, or barley and rye, this 33-mer peptide survives – possibly because of the high proline content – and resists digestion by the brush border, crossing the epithelial cell membrane and getting into the cytosol. This glutamine-rich peptide is then deamidated by transglutaminase enzymes. The deamidated epitope cross-links and has a high affinity to HLA-DQ2 molecule, which is then presented to CD4+ T-cells. These become activated, secrete inflammatory cytokines, and cause tissue damage. T-cell lines from CD patients also recognise peptide sequences from barley and rye, but not from oats. These changes start to occur within four to six hours of exposure to the toxic peptide (Shan *et al.* 2002; Mowat, 2003).

Coeliac disease is a common condition treated and prevented by diet and specific foods. Such an association of food with health and disease is widely accepted by the general public, while food intolerances or allergies are recognised internationally and legislation like the EC Labelling Directive[5] and Codex Alimentarius 2007[6] requires the labelling of foods containing common allergens.

Some might argue that a food from which something is omitted to ensure health does not represent a truly therapeutic approach, but variations in the composition of foods and diets, including omissions, are the essence of diets and foods for diabetes, coronary heart disease, renal disease, etc. Moreover, there are growing numbers of foods that are truly therapeutic and preventive, of which the best current example is probably the use of probiotic-containing foods to treat and prevent antibiotic-associated diarrhoea (AAD).

[5] *www.foodallergens.info/Legal/Labelling/Labelling.html*

[6] *www.codexalimentarius.net/web/index_en.jsp*

Probiotics and AAD

It would appear counterintuitive to give a patient a relatively small bacterial culture of known organisms when he or she starts a course of antibiotics and to expect a benefit to health. In fact, probiotic bacteria have been used in the treatment of diarrhoea for at least 50 years (Winkelstein, 1955), with the idea of taking lactobacilli in the diet to ensure gut health being credited to Metchnikov (Metchnikov, 1908). Figure 4 (below), taken from McFarland's 2006 systematic review, is a forest plot of the results of 25 "randomised, controlled, blinded efficacy trials in humans published in peer-reviewed journals". It shows a highly significant reduction in the risk of AAD when probiotics are used. Although the hospitalised elderly, for whom AAD can be a killer disease, are the population principally at risk, the review included nine studies in children.

What does this systematic review tell us? That many different probiotics were used in the studies and no single species was clearly the recommended choice. McFarland mentions *Saccharomyces boulardii, Lactobacillus rhamnosus GG*, and probiotic mixtures as showing the most promise, due probably to the fact that they are the probiotics most frequently used in clinical trials to date.

Whether strain specificity exists for the therapeutic benefits of probiotics remains to be seen, although it is highly likely that when the – as yet undetermined – mechanisms are identified, specific strains will be targeted at the effector system. The problem in establishing strain specificity is that few comparative studies are reported in the literature. Similarly, dose response studies are rare (see "Acute Infectious Diarrhoea" below), although McFarland does note that a dose of at least 10^{10}/day is needed for efficacy.

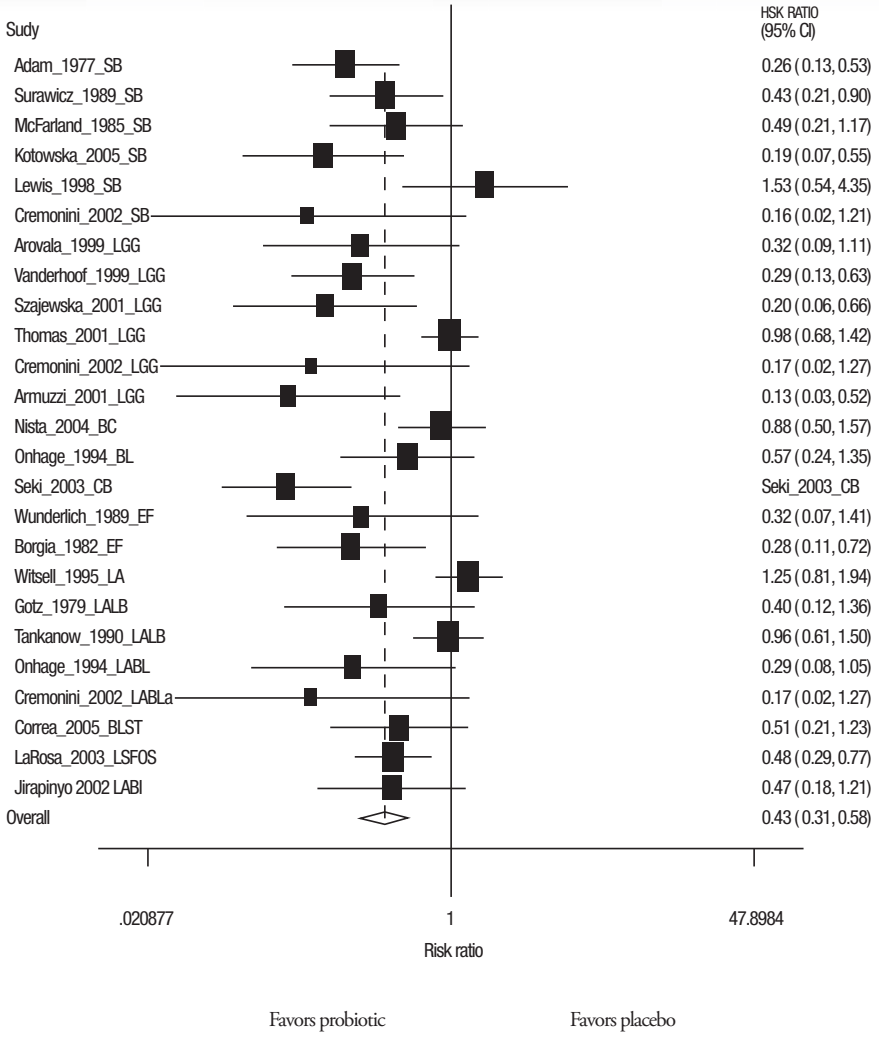

Figure 4

Forest plot of 25 randomized, controlled trials of probiotics for the prevention of antibiotic-associated diarrhoea showing crude and pooled risk ratios (SB = Saccharomyces boulardii; LGG = Lactobacillus rhamnosus GG; BC = Bacillus clausii; BL = Bifidobacterium longum; CB = Clostridium butyricum MIYAIRI; EF = Enterococcus faecium SF68; LA = Lactobacillus acidophilus; LALB = Lactinex = L. acidophilus and L. bulgaricus; LABL = Lactobacillus acidophilus and Bifidobacterium longum; LABLa = Lactobacillus acidophilus and Bifidobacterium lactis; BLST = Bifidobacterium lactis and Streptococcus thermophilus; LSFOS = Lactobacillus sporogenes and fructo-oligosaccharide; LABI = Lactobacillus acidophilus and Bifidobacterium infantis.) Mac farland, 2006.

One aspect of AAD that compels us to take this problem seriously is the occurrence of *Clostrium difficile* in elderly hospitalised patients. It is identified in 10-20% of cases of AAD and is associated with the severest form of the disease and significant mortality (Bartlett, 2002). Case reporting of C *difficile* infection is now mandatory in the UK. In 2007 UK National Statistics[5] reported a rise to almost 60,000 cases a year in England and Wales (population 52 million), with deaths increasing exponentially to over 8,000 – a rise of 30%. Systematic reviews of the data relating C *difficile* infection and probiotics suggest there maybe a significant benefit (McFarland, 2006), although better-designed and larger studies are needed (Dendukuri *et al.* 2005). However, a recent randomised, double-blind, placebo-controlled study in 135 patients aged 74 on average, who had been prescribed antibiotics and were asked to consume either a placebo or a probiotic drink sold in supermarkets, showed complete elimination of C *difficile* in stools (Hickson *et al.* 2007). AAD was reduced from 34% in the placebo group to 12% in the probiotic drink group and C *difficile* toxin positive stools fell from 17% to zero. While no study has been perfect, it is remarkable that a food available in the supermarket can possibly eliminate the risk of C *difficile* infection and its consequences. If there were a drug so effective, it would be widely prescribed. Yet probiotic drinks are currently used prophylactically in only a handful of UK hospitals. In the Vale of Leven hospital in Scotland in 2008 there was an outbreak of C *difficile* associated diarrhoea affecting 55 people of whom 18 died. In devising strategy to reduce this problem in the future the Scottish Executive report does not mention probiotics.

[5] *www.statistics.gov.uk/hub/*

Probiotics and Acute Infectious Diarrhoea

Acute infectious diarrhoea is a common illness in both adults and young children and is a major killer of infants in developing countries. Because probiotics are safe and easy to use, there have been many studies into their benefits for this condition. In a recent Cochrane review Allen and colleagues (Allen *et al.* 2008) convincingly showed from 23 good, randomised, controlled trials – the majority of which involved children – that probiotics benefit acute infectious diarrhoea in both adults and children. The relative risk of diarrhoea lasting more than three days was reduced to 0.66 (confidence intervals 0.55, 0.77) and of lasting more than four days to 0.31 (0.19, 0.50). The mean duration of diarrhoea was reduced by 30.5 hours (-42.5, -18.5) and by Day 2 stool frequency was down by 1.51 stools per day (-1.85, -1.17). Earlier systematic reviews yielded similar findings (Sazawal *et al.* 2006; Van Niel et al. 2002; Szajewska *et al.* 2001).

So which, then, is the ideal probiotic for management of acute diarrhoea? A wide variety of bacterial species and yeasts were used in the trials cited above. They are predominantly from the genera Lactobacilli, Bifidobacteria, Enterococci, and Saccharomyces, which, together with varying treatment regimes and criteria for end-points, means that no clear winner emerges. *Lactobacillus rhamnosus GG* gets frequent mention, but again mainly because it is often selected for trials.

Trials in which probiotics are compared are seldom reported. When they are, the results are important. Canini and colleagues (Canini *et al.* 2007) used five probiotic regimes in a randomised, controlled trial of 571 children who went to their family doctor with acute diarrhoea. Children who had had antibiotics were excluded. The control was an oral rehydration solution (ORS). The duration of diarrhoea was 115 hours with the ORS and significantly shorter

with *Lactobacillus casei subsp. rhamnosus GG* at 78.5 hours. Also significantly better than ORS was a mixture of species, which included *delbrueckii var. bulgaricus, L acidophilus, Streptococcus thermophilus, and B bifidum* (70 hours). Not effective were *Saccharomyces boulardii, Bacillus clausii*, and *Enterococcus faecium*. This is clearly not the final word on the subject, as each population of patients studied will have different racial, environmental, cultural, and demographic characteristics that may affect the outcome. More comparative studies are needed.

What might be more important than species, however, is the "dose" or number of probiotic bacteria given to the patient to achieve an effect. In her review of AAD, McFarland (2006) notes that "use of a high dose (>10^{10}/day) of probiotic was associated with a significant efficacy for AAD". The question of dose is addressed by Van Niel (2002) in his meta-analysis of randomised, controlled trials of *Lactobacillus sp.* for acute infectious diarrhoea in children. Taken from his paper, Figure 5 below shows a clear dose response across eight included studies for the reduction of the duration of diarrhoea with, again, amounts in excess of 10^{10}/48 hours being crucial. No pattern of dosing or duration emerges from any of these studies.

Other Uses of Probiotics

Probiotics have been tried in many other clinical situations for both the prevention and treatment of disease. These include necrotising enterocolitis, ulcerative colitis, Crohn's disease, pouchitis, irritable bowel syndrome, non-alcoholic fatty liver disease, constipation, pancreatitis, eczema, childhood atopy, cancer prevention and genito-urinary infection. Some clinical situations have been crowned with considerable success (Sandborn *et al.* 2008), some have revealed intriguing opportunities (Nanno, 2008), and others have shown no benefit (Boyle *et al.* 2008).

More importantly, probiotic-containing foods are seen as functional foods and are promoted as helping to improve health in the general population. There are reports that probiotics have been of benefit to the training regime of elite athletes (Cox *et al.* 2007), in enhancing immunity in the elderly (Samson *et al.* 2008), and improving intestinal transit (Marteau *et al.* 2002). ■

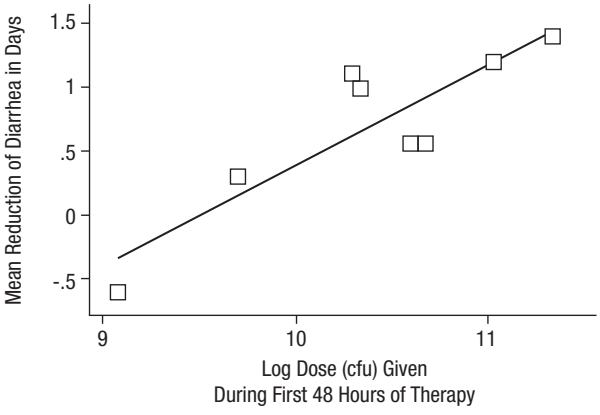

Figure 5

Dose-effect relationship between Lactobacillus doses and reduction in diarrhoea duration in eight included studies that reported diarrhoea as an outcome. CFU, colony-forming units. From Van Niel et al. 2002

Modifying Physiological Function

Prebiotics

These sugar-like carbohydrates, which are mostly oligosaccharides with non-alpha glycosidic bonds, have occurred naturally in our diets for millennia. They have risen to prominence only in the past few years, however, specifically because they are thought to have benefits to health beyond simply providing the body with energy. The recent report from the Food Quality and Standards Service of the FAO defined prebiotics as "a non-viable food component that confers a health benefit on the host associated with modulation of the microbiota". This is a considerably wider definition than the original one (Gibson *et al.* 2004), which has traditionally included only non-digestible carbohydrates, but was agreed by the Technical Group in order "to encompass new prebiotics, and to more accurately reflect current understanding of the microbial ecology of the human microbiota." Definitions aside, however, prebiotic carbohydrates such as inulin, fructo-oligosaccharides, transgalacto-oligosaccharides and lactulose, have been shown, when taken in the diet in relatively small amounts (5-20 grams/day) to stimulate the growth of health-promoting species belonging to the genera Bifidobacterium and Lactobacillus, not ordinarily the most numerous organisms in the gut, except in breastfed babies (Gibson *et al.* 2004). This change in the microbiota was initially observed by Japanese researchers and reported in the first issue of a new journal, *Bifidobacteria and Microflora* in March 1982.

Changing the gut microflora in this way must count as "correcting or modifying physiological functions", which defines a medicinal product in the European Community (Directive 2001/83/EC). Whilst Community legislation specifically excludes products that come under the definition of food – Amended Proposal (COM(2003)163) – prebiotics nevertheless provide a good example of a food ingredient that is added with the specific purpose of changing the composition of gut microflora in order to benefit health. Prebiotics also affect calcium absorption (Macfarlane *et al.* 2006) and an increase in bone mineral density has been shown in one human study (Abrams *et al.* 2005). These carbohydrates could one day be used as part of a diet to prevent osteoporosis.

Although it is still too early to ascribe clear health benefits to prebiotics (Macfarlane *et al.* 2006; 2008), much current research into prebiotics is aimed at demonstrating health benefits from modified physiological function. Such changes to gut microflora are unlikely to be achievable with drugs, such as antibiotics – which gives us food providing a unique benefit to health beyond drugs. ■

The Therapeutic Spectrum of Diet

There are many other examples of the use of diet in therapeutics. Table 2 below lists conditions where it is accepted that diet plays a part in either their prevention or treatment.

In addition to such well-established therapeutic uses, diets and foods can also be used to treat protein-energy malnutrition (marasmus and kwashiorkor), inherited metabolic disorders, *e.g.* amino acid disorders (phenylketonuria, Maple Syrup urine disease, homocystinuria), glycogen storage disease, galactosaemia, Refsum disease and adrenoleukodystrophy. Diet is also valuable for pre-term infants, the prevention of dental caries and for specialised conditions such as post-gastrectomy syndromes and cystic fibrosis. There are also diet-drug interactions. All of these reinforce the important links between diet and health. ■

Table 2 ➜

Conditions which diet can help prevent or treat

Disease	Diet, Foods, and Nutrients for Prevention or Treatment
• Trace element deficiencies.	• Mainly iron, iodine and occasionally zinc.
• Vitamin deficiencies (A – blindness. D – osteomalacia. K – newborn; C – scurvy. Folic acid – neural tube defects. Thiamine – beri-beri and alcohol-related disorders.)	• Vitamin supplements of A, D, K, C, thiamine and folic acid.
• Obesity.	• Low energy.
• Food intolerance and allergy (common allergens such as wheat, dairy, fish, eggs, tree and ground nuts, crustaceans and molluscs, mustard, celery, sulphite, sesame, soya, and lupin).	• Avoidance of specific foods.
• Immune system disorders – *e.g.* coeliac disease, HIV/AIDS.	• Avoid wheat, barley and rye. • Maintain "good" diet, supplements, artificial feeding.
• Diabetes.	• Avoid obesity. • Fat no more than 35% energy. Wholegrain foods, fruit and vegetables. • Low glycaemic index foods.
• Bone disease – mainly osteoporosis.	• Dairy foods and calcium/Vitamin D supplements.
• Renal disease – principally impaired renal function.	• Can be complex requirements. Control of protein, fluid and electrolytes.
• Cardiovascular disease: - coronary heart disease - hypertension and stroke.	• Lower cholesterol by reducing saturated fat and increasing omega-6 PUFA. • Increase omega-3 PUFA. Wholegrain cereals and NSP. • Low sodium and low alcohol.
• Gastrointestinal Diseases: - Acute diarrhoea - Crohn's disease - Constipation - Diverticular disease - Irritable bowel syndrome.	• Oral rehydration solutions Probiotics. • Maintenance of weight. • Supplements. • High fibre. • High fibre. • Diets to reduce gas formation sometimes useful. Probiotics.
• Dietary recommendations for health: - national and international guidelines, *e.g.* WHO, 2003.	• Fat 15-30% of energy. • Saturated fat <10% energy. • Carbohydrate 55-75% energy. • Sugars <10% energy. • Protein 10-15% energy. • Salt <5g/day. • Fruit and vegetables (5 a day) 400g/day. • Fibre/NSP 20g/day.

Conclusion

Foods and diets are an essential part of the treatment and prevention of disease. This has been true historically, but is now even more so with the development of functional foods designed specifically to modify physiological function and provide health benefits as well as energy and nutrients for growth and the maintenance of body function. Food can do things that drugs cannot. It can supplement their actions and reduce the need for them.

Food is part of any lifestyle approach to health that also includes physical exercise, not smoking, moderate alcohol intake, and lower stress. Foods and diets can both contribute to and prevent diseases and are, quite correctly, an important part of the public health policy of almost all countries in the world.

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The Foods of Longevity

Food and Drugs from a Comparative Perspective, with Special Reference to China

by Professor
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Abstract

Anthropological exploration of the relationship between foods and the human quest for longer life reveal that most, if not all ancient civilisations, believed in substances that bestowed long life and even immortality. These were foods of the gods. Such near-universal practices and representations underwent, however, deep paradigmatic shifts as societies evolved. What Jaspers terms the "Axial Age" saw the gift of immortality evolve away from the gods to humans and the awakening of the notion of "individuality", summarised as: "My fate depends on myself, not on the will of Heaven".

The shift was particularly pronounced in East Asia, notably in China, where the Taoist cults of the 4th and 3rd centuries BCE came to believe that individuals may empower themselves to improve their lives and enhance the possibilities of healthy longevity and even physical immortality. Just as the great goddess, Xiwangmu, feasted on her own sacred peaches, so the Taoists lived on fruit, nuts, vegetables, water, and herbal teas. The shift from meat and alcoholic beverages to the "natural" diets of the initiates of Late Antiquity and beyond was of tremendous significance. It marked the beginning of an evolution in human diets that has lasted to the present day.

Concomitantly to the great dietary shift, herbal medicine developed as a distinct therapeutic technique. Chinese scholars of the 2nd century BCE codified medicinal herbs (yao) in medical manuals. The herbs were used not only for healing specific diseases, but to lengthen life as part of the quest for bodily immortality. They, too, became part of the long life, natural diet.

In the development of modern Western cultural phenomena like the search for such alternative foodways as health foods and longevity-enhancing nutrition, the influence of Chinese and other Asian dietary and medical practices may be greater than is generally realised.

On the Etymology of Food and Drugs

Marcel Mauss coined the term "habitus" in order to characterize the many ways bodily techniques, styles and skills belong to a given culture and the ways in which they do so.

Habitus is prominently present in what we now call "foodways". Our present-day nutritional customs – our likes and dislikes, the foodstuffs we select on most occasions, table manners, and so on – perpetuate ways and techniques that may have been acquired in a very remote past. Social scientists of our times, such as Pierre Bourdieu, Norbert Elias, Claude Lévi-Strauss, Pierre Vernant, Marcel Detienne, and Charles Malamoud, have shown that what and how ancient peoples ate was much determined by their cultural systems – their habitus – and how these same systems remain pertinent in the ways we think about food today.

This point is borne out by the etymology of words for food still in use in French and English. The French words, *nourriture* and *nourrir* originate from the Latin verb *nutrire*, meaning to "nurse with milk", while the English "nursing" and "nurture" remain close to the original meaning of "breastfeeding", rendered in French by *allaiter*.

If we consider China and the East Asian cultures it has influenced etymological research is complicated. For the Chinese world the notions of the sacred nature of food as an offering is essential. According to this idea, "feeding" in China is associated not so much with bestowing food on offspring, as evidenced in the French *nourrir* or the English "nurture", but with an offering to higher beings, like elders, ancestors, or deities. In other words, food in Western thought is seen as a *gift* (from god, kings, parents, etc.), whereas Chinese culture considers it rather as an *offering* – to the gods and ancestors, to one's parents, to one's own body. We will see that this fundamental difference may perhaps account for the evolution of food culture in China.

The now hybrid word "drug" is a poor scientific concept and its imprecision makes it difficult to use in legislation and regulations. French is better off with *médicament* and *médication*, words that clearly denote substances used in therapy.

The word for medication in Chinese is yao, "vegetal substances that can heal diseases" – in other words, medicinal herbs, a notion often enlarged to include healing substances of animal or mineral origin. As to the healing function in general, it is conceived as comprising not only medication (yao) but food, too. This inclusive notion reflects an important cultural characteristic: the sacred nature of food, which mirrors the sacred – and immortal – nature of the human body. The Chinese view of the human body as sacred is strikingly different from traditional Western thinking, which considers that the body is by essence mortal and the source of the corruption of the immortal soul and the repository of mankind's iniquities. At root lies the duality of spirit and matter, of body and soul.

We shall now try to follow this lead by looking at a special and, to the best of our knowledge, little studied aspect of human food culture. It relates to the idea that there are nutritional substances and food rituals which can contribute to lengthening our lives and even to making us immortal. ■

The Sacrificial Feast and Immortality

Myths and beliefs about special substances believed to bring long life are found in all ancient civilizations.The myths of the Bororo and Tukuna people of Brasilia studied by Claude Lévi-Strauss speak of immortal gods who seek, in the guise of different animals, to marry female humans. They possess a special kind of alcoholic beverage that makes them immortal.

Closer to us, but in fact very similar, are ambrosia and nectar. Both words, which actually mean "not to die", denote substances that conferred the immortality of the gods on humans in ancient Greece and Rome. Similarly, the Vedic rituals in ancient India, were centred on the offering of *soma*, a drink obtained from pressing certain plants and considered to be a divine agent conferring power and immortality on the gods. Exactly what *soma* was remains an open question, but there is a general theory that it must have had hallucinogenic properties. Its oblation – and, possibly, its consumption by priests – provided a kind of communion between humans and gods. Consciousness-altering alcoholic beverages (wine, beer, jiu, sake, etc.) were also often seen as gateways to transcendence. In classical China, the oblation of *jiu* (fermented sorghum or rice) is the foundation of all ritual, both religious and secular, while wine fests have been known since Antiquity as "banquets of happiness and long life".

Although wine and conscience-altering substances are still popular and part of the contemporary scene, we do not think of them as being able to confer longevity. The opposite, rather. Yet the idea of food as a way of enhancing longevity is by no means absent from today's nutritional thinking, which considers that health foods and macrobiotic diets have virtues that may lengthen human life[7]. In the late 20th and early 21st centuries this search for long life has expanded to so-called nutritional supplements and to diets that claim to be able to make us live much longer than before, and even to make us almost immortal.

The present paper focuses on the foundations of the present-day individual search for food that brings longevity. It is necessary, first, however, to say a few words about the food lore which, from a socio-historical point of view, preceded it.

The importance of the sacrificial banquet, and the way in which the special kind of collective feasting it involved has shaped human foodways to the present day, can hardly be overestimated. Festive celebrations with high protein intakes were held to mark the taking of large animals by hunting parties. But real abundance came with animal husbandry, which made supplies of animals available at any given moment.

Fundamental cultural dichotomies like "cooked" versus "raw" (*le cru et le cuit*) studied by Lévi-Strauss are derived from the value system established by the great sacrificial

[7] *The founder of the "macrobiotic" diet is Georges Ohsawa (1893-1966). This diet rests on the belief that food and food quality are vital to health, well-being, and happiness. Food should "nature food" and therefore not or hardly be processed. Ohsawa was strongly influenced by Chinese and Japanese foodways. His "philosophy" was based on the Chinese yin-yang and Five Elements theories that we present here.*

feasts of prehistoric and preliterate societies. Many other customs also derive therefrom: wine-drinking protocols like the mutual toasting still prevalent in Scandinavia and China come to mind. Less immediately evident are important changes in foodways like the habit of eating boiled or steamed polished white rice, nowadays consumed throughout the Far East. It certainly derives from the fact that pure white rice, together with white sacrificial animals, were prescribed offerings in solemn sacrifices in ancient China. Eating white rice thus became a sign of social standing and piety. Confucius would not eat any other kind.

Big roasts, ceremonial wine drinking, specially prepared food, and the intricate protocols of seating at festive dinners all originate in the sacrificial banquet. So, too, does the universal custom of holding large dinner parties on important occasions such as marriages, birthdays, and funerals. Even neighbourhood barbecue parties ultimately derive from the sacrificial feast.

The belief system related to food offerings and festive banquets is duly documented in texts produced by ancient societies that have since become the sacred books of the great world civilizations. They include the *Pentateuch* (the five books of Moses"), the four holy *Vedas*, the *Five Classics* of ancient China and many others. They invariably show that human beings were defined as primarily belonging to agnatic ancestral lineages and tribes that had the sacred obligation of perpetuating the practice of sacrifice to their ancestors and gods. The framework of the family, group, or tribe to which people belonged defined their position in life. **Each person was considered to be part of a whole**, a "dividual" as opposed to "individual", a notion that would appear in later times.

Belonging to a lineage or agnatic tribe implied the transmission of a kind of inherited – we would say "genetic" – legacy. Each person lived by the grace of a vital essence or transmitted energy inherited from his, or her, forebears. This essence was what differentiated one group from another and, within a group, one person from another. In this way ancestors would continue to live in their offspring and the creator god would thus exist forever through his creations. By feeding the gods and ancestors through sacrifices a given group also ensured its own survival. **As long as oblation kept the gods and ancestors alive, the tribe or lineage remained alive too.** The sacrificial feast nourished all: gods, ancestors, and living people. In other words, the divine banquet ensured the **collective immortality** of the entire tribe and its lineage or sibs.

These ideas remain latent in the foodways of today, if not materially, at least symbolically. Over time, the rules for performing ritual sacrifice became the dietary laws that delineate fundamental differences between so many religious groupings even today. Jews and Muslims do not eat pork, whereas traditional Chinese ritual laws forbade beef and considered only pork as truly pure. Such rules persist, although Jews no longer perform their great sacrifices in the temple that once stood in Jerusalem, Islam has moved the practice of animal sacrifice to the domestic sphere, and China's religious tradition was severely repressed during most of the 20th century.

On a more general level, the whole construct of oblation and immortality as discussed above has informed the ritual of many of the liturgies of the world's religions, in particular the Christian Holy Communion. In the Byzantine church, the Lord's Supper (bread and wine symbolising Christ's body and blood) was considered to bestow immortality and has kept this function ever since in Roman Catholic liturgy. The Sacrifice of the Mass (or Eucharist) is indeed a metaphor for the sacrifice by the Church, as a community of the faithful, to the Covenant and for **the eternal life, or salvation, of the individual**. ■

The Paradigm Shift

The shift from the collective, composed of dividuals, to the individual appears with crucial changes that began in what the philosopher Karl Jaspers (1883-1969) called the "Axial Age", a period during the second half of the first millennium BCE, during which many new ways of thought emerged in the Mediterranean world, the Near East, India and China. They were Platonism, Buddhism, Zoroastrianism, Taoism, and, finally, Christianity.

A common characteristic of these great persuasions is that they emerged from what is generally called "mystery cults". They introduced the notion of the individual and his or her personal experience and conscience as the very foundation of the human being, something we now take for granted. Yet the belief in individual salvation marked an important departure from ancient sacrificial religions in that it took the gods' and ancestors' gift of immortality and bestowed it on ordinary humans.

In the Mediterranean world the advent of the individual went through many phases before giving rise to a new faith that transformed ancient sacrificial rituals into an institutionalized liturgy entirely composed of metaphorical and symbolic acts. In doing so, the Christian liturgy resolutely placed itself in the continuity of the ritual Law of Moses. In other instances, notably Buddhism in India and Taoism in China, the same social and intellectual evolution towards individual salvation resulted **in a far more radical departure from ancient sacrificial religions.**

Although far less well known or studied, this "axial" change in the Far East greatly transformed foodways in that part of the world, with Buddhism and Taoism extremely influential.

In more general terms, the evolution outlined above shows that, although the search for long life is universal, ideas about how to obtain it have considerably changed. It is not merely about replacing meat, wine, or peyote with bean sprouts, green tea, or incense sticks, but something far more fundamental – a new approach to human life in general.

The Axial Age Paradigm Shift in China

The teachings of the Buddha proscribed the killing of any living being, thereby rendering the practice of ancient Vedic sacrifice impossible. It promised eternity to its adepts through the renunciation of worldly things and the extinction of all desire. The complete break with the ancient sacrificial religion of India is manifest, although, to this author's knowledge, the issue is nowhere directly addressed in Buddhist scriptures.

This is not so in China. The earliest maieutic writings of Taoism explicitly criticize and deride the animal sacrifices that were central to the most solemn and holy ceremonies of the Chinese state. They also scoffed at the gods, ancestors, and the ancient founders of the royal dynasties and their sage councillors, describing them as inept bunglers and dubious characters. In their place the early Taoists honoured "divine human beings" who lived free and happy in the unspoiled natural surroundings of the great holy mountain ranges:

"In the far-away mountain of Gushe live divine human beings. Their skin is as white as frost or snow; they are as shy as virgins. They do not eat cereals; they inhale the wind and drink the dew. They ride on clouds that are drawn by flying dragons; so they go roaming beyond the limits of the world. Through the concentration of their spirit they can put an end to the plague and ripen harvests."[7]

The divine beings introduced here would later receive the Chinese name, *xianren*. Initially, the term literally meant "someone capable of moving through the air", although it is now generally translated as "transcendent immortal" or simply "immortal". These translations imply that the *xianren* have overcome death thanks to their diet characterized by abstention from cereals and other starchy foods. Their "inhaling the wind" refers to breathing exercises, also an early technique in the search for health and longevity. Furthermore, they had the power to free the world from fearful epidemics and, in response to prayers, to safeguard harvests.

In the process of discovery of the individual that marked the Axial Change, the Chinese were exceptional in that they did away not only with ancient sacrificial religion, but with the duality that it implied, *i.e.* that people died, but the tribal *manna*, the spirit of the ancestors, lived on forever, or for at least as long as sacrifices were offered. Not only was the notion of sacrifice eschewed, so too was the unavoidability of death. **Whereas most of the civilized world continued to adhere to the food habits inherited from the sacrificial religions of the New Stone and Bronze Ages, China rejected them and developed a new nutritional habitus.** Central to this paradigm shift was the concept of the immortality of the individual, whereby **each human being was personally responsible for his or her health.**

The Chinese departure from the sacrificial religion had, as we shall see, a profound influence on the Chinese food system. It also spawned the development of a new religious system to which the individual and the search for immortality were central. We call this system "Taoism". Yet ancient rituals in honour of the ancestors did not disappear altogether. They continued to play an important role in social spheres where family and kinship were of paramount importance – *e.g.* in royal and, later, imperial institutions – and in the extended family organizations that would emerge later in history. This traditional ancestor worship and the moral doctrine that grew out of it are known as "Confucianism". ■

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[7] *From The Complete Works of Chuang Tzu (late 4th and early 3rd century BCE) translated by the author of this essay.*

The Immortals

During the 2nd century BCE mentions of the *xianren* become more and more numerous. These immortals formed an entirely new pantheon that now completely replaced the ancestors and gods who had been worshipped in China until then.

They did not belong to a lineage, nor were they founders of dynasties or divine kings. They had metaphorical names, like Xiwangmu, the Sovereign Mother of the West. She did not reside in the human world, but had her abode on great Mount Kunlun outside China. There she lived among the Immortals, with whom she would periodically celebrate the great Banquet of Immortality. Typically, this goddess and her court of transcendent beings did not feast on meat and wine, but only on delicious peaches that grew in her orchard.

While peaches were the hallmark of the Sovereign Mother of the West, many other immortals had their special diet, too. For instance, Chisongzi (Master Red Pine), was, according to a well-known legend, a shepherd boy who once lost his way in the mountains and learned how to sustain himself on pine nuts. These rendered him immortal.

Other immortals ate exclusive diets of asparagus, Angelica root, mushrooms of the ganoderma species, citrus fruits, pears, and so on. They could survive indefinitely in any natural environment, whereas the "civilized" world was highly detrimental. Also remarkable was that, while in earlier times the sacrificial fest culture encouraged people to eat as much as possible, the ideal was now to "eat like birds", *i.e.* as little as possible.

This belief in the life-giving properties of Nature as opposed to the degradation of civilisation was the subject of many ancient legends. The most famous is perhaps "the White-Haired Woman". Still popular today, it has even been reworked to fit contemporary Chinese ideology. The story is about a woman who, during a time of war and upheaval, fled her home and found herself in a vast forest on an uninhabited mountain. She learned from the animals how to sustain herself by eating all kinds of herbs and fruits. Instead of dying, she steadily become healthier and more agile, able to swing through the forest like apes and monkeys. She discarded her clothes, for white fur now covered her body (hence her name), and she remained full of vitality. Several centuries later hunters captured her and brought her back to civilization, where she was fed meat and cereal. As a result, her fur dropped out, her skin grew old and wrinkled, her teeth decayed, and she soon died.

The proscription of cereals – in fact of all starch-bearing crops, including tubers – appeared very early, before later Taoist dietetic precepts extensively elaborated upon it. According to Taoist belief, crops and other staple foodstuffs nourish and strengthen the Three Worms, the negative energies in our bodies that are the very agents of decay and death. They dwell in the lower digestive system, which they make into a cesspool that poisons the entire body. ■

Yin, Yang and the Five Elements

The point of departure of the Taoist system is "the self". The self is the limitless human body.

It encompasses the entire universe and all of creation – the sun, the moon, the stars, mountains, seas, lands and all their inhabitants. Gods and demons also reside in the self.

This mystical thought grew out of ascetic meditation practices that concentrated on the body and the energies of its constituent parts, divided into a dual system of light and darkness. While the lower part of the trunk (kidneys, bladder, gut and sexual organs) was a dark aquatic region, the heart had the opposite qualities of light and fire. It radiated a bright energy, termed the "sunny side", or *yang*, while the dark force from the lower belly was called the "shadowy side", *yin*. These two opposite yet complementary categories would become the guiding principles of Chinese cosmology in general.

The dual system was further extended to the other main viscera of the body: the lungs were identified with the early growing stage of *yin* energies that culminated in the kidney, and the liver with the budding stage of *yang* energy that culminated in the heart. In the centre was the spleen (and with it the stomach), which represented the neutral ground through which the other four energies might transit.

Each energy stage was assimilated to an element: greater yang with fire; greater *yin* with its opposite, water; rising *yang* with wood; rising *yin* with metal. The intermediate stage, which enable the transition of the four elemental forces, was the central element, earth. The five elements were identified with the five planets that early Chinese astronomy had identified.

In this way the five stages, or elements, (*wuxing*) of the transformation of cosmic energy (*qi*) became identified with the five viscera: the heart (greater *yang*), the liver (rising *yang*), kidneys (greater *yin*), the lungs (rising *yin*), and spleen (neutral). The table below sets out the fundamental components of the *wuxing* correlative classification system:

Elements	Metal	Wood	Water	Fire	Earth
Stages	Rising *yin*	Rising yang	Greater *yin*	Greater *yang*	Neutral
Planets	Venus	Jupiter	Mercury	Mars	Saturn
Seasons	Autumn	Spring	Winter	Summer	Last month of each season
Directions	West	East	North	South	Centre
Organs	Lungs	Liver	Kidneys	Heart	Spleen
Bowels	Large intestine	Gall bladder	Bladder	Small intestine	Stomach
Sense organs	Nose	Eyes	Ears	Tongue	Mouth
Flavours	Acrid	Sour	Salty	Bitter	Sweet
Emotions	Sorrow	Anger	Fear	Joy	Worry
Tissue	Nails, skin, hair	Muscles	Bones	Blood	Flesh

Table 1

The wuxing correlative classification system

This system is boundless, as all phenomena can be ascribed a place within its framework. Infinitely flexible, it enables everything to be classified according to empirical observation. As Marcel Granet, the great French sinologist and one of the founders of modern anthropology, pointed out, although the system is not based on causal, but correlative, logic, it contains few fundamental errors. As such, it has maintained its place as the very foundation of Chinese science for more than two thousand years. ■

Traditional Chinese Medicine

The correlative system is now universally known. It has been widely propagated in the West and become the foundation of Traditional Chinese medicine (TCM).

The ancient and most important handbook of TCM, generally known as *The Yellow Emperor's Classic of Internal Medicine*, is solely devoted to applying the system to the arts of healing. This work, still considered today as fundamental to the theory and practice of TCM, dates from the very same period under consideration here, *i.e.* the 3rd and 2nd centuries BCE.

The healing techniques of foremost importance in *The Yellow Emperor's Classic* are acupuncture and moxibustion, which regulate the different vital energies (qi) in the body. Where energies are blocked or weakened, they should be freed and strengthened. Where they are too strong, they should be weakened. Health is conceived as a system of harmony and equilibrium within the ever-changing evolution of nature.

The medical system expounded in *The Yellow Emperor's Classic* is built on the theory of the meridians, which conduct qi through the body. The typology of the meridians is derived from the cosmology of *yin*, *yang*, and the five elemental energies considered above.

Because it propounds techniques of achieving inner equilibrium to heal, *The Yellow Emperor's Classic* is not directly concerned with drugs and gives no prescriptions. Although it does acknowledge the use of drugs, it does so only as a secondary method for dealing with disease. Where drugs are mentioned, they are often called "poison drugs" (*duyao*). This is not to be understood in a negative sense, but as referring to the fact that, in contrast to acupuncture, drugs introduce external substances into the body in order to *attack* pathogenic agents and, in so doing, cause reactions. Pathogenic agents being essentially harmful, or poisonous, the drugs that attack them are considered counter-poisons. This is the principle of "categorical similitude" (*tonglei*) that is the very basis of Chinese pharmacology. In this respect is has some resemblance with the 18th century therapeutic doctrine of homeopathy, which is still popular today. But the comparison ends here, as codified Chinese herbology uses very different techniques.

The first true pharmaceutical handbook was the *Treatise on Cold Disease (Shanghan lun)* by Zhang Zhongjing, which dates back to 220 CE. It offers over 100 herbal prescriptions, presented as part of a more general therapeutic framework dominated by the theory and practice of acupuncture. In the extremely sophisticated composition of herbal, mineral, and zoological drugs the leading principle is once again **equilibrium**. The prime therapeutic substance for attacking a given pathology is, therefore, combined with a number of other substances considered to **counterbalance** its "toxicity". Consequently, prescriptions are invariably made up from **combinations** of herbal and other medical substances in order to achieve a certain balance. Many formulae consist of between five and twenty, or more, ingredients.

Among these multiple interactive substances, TCM distinguishes between four kinds. The first is the "king" ingredient, the principal therapeutic agent. Others with similar virtues

may be added as "ministers". Then come the "assistant" ingredients, whose role is to counterbalance the king and ministers. Finally come the "guides", which allow the active therapeutic ingredients to reach the root of the disease in question.

As to the classification of different drugs, the now familiar *yin*, *yang* and five elemental forces again apply. In general, TCM carefully classifies all herbs and other *materia medica* according to three kinds of criteria:

- how they relate to the body's meridians;
- the five elements and the stages to which they belong;
- and the nature, or *xing*, of the drug, in other words, what makes it cold (extreme *yin*), cool, neutral, warm, or hot (extreme yang).

When the disease is thought to be caused by a "cold" pathology, then the formula and the king substance it contains, should be "hot". However, it should also include therapeutic substances that offset the heat of the king. In this way, the prescription conforms to the ideal of equilibrium and harmony that is also the ideal of the self, or cosmic body, in its totality.

Again, the same cosmology – *yin*, *yang*, and the five elements – applies to food. The classification of foodstuffs into cold, cool, warm, hot, and neutral is very widely known and taken into consideration for all diets even today. There is thus a very close, mutual relationship between food and drugs, with Chinese practice most certainly offering the clearest example of how they are used to complementary effect. ■

Food and Drug in Chinese Culture

The notion that food should be good for the health is essential in China. Indeed, whether a particular foodstuff is healthy or not regularly outweighs considerations of taste.

General notions of quality and culinary preparations with a view to physical well-being and equilibrium are very present in literature as well as in daily life. As we have seen, foodstuffs in China are classified primarily according to whether they are hot, cool, wet, or dry. Balancing these characteristics in a meal and the overall diet is a first necessity, just as the prime aim at times of illness remains to this day to restore balance.

There exists a clear divide between food and drugs (medication) in China. Whereas foodstuffs and prepared dishes generally retain their distinctive characteristics, drugs, as we have seen, should always be fully balanced against each other. There is, in consequence, no such thing as a single-ingredient drug in China. Moreover, all drugs are prepared by cooking or, to be precise, stewing or simmering in a special earthenware pot. They are never absorbed raw. Food is stir-fried in a wok, something that is never done with medicinal preparations.

There are many other differences between food and drugs in China. They include the practice of offering gifts which are not only, as in the West, tasty, prestigious foods (pastries, chocolates, caviar, champagne), but healthy food, too, such as the much-prized dried cuttlefish, fine noodles, and dried mushrooms. Favourite health gifts also include drugs like ginseng and cordyceps, as well as dried white tree fungus *(bai mu'er)* for women.

Western food presents are not intended for daily consumption but to celebrate special occasions. In China they invariably have the (supposed) quality of being *pu*, which can be translated as "strengthening", "supplementing", or "patching up". They, too, are intended for a special purpose – that of repairing the body. And just as most Westerners do not consume caviar and champagne on a daily basis, so the Chinese use *pu* food only exceptionally.

It is the distinction between, on one hand, what is regular and ordinary (*chang*) and, on the other hand, irregular or exceptional (*feichang*) that defines the dividing line between "food" and "drug" in China. This normative distinction is reinforced by the notion that all drugs must be ill-tasting in order to be effective.

Another important criterion is that food should always and indefinitely be available, not only during our lifetimes but also after death. Even today the Confucian ethos makes feeding the ancestors an absolute obligation. Drugs, on the other hand, serve a limited purpose. They should be capable of healing a disease, and, once this has been achieved, they should be discarded. Indeed, there is something eschatological about drugs, especially in China. They mark a terminal phase along the lines of "either one recovers or one dies". This thinking is clearly present in Chinese mythology. The Divine Husbandman (Shennong) – to whom, as we have seen, the earliest compendium of *materia medica* is (spuriously) attributed – is believed to have farmed in his youth in order to produce food. In his old age he invented drugs in order to heal the diseases that inevitably come with advanced years. As a consequence, the Divine Husbandman is the patron deity both of farmers and of medicinal herb doctors – a good example of what may termed a "continuum".

The table below illustrates the properties and purposes of food and drugs:

Food	Drug (medication)
For everybody	For the ill
Youth, prime of life	Old age and death
Distinct properties	Balanced composition
Regular	Exceptional
Always needed	To be used for a limited time
Tasty	Bitter
Good government	Bad government
Stir-fried	Stewed (simmered)

Table 2.

The properties of food and drugs

Alchemy and the Quest for Immortality

Chinese herbal medicine is still popular – and has become more so in recent years. It has also, historically speaking, contributed many healing herbs and recipes to Western medicine. But, if the Chinese pharmacological tradition has proven useful in healing disease, its aim is not to confer longevity, let alone immortality. This quest was the purpose of Chinese alchemy.

If there is one case where the life-bestowing virtues of drugs are closely linked to their eschatological nature, it is that of the Chinese alchemical elixirs for bringing immortality. Once more, the difference with the Middle East and the West is striking. Even if longevity and immortality were not absent from the agendas of Western and Middle Eastern alchemists from Antiquity and the Middle Ages, their main avowed reason for the pursuit of their art was to make gold. From the outset Chinese alchemy's stated, almost exclusive, aim was physical longevity.

Alchemy emerged as a secret art towards the end of the Axial Age. Its main ingredient was then cinnabar, or mercury sulphide, the common ore of mercury, in which Southern China, especially the province of Guizhou, and North Vietnam (Tonkin) were rich. Heating or roasting crystals separated the mercury from the sulphur and caused it to evaporate. Once condensed, it yielded quicksilver (liquid mercury) which, when reheated, oxidized and reverted to red cinnabar powder. It was this transmutation that the Chinese alchemists sought to achieve. For them the sublimation of the Great Elixir reproduced the cosmic process by which *yin* (quicksilver) was transformed into yang (red cinnabar powder), and vice versa: nine-times-transmuted cinnabar was considered the most powerful *yang* essence in the universe. Ingesting it would bring immortality.

This belief held sway although mercury and its derivatives were well known to be toxic. It had been used in China since ancient times as rat poison. When mercury sulphide was heated, the fumes from the crucible which contained lead caused fainting fits and hallucinations. This protracted, and at the times very costly, experiment in fact amounted to a highly elaborate form of suicide. Yet the deceased could also be seen as still alive: the toxic transmuted cinnabar also had the power of preserving human tissue. In early alchemy manuals the adept was to take infinitesimal quantities of the elixir over a long period, thereby impregnating his body with the poison. After his demise, his body would not immediately decompose.

This kind of mummification has been confirmed by recent archaeological finds. In 1973, Chinese archaeologists discovered a large tomb at Mawangdui in Hunan Province. It was that of a noblewoman who had died in 168 BCE. Her perfectly watertight coffin held an aqueous solution of cinnabar that had preserved her body so well that Chinese physicians were able to practice an autopsy and prove that she died of a heart attack.

Cinnabar was expensive and hard to come by, and only the very rich could indulge in this kind of alchemical experiments and have their bodies mummified. One far cheaper compound mixture was discovered around 100 BCE. It had the side effect of greatly

increasing the body temperature so that those who took it refused hot food. Consequently the drug was named "cold food powder" *(hanshi san)*. It was not only addictive, but provoked painful reactions and withdrawal symptoms, so that once hooked it was virtually impossible to stop using it and most addicts would die in great suffering some four or five years after their first intake. As a derivative of an elixir that promised to convey immortality, cold food powder did exactly the opposite.

Another derivative of the Chinese alchemists' search for the immortality pill was to have truly global repercussions. According to the early tenth-century Taoist handbook, *The Synopsis of the Essentials of the Mysterious Tao of the True Origin (Zhenyuan miaodao yaolüe)*, the explosive mixture of sulphur and saltpetre was discovered accidentally during an alchemy experiment. This is the earliest historical source of the lethal mixture that, mixed with charcoal, became known as gunpowder. The invention of gunpowder and its military application, together with the contemporary, widely implemented invention of printing, brought the Chinese Middle Ages to a close and modern times began. The ancient search for immortality through alchemy came to an end, having given rise to drug abuse and warfare.

The new era, like the Renaissance in the West, spelled a return to classical sources. The ways of the ancient Immortals were rehabilitated and, with them, the primacy of the human body in a healthy state. It was now argued that the recipes for the Great Elixir of alchemy should be understood in a symbolic, sense. Lead and quicksilver, sulphur and orpiment were not crude minerals, but the figurative names of different vital energies distilled by the viscera in the body. Through blending and sublimation these vital energies could then be transmuted so as to gradually transform the body and make it immortal. This spiritual alchemy was called the "Art of the Inner Elixir" *(neidan)*.

Spiritual alchemy is a special kind of meditation technique whereby disciples would visualize their body and its inner workings according to the cosmological system of *yin-yang* and the five elements. They think of it as a landscape, a magic garden populated by divine beings with whom they can converse and interact. In this wonderland a hierogamy (sacred wedding) between the Lady of the Heart and the Lad of the Kidneys takes place. The offspring produced by this marriage is the Cinnabar Infant, the embodiment of the elixir of immortality.

The practice of spiritual alchemy has been highly influential in Chinese health techniques. It has given rise to many forms, including the highly popular, present-day *qigong* exercises, where the practitioner learns to guide the flow of vital energies in his or her body. Also profoundly influenced are Chinese martial arts, such as the ever more popular *tai-chi chuan*.

The pursuit of the spiritual elixir of immortality should be seen as the quest for an ideal of total autonomy and self-sufficiency, in which one does not depend on others, is not driven by desire, is without action, and at one with nature. The idea is that each human being should be the master of his or her destiny, or, as the Taoists themselves say: "My destiny depends on me, not on the will of Heaven." ■

Chinese Food Culture in the West

Much of the above may, at first sight, seem rather outlandish. Yet closer scrutiny reveals that many of the preoccupations discussed are those of our contemporary societies.

The great progress in science and technology has not rendered the search for longer life, or even for immortality, a thing of the past. Quite the contrary is true. The number of recently published books on anti-aging, living longer, and physically living forever is impressive. So is their success.

Terry Grossman's *The Baby Boomers Guide to Living Forever*, first published in 2000, sold well over a million copies and was translated into 15 languages. It advocates, among many other recipes and supplements, the use of a mineral drug for chelation therapy. Even more successful is Roy Walford's *The One-Hundred Year Diet*. Its main tenet is that drastic calorie reduction is the key to longevity, something that ancient Taoists would have understood. Nothing in the way of diet guides can compare, however, to the books of the famous Dr. Atkins, which sold in their tens of millions. His main thesis is that in order to slim carbohydrates must be avoided at all costs, a view that has a familiar ring to those who are acquainted with ancient Taoist longevity techniques.

The authors of best-selling diet books are certainly not aware of it, but their strong recommendations like eating fruit and fresh vegetables, drinking lots of water and a little wine, eating what is in season, avoiding fat, sugar, carbohydrates, and refined food, and eating little or no meat, can all be found in the ancient Taoist books of one to two thousand years ago. The direct or indirect influence of China is obvious in many instances. No well-established diet is nowadays complete without wok stir-fried vegetables or tofu dishes.

A vast study that credits Chinese food culture with being nutritional and health-enhancing is *The China Study: The Most Comprehensive Study of Nutrition Ever Conducted and the Startling Implications for Diet, Weight Loss and Long-term Health* by T. Colin Campbell and Thomas M. Campbell (2007). On the basis of the examination of over 350 health and nutrition variables, with surveys taking in 6,500 adults in more than 2,500 counties across China and Taiwan, the book demonstrates the numerous links between nutrition and disease. It also shows that proper nutrition can have a dramatic effect on reducing and reversing ailments as well as curbing obesity. The authors conclude that the Chinese diet stands out as a model to for all those concerned with health and longevity.

But long before this great scientific inquiry, the general public had already concluded in favour of Chinese food. One of the most striking statistics in this respect is the mutual interpenetration of Western and Chinese food habits. Powerful fast food chains like McDonald's and Kentucky Fried Chicken have, for twenty years now, attempted to find a niche in China through much publicized and costly investments. McDonald boasts about its success in opening 900 outlets in the whole of China, whereas KFC is proud of its 1,100. Yet these figures pale in comparison to the number of Chinese restaurants and take-out outlets in the United States. Although

there are no hard and fast numbers available, it is generally agreed that there are at least 35,000 Chinese restaurants in the United States alone. And this has been achieved solely by small family investment, without any large capital outlay or great publicity!

Why is Chinese food so popular? Because it is healthy – or at least healthier than the food systems that have never fundamentally broken with the sacrificial feasting tradition of Antiquity. Indeed, it can be shown that in the current global transformation of eating habits, the influence of China and other Asian cultures, especially Japan, is far larger than is generally realized.

These dietary developments are a cultural phenomenon must also be linked to the changing perception of the human body in the contemporary world. By saying "my fate depends on myself, not on the will of Heaven", men and women are affirming that irrespective of any divine predestination, all human beings have the power to seek to improve their lives and to enhance the possibilities of healthy longevity and even physical immortality. As we have seen, this fundamental change can be traced back to rise of the notion of "individuality" during the Axial Age in China.

Individually, people everywhere are exploring a vast range of alternative foodways, such as fasting, special diets and, last but not least, all kinds of drugs and supplements in order to find spiritual and physical well-being. This long quest continues unabated, creating ever greater markets. Indeed, there is today, more than ever, a universal hope that food may bring us greater longevity. The result is a search for foodways that may effectively contribute to this aim.

Although the historical and cultural facts examined in this chapter may seem a quirky and slightly nonsensical search for the impossible, they form what may be termed a "mystical empiricism" that builds on thousands of years of experience of searching for the valid foodways that can most effectively contribute to human well-being and greater life expectancy. Without this very ancient hope there would be no such search, which is what human progress is all about.

In the light of the present discussion we may feel that more modern research is still necessary. Perhaps the arguments we have considered may even be considered important enough to warrant a new research program into the Chinese traditions of longevity that in the past have so successfully combined diet and personal development. ■

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Blurred Boundaries: the changing Nature of *good* and *bad* food

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Abstract

Food consumption patterns evolve and adapt over individuals' lifetimes, influenced and driven by various factors. A survey of food habits and consumption behaviour from a purely observational perspective can help identify the roles played by different food components. In other words, without passing judgement or seeking to explain or recommend, it is possible to single out the essential nature, the added value, the real benefit, the risk, or the toxicity of specific food components during their life cycles.

Eating behaviour can be driven by the availability of food, while adaptations in the consumption of foods or the preparation of meals (cooking) can help to facilitate the absorption of nutrients and the elimination of toxins. Dependent, vulnerable individuals, like the elderly and neonates, are particularly sensitive to food components, preparation processes, and changes in consumption patterns.

The body adapts naturally in a wide range of ways to local situations, over time, with the seasons, and according to access to food. A description of how the status of a nutrient can change (from essential to dispensable, from healthy to harmful) depending on an individual's health, age, and/or bodily change, on one hand, and on the advancement of scientific knowledge, on the other hand, can shed new light on the real need to classify substances (food or drugs) and on any limitations such classification may entail.

People often wonder why nutritional recommendations tend to evolve and change so frequently, why there are no single global trends, and why some foods that are hyped as beneficial are then banned a few decades later.

One answer is that things evolve, grow to maturity, then slip slowly into senescence. Knowledge of food's effect on health and its nutritional components increases with the progress of science, while ethnicity and gene expression suppose adaptation to a changing environment, be it in the form of migration, climate change, or the availability of food.

In point of fact, nothing in people's nutritional needs and mineral-organic makeup remains constant – from their living conditions to the sources of energy and essential nutrients they use. The result is that the genotypical mechanisms of homeostatic control seek out the best adapted metabolic pathways, so producing various phenotypes. Understanding that all these moving targets – ageing individuals, different milieus and living conditions, proactive and reactive genotypical mutations and gene expression – interact makes it easy to understand, in turn, that recommendations on nutritional and food intake require, by their very nature, constant fine-tuning. Easy to understand? In theory, yes.

The practical approach, however, is far less simple to exemplify as it involves factoring too many variables into the same equation. Still, considering each variable one by one yields a more comprehensive view of the qualitative impact of many factors influencing shifting nutritional needs and different feeding habits. To examine how perceptions and understandings evolve, we will look at the following examples: a product – milk; a nutrient – vitamin A; the body's needs as it matures and ages; changing historical and cultural perceptions of selenium and proteins; and notions of artificial and natural.

Milk throughout Life: Fat-Driven Recommendations

The example of fat in cow's milk and dairy products illustrates how nutrient recommendations can change in the course of a single lifetime.

Fat is not, of course, the only milk nutrient for which nutritional advice has undergone change. The high mineral content in cow's milk prevents its inclusion in the diet of new-born babies, while its low levels of iron mean it cannot be the sole food source of iron for growing children and young people. Further contraindications could be mentioned – the protein load on the kidneys and some very low vitamin contents, for example. But putting milk into a fat-related perspective shows just how complex and difficult it can be to advise on only one single nutrient.

Mother's Milk

Milk is a mammal's first food. The composition of maternal milk meets the needs of the offspring in each mammal species during a key period. Natural selection is the most likely explanation for such specific variations.

With few exceptions, the content of human maternal milk nutrients varies within a narrow range during lactation. The quantity of fat changes with time and season – or, rather, with maternal feeding habits or food availability. This holds true for fatty acids and phospholipids which are major tissue-building factors in brain development.

Unsaturated fatty acids (linoleic, linolenic, arachidonic fatty acids and the long-chain acid DHA) and saturated fatty acids like stearic acid probably have a critical role in building axonal structure and neuronal connexions. Indeed, stearic acid is thought to be particularly important because it converts into oleic acid, a monounsaturated compound that is the most common fatty acid in myelin. The presence of cholesterol in human milk (contrary to cow's milk) does not constitute real proof of essentiality, though it might indicate some evolutionary advantage. After weaning, cholesterol is no longer a mandatory component of diets: humans can do without it for the rest of their lives. In other words, what might well be a beneficial nutrient after birth and during early infancy is regarded, at worst, as potentially risky and, at best, as superfluous thereafter, even though it is hardly avoidable.

Exclusive breastfeeding can last for months and even for the first year of life in some countries or groups. Weaning or, at least, the introduction of *beikost*, usually occurs at the baby's demand when the energy intake from its mother's milk no longer suffices. Here again, the milk's fat content supplies more than half of a baby's energy requirements. In most instances, however, milk yield conditions the food supply to the breastfed baby. It is dramatically reduced when a mother suffers from malnutrition and is forced to offer her crying baby solid food. The quality of her milk is not really altered. It is simply that there is not enough to meet the needs of her growing infant whose weight may have doubled over the first three months of its life.

The common question as to how long a baby should be breastfed – expressed in a mother's mind as "How long will my milk be nutritionally adequate?" – is a non-issue.

Human milk is in fact a food that can be taken for years, but the amount available limits such long-term use. Suckling infants must therefore been weaned, since unlimited breastfeeding is not sustainable for a woman's health, particularly if she becomes pregnant again. In simple terms, breast milk might, nutritionally speaking, be adequate for life but cannot be recommended for obvious reasons.

Animal Milk

Milk or dairy product consumption in adolescence together with vitamin D is considered of paramount importance to building solid bone mass. However, unless it is processed to substantially reduce protein content and adapt the lipid profile, milk intake can overload the kidneys and supply too many saturated fatty acids. Access to cow's milk is not a problem in industrialised countries, but processes are needed to "humanise" it, to adapt it as a potential infant formula, and make it suitable for older age groups. Its fat content must be reduced (skimming the cream) before it is nutritionally acceptable as a calcium source.

Contrary to human milk, the composition of unmodified animal milk – be it from cows, goats, sheep, buffaloes, or camels – makes it unfit for human consumption above certain levels of intake, with major limiting factors being the saturated fat content, fatty acid profile, and protein load.

Lactose

Lactose is the main carbohydrate found in milk. It is, in fact, found only in milk, thus only in the animal world. A disaccharide, which consists of bonded glucose and galactose molecules, is found in the highest quantities in human milk but is totally absent from sea lion milk, for example. Amounts are inversely proportionate to total fat contents. Lactose is an important energy source, helps absorb calcium, and greatly influences gut flora (*e.g.* the growth of lactobacillus).

It is digested in the gut, where it is broken down into the monosaccharides glucose and galactose, which can then be absorbed by the body. The hydrolysing enzyme that breaks down lactose for digestion is called lactase. It is present in the human body weeks before birth, while levels drop and nearly disappear in later life. The age at which the enzyme is no longer really active varies amongst individuals and ethnic groups. In some children it disappears after weaning; in others not until their teens.

A sizeable minority of the global population – 30% according to some estimates – have a genetic trait that prevents lactase from declining and switching off. Such individuals are called "lactase persistent" or "lactose tolerant". They may drink plain milk without any trouble, while lactose-intolerant people suffer discomfort like bowel movements, bloating, and even diarrhoea when their lactase production drops. Such symptoms are caused by the undigested lactose that remains in the gut lumen. It exerts an osmotic effect that causes water retention or fermenting, which produces organic acid and gas. The lactose intolerant tend to reduce their milk consumption naturally when their lactase production begins to drop. As teenagers, they might not be aware that they are changing their eating habits and simply believe that they have chosen to switch to low-lactose products like cheese or yoghurt and are simply not adding milk to their tea or coffee.

Lactose intolerance is not a disease, but simply reveals a change in gene expression leading to a different phenotype – namely, a reduced ability to digest the lactose in milk. Although the reason for the onset of lactose intolerance is not fully understood, it is certainly unrelated to the maintenance of milk in the diet, which would induce lactase activity. It is, rather,

the opposite: the natural decline in lactase production forces people to adapt their consumption of milk.

Because the lactose tolerant and intolerant live side by side in many parts of the world it is not possible to make sweeping recommendations on milk consumption. Food recipes in communities are nonetheless useful indicators of prevailing dietary practices. In Belgium, for example, Flemish people add milk and cream to their cooked food, whereas Wallons generally prefer butter and eating cheese. However, the mixing of populations and ethnic groups in Europe and in the US can make it difficult to predict on an individual basis who might tolerate lactose and who might not.

The example of lactose illustrates how "clinical" tolerance can orient food choices independently of any cultural or educational background.

Staying with the example of lactase persistence, ethnologists and anthropologists have hypothesized that it originates in the close interaction between humans, their genetic characteristics, and the environment, hostile or not. The mutation leading to the dominant lactase-persistent gene occurred some 10,000 years ago, somewhere in the Far East, where hunter-gatherers were breeding cattle and consuming their milk. Unlike harvesters, cattle breeders had to be constantly on the move in order to feed their livestock, which drove them to migrate towards new horizons. In this case the ability to tolerate and digest new food would not only have conditioned consumption but also behaviour. Such a hypothesis can be taken even further: cattle breeders would not survive where their cattle would not settle. In regions where the tsetse fly prevailed there were no cattle breeders, just as their numbers are today declining in the sub-Saharan belt stricken by chronic drought and desertification.

Milk from Meadow to Bottle

The composition of milk is generally stable if it is not adulterated or allowed to ferment. Fat levels in dairy milk are determined chiefly by a cow's stage of lactation and diet (whether it grazes or is fed hay), although today's production and processing methods have eliminated the influence of such factors. It is nevertheless interesting to note that if the practice of milk pooling is not used to homogenise milk composition, substantial differences may lead to conflicting recommendations and nutritional advice. Cattle fed on barley, hay, or corn might double their essential fatty acid production compared to those fed merely on forage. A similar approach is used to modify the composition, fat content, and fatty acid profile of meat.

Another interesting factor relates to ruminal biohydrogenation, which reduces the amount of poly-unsaturated fatty acids and accounts for the presence of trans, and other positional, fatty acid isomers in milk fat. Trans fatty acids, sometimes regarded as beneficial for health due to unsaturation, are now considered undesirable as they are as atherogenic as saturated fatty acids. This new understanding, based on epidemiological data, illustrates how a widely promoted, healthy nutrient can be banned a couple of decades later. ■

Vitamin A revisited

Vitamin A is a typical example of a nutrient for which both deficiency and toxicity are widely documented.

Blindness and xerophtalmia affect millions of children around the world, mostly in regions suffering from low fat diets and malnutrition.

Conversely, hypervitaminosis A is probably the most common kind of vitamin intoxication. Levels of chronic intake only five to ten times higher than recommended intakes during months or years can cause severe liver damage. A better understanding of the risks linked to both low and high intakes have seen recommendations change drastically over the last 20 years. Looking at the absolute and relative values recommended from infancy to adulthood is informative.

In the mid-1970s proposed levels of daily intake would vary between 1,000 and 1,200 RE/d. Today amounts that are half of those (600-700 RE/d) are considered more than sufficient in many cases, while half again is advised 350 RE/d for neonates and infants, leaving vitamin A with the narrowest ranges of age-related variations (a factor of 1.5–2) of any vitamin. Even levels only three to five times greater than the recommended amount (3000 RE/d) can display harmful effects in sensitive pregnant women. Vitamin A is probably the only teratogenic compound in its class of nutrients – or at least the only one clearly established as being so.

To make a long story short, and erring on the side of caution, the *highest* level of vitamin A intake proposed today for anyone should not exceed 1000 RE/d, which is still below the average amount advocated only 25 years ago. ■

Age and Maturation

A quick look at tables of nutritional recommendations suffices to illustrate some apparent inconsistencies across age groups for the same class of nutrients.

Take vitamins, for example. Recommendations increase three- to six-fold between infancy and adulthood, while body weight grows on average by between 8kg and 60kg (a factor of around 7.5). The slightly higher proportion recommended in childhood is ascribed to growth.

Such trends seem to obey common sense: when bodily growth and daily activity increase, needs grow more or less proportionately. However, for some vitamins, *e.g.* vitamin D, the trend moves in an opposite direction, from 25µg in infants, for example, to 5µg in adulthood. It then climbs back up to 15µg for the elderly, particularly women. A similar U-shaped curve is also observed for vitamin K between 18 and 75 years old.

The pattern is difficult to understand at first sight, although it can be explained for vitamin D by very rapid bone growth during early infancy, followed by a fresh spurt in puberty.

An examination of folic acid and cobalamin recommendations, however, reveals that they are at their highest after the age of …75! They are mostly based on the higher frequency of deficiencies in this age group and controversy persists in medical literature as to whether deficiencies point to poorer absorption or to greater age-related requirements.

Another example of opposite trends comes with the comparison between the iron and zinc needs of adolescent boys and girls. Recommendations for both minerals start at around the same amount (10-12 mg/d at 10 years old) for both sexes. However a lower zinc intake is recommended for girls and a higher one for boys as they grow older, while for iron the pattern is exactly the opposite. What appears to be a paradox at first sight (both minerals are mostly incorporated into protein in the muscle mass) can now be easily explained. The answer lies with iron. Although girls have lower body weights and lean mass than boys, menarche and ensuing menstrual periods dramatically increase their iron loss – hence the reason for such an increase in need, which nearly doubles up to menopause.

The examples of iron and zinc illustrate differences linked to age and gender or, in simple terms, to maturation. ■

Selenium: from Poison to Essential Nutrient

Selenium was discovered nearly 200 years ago by two chemists in sulphuric acid residue, which caused it to be considered a dangerous toxic.

It would subsequently emerge that selenium was closely associated with lead, copper, and nickel, and in the electrolysis residues of those metals. However, veterinarians in New Zealand and Australia had long recognized that selenium supplementation in livestock feed prior to or during gestation could prevent the myodegeneration (white muscle or stiff lamb disease) that frequently affected calves and lambs. Many years later it was confirmed that forage legumes in pasture land where selenium was either deficient or unavailable were an important contributory factor. They appeared to be less effective in taking up selenium from the soil than grasses. When cattle and sheep graze on such land, cows' and ewes' selenium uptake may be inadequate. Numerous countries have recorded instances of myodegeneration, which has also been produced experimentally in several species by restricting intakes of selenium and vitamin E.

It took another 160 years after its discovery before US researchers demonstrated that selenium was a constituent of glutathion peroxydase, an enzyme produced by the human body that plays a major role in the detoxification of potentially cell-damaging peroxides. Additional physiological roles have now been attributed to selenium, which notably plays a part in the production of thyroid hormones, and has been further identified as a component in a number of proteins with the highest levels of enzyme activity. Intake should vary between 20 and 60 µg/d from infancy to adulthood respectively.

Interestingly, selenium is said to have some beneficial health effects, some of which are well established, while others are far more controversial. Whereas some studies have shown that selenium supplementation seems to decrease the overall risk of developing cancer, research into specific types of disease (*e.g.* skin cancer) could not confirm initial findings. It did, however, generate interesting findings on the reduced risk of other types of cancer, like prostate and colon cancer. Other studies still have yielded unexpected results.

The SU.VI.MAX study in France, for example, showed that selenium afforded male subjects protection against disease for reasons that remain little understood. There appears to be some correlation between low selenium levels in the soil and blood with higher peak incidences of AIDS, which can thus be associated with a faster progression of the disease. Selenium apparently plays an important role in the body's immune systems. Conversely, excessive intakes of selenium lead to selenosis in some regions. Sufferers develop symptoms like the loss of hair and nails, dermatosis, liver damage, and neurological troubles like convulsions.

Selenium is a graphic illustration of how a compound of no initial nutritional interest when first discovered by chemists, and then considered a poison, turned out to be an essential, life-supporting nutrient that protects cells against acute oxidative damage. Understanding of selenium evolved from fatal to vital in just 150 years. ■

Protein Intake, from Beneficial to Prejudicial

Zakuski are plentiful Russian hors d'oeuvres which were once traditionally offered to arriving guests to take the edge off their appetite as they waited for the meal.

They also historically demonstrated the host's power and wealth, with generous amounts of high-protein foods like caviar, salmon, ham, or hard cheese denoting great health and wealth. The custom of serving *zakuski* persists, even though its original meaning is now lost. It makes less sense today than it once did in a world where starvation was rife and very many people suffered from protein-energy malnutrition. It was his awareness of just such widespread malnutrition that prompted Henri IV of France, in the late 16th century, to pledge that every working family would have chicken on its table each Sunday.

Protein consumption has evolved gradually and unnoticed from ancestral customs to levels of intake that endanger health. Kwashiorkor and starvation oedema are no longer Western health issues. Excessive protein consumption is. Indeed, daily adult intakes in excess of 100 g/d have been common findings in recent surveys in the US and Europe. Even infants are consuming equivalent amounts – over 5 g/kgBW on a daily basis in some cases.

The diseases engendered by, or at least linked to, such dietary practices are numerous. They include chronic renal disease and hypertension with cardio-vascular complications, and potentially high chronic calcium loss leading to bone disorders, particularly in women. Furthermore, the epidemic of allergic disorders observed in the past two decades can in part be related to such protein consumption. Last but not least, more recent data indicate that infants fed on cow's milk reformulated to be particularly low in protein, and so mimic human milk, developed obesity patterns five years later and far less frequently than infants receiving "classic" adapted formulae.

The example of protein further stresses that more and bigger are not better. ■

Natural and Artificial

Humanity has survived the struggle for life for millennia. This success story in a hostile environment has led some to conclude that nature is in fact protective of humans.

In that light, nature should not only be respected (which seems fair in itself) but mimicked, too, and all that it produces of itself should be considered good. In other words, every human intervention in nature's bounty is considered to be denaturing and artificial.

Yet, with all due respect for such a concept, naturally available food is not necessarily safe even for those able to recognize poisons and toxics. Although cassava grown in soils containing cyanogens produces cyanide in the human body, retting it for several days eliminates the undesired compound. Such detoxification processes have long existed for cassava, which is an important food source in Africa. Many other techniques and practices have been developed across the centuries to grow food (fertilizers and manure), to sterilize or store food (smoking, salting and curing) and beverages (brewing and fermenting). All are artificial "by nature" but have greatly contributed to feeding humanity.

The increasingly wide use of pesticides and herbicides and large amounts of fertilizers have brought even more artificial usage of well-accepted techniques, leading to a parting of the ways in different perceptions. Some approaches indeed involve risk that is often insufficiently measured or controlled in the long run. Risk management is nowadays a component of risk assessment – first identifying it, then understanding it better, and finally reducing it as much as possible, and communicating ways of limiting its potential impact. Refusing risk is surely more dangerous than understanding and managing it.

This appears to be an important clue for further discussions and probable controversies, such as: How organic is organic food? How genetically modified is cross-fertilisation compared to gene modification?

Once again there is no clear-cut border between the unexpected and random changes nature generates "naturally" (though often described as "accidentally") and what humans try to modify using more systematic, "artificial" approaches (sometimes cited as medical and scientific "success stories"). ■

Conclusion

The purpose of this short overview has been to argue that borders between good and bad, beneficial and dangerous, natural and artificial do not exist as such.

As soon as any attempt is made to delineate differences and opposites, dividing lines shift as science progresses, knowledge grows, or needs change according to age, living conditions and locations, climates, behaviours, and lifestyles.

Laying down rules and setting limits probably reflect the needs of people to codify their behaviour (food consumption is a good example), of regulators to set rules, and of public health professionals to decide how and where to intervene.

Rules and limits should be regarded as tools not as delineations of what is right. They should be adaptable and meet the real needs of those who have agreed to use them at and for a certain time. Such an approach enables insight into what is really needed and can be improved upon for the benefit of all.

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Food or Drug: Definitions and Perspectives

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Absract

Foods and drugs may be regulated by different legislation in the same country or region, while in other countries a single body sometimes governs both (*e.g.* the FDA in the US). In the Europe Union, the authorities have tried to define the remits of potentially divergent legal provisions. International organisations like the FAO and WHO and national competent authorities have also sought to define items like food, nutrients, supplements, additives, medicines, and drugs as well as techniques and procedures like enrichment, preservation, sterilisation, validation, and shelf life. Their aim has been to produce definitions that could serve and facilitate the common acceptance of terms and underlying concepts. It is, however, a task that is fraught with difficulty, as becomes evident when the definitions fail to coincide and, in most cases, overlap, so generating grey zones and debate.

In last instance, regardless of definition, what matters to the consumer/patient is what is healthy and what can combat disease or even restore health. Any attempt to reconcile definitions of food on one hand and disease on the other unavoidably comes up against the very concepts of health and disease and the need to finetune the more subtle perceptions of sickness and illness in terms of well-being.

Comparing legal and scientific concepts of pharmaceuticals and food items with sound, everyday, common-sense perceptions helps to understand whether they should be defined by their composition or their intended use. To that end, this chapter proposes a number of legal provisions, consensus definitions, and supporting references.

To sustain life as long as possible human beings interact with their environment in ways that are complex and numerous. The most crucial and fundamental are those which meet the needs of the body and ensure its homeostasis. A number of models define primary needs. Some – those of William Glasser and Robert Ardrey, for example – are simple, while others are complex, such as those proposed by Manfred Max Neef, Abraham Maslow, and Virginia Henderson. All, however, consider that breathing and feeding are the two vital requirements. Together with rest, sleep, and sufficient protection to allow the body to maintain its temperature, food and air represent the minimal conditions required for physiological human life. They are the fuels which the body needs to function.

The quality and availability of food determines bodily performance, which suggests that foodstuffs and their components may be ranked. This, in turn, leads to the idea that some foods can be more useful than others, improving metabolic pathways and increasing feelings of well being, encapsulated in the notion of "good health". When food quality and quantity decrease, during periods of shortage, for example, physiological performance may be affected, which implies the existence of different degrees of well-being (or quality of life). Conversely, with the return of favourable conditions, health may be restored.

Food can combat fatigue by providing, not only energy, but stimulating effects (*e.g.* coffee). Moving along this observational path of reasoning, some foodstuffs may also contribute to the alleviation of acute, unusual conditions, like fever (cinchona tea) or diarrhoea (salt water). Such conditions, associated with feelings of discomfort, may be described as a lack of ease, unease or "disease". To alleviate them early humans sought out edible plants, from which they brewed herbal teas or which ground into powder form. Some individuals or groups discovered the special effects of certain foods or substances, keeping the knowledge for themselves and future generations.

The dividing line between food and medicines was probably drawn by shamans or "medicine men" who used their secret knowledge and special powers to consolidate their power. In the Yoga Sutras of Patanjali (Chapter IV, verse 1) it is stated that supernormal perceptual powers *(siddhi)* can be attained through the use of certain plants, briefly giving whoever takes them mental acuity and powers similar, or equal, to *siddhi* achieved at the highest levels of spiritual practice.

Mixed with others, such substances could be toxic, which made it easier for prescribers of cures to emphasise the risks of misuse with warnings of death or divine wrath. This contributed to the creation of an artificial frontier between health and illness, and food and remedies, or drugs.

Such differences are nowadays firmly fixed in our minds. Defining them, however, is a more difficult task and consensus seems hard to achieve. Yet our 21st century societies are today sorely in need of some clarity as to what constitutes health and disease. We are accepting greater individual responsibility for the conduct of our own lives. To stay fit and healthy, we choose our own food and eating habits and buy self-prescribed drugs over-the-counter in pharmacies.

Changing notions of what constitutes states of health and sickness can, however, turn previously healthy individuals into patients, at least from a societal point of view. They will experience great difficulty in changing status unless they can clearly demonstrate strong evidence of good health. Indeed, the limit between health and sickness might be a matter of personal acceptance, reluctance, or reliance, and it may well be easier to define for others than for ourselves.

Whatever the hurdles, the most logical approach to reducing the grey area between health and disease, and food and drugs could well be to consider – while keeping an open mind to necessary nuances – available definitions currently published by the main bodies involved in the field. It might thus be possible to circumscribe the dominant current perceptions in society and arrive at a common definition. A staggered approach from simple to complex, objective to subjective might also facilitate a final understanding of the issue.

Food

Good Common Sense Definitions of Food from Dictionaries

- "What living things eat."
- "Any substance that can be metabolised by an 'animal' to give energy and build tissue."
- "Any substance (solid or liquid) that is used as a source of nourishment (food and drink)."
- "Any substance that is or can be consumed by living organisms, especially by eating, in order to sustain life. Anything intended to supply energy or nourishment of an entity idea. A foodstuff."
- "Any nourishing substance that is eaten, drunk, or otherwise taken into the body to sustain life, provide energy, promote growth, etc."

Synonyms: nutriment, aliment, bread, sustenance, victuals; meat, viands; diet, menu; food, fare; provisions, rations; all refer to nutriment.

- "What is fed upon; that which goes to support life by being received within, and assimilated by, the organism of an animal or a plant; nutriment; aliment; especially, what is eaten by animals for nourishment."
- "That which is eaten to supply necessary nutritive elements."
- "Anything that provides mental stimulus for thinking."
- "Anything which, when taken into the body, serves to nourish or build up the tissues or to supply body heat."

Scientific Textbook Definitions of Food

- "Material consisting essentially of protein, carbohydrate, and fat used in the body of an organism to sustain growth, repair damage, sustain vital processes, and furnish energy."
- "Food is any substance, usually composed primarily of carbohydrates, fats, water and/or proteins, that can be eaten or drunk by an animal for nutrition or pleasure. Items considered food may be sourced from plants, animals, life forms such as fungus, or fermented products like alcohol. Although many human cultures sustained themselves through hunting and gathering, today most do so through farming, ranching, and fishing, with hunting, foraging and other methods of a local nature still used, but playing a minor role."
- "Food and nutrients: any substance that can be metabolised by an animal to supply energy and build tissue."
- "In a physiological sense, the portion of food that is true aliment is that which can be digested and absorbed into the blood, thus furnishing nourishment, as distinct from the indigestible matter which passes out through the alimentary canal as faeces."
- "Food: anything eaten by human beings and other animals, or absorbed by plants, to sustain life and health. The building blocks of food are nutrients, and humans can utilize the following nutrients: carbohydrates in the form of starch (bread, potatoes, pasta), simple sugars (sucrose and honey), and fibres (cereals, fruit, and vegetables); proteins from nuts, fish, meat, eggs, milk, and some vegetables; fats as found in most animal products (meat, lard, dairy products, fish), margarine, nuts and seeds, olives, and edible oils; vitamins, found in a wide variety of foods, except for vitamin B12 which is found mainly in foods of animal origin; and minerals, found in a wide variety of foods (*e.g.* calcium from milk and broccoli, iodine from seafood, and iron from liver and green vegetables)."

Legal and Regulatory Definitions of Food

• ***International Organizations***

Joint FAO/WHO Codex Committee on General Principles (May, 2004):

• "'Food' means any substance, whether processed, semi-processed or raw which is intended for human consumption and includes drink and any substance which has been used in the manufacture, preparation or treatment of food."

• ***European Union***[10]

In 2002 the EU established the European Food Safety Agency (EFSA). EFSA's founding regulation was an opportunity to set in stone some common definitions of precisely what a foodstuff should or should not be.

A definition of "food" from regulation EC 178/2002 establishing EFSA:

• "'Food', or 'foodstuff', means any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans.

• "Food includes drink, chewing gum, and any substance, including water, intentionally incorporated into the food during its manufacture, preparation or treatment. It includes water after the points of compliance [defined in other Directives]."

• ***United States of America***

In the United States Congress enacted the stringent Federal Food, Drug, and Cosmetic Act (21 U.S.C.A. § 301 et seq.), which superseded the provisions of the Pure Food and Drug Act of 1906.

It defined "food" as meaning (1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.

Comment on Definitions of Food

Common sense definitions all seem to call upon the idea of food being a visible intake – as opposed to the intake of air – converted by metabolism into energy or substances for the maintenance of bodily functions (growth) and the construction of cells.

Scientific definitions refer mainly to two different, more dynamic dimensions of food – namely where it comes from and where it goes; and what for. They mention origins and sources, some production processes, and expand on the end result or outcome of food transformation (*e.g.* digestion, metabolism) into simple biochemical components (*e.g.* nutrients, energy compounds).

Legal definitions are descriptive. They focus on technical elements, such as manufacturing processes, in order to allow and facilitate quality control inspections and prevent fraud.

In summary, whereas the lay person would speak of the use of food, (*i.e.* what we should eat), the lawyer thinks of preventing misuse (what food should consist of), and the scientist will emphasise the purpose of food (why we should eat). ■

[10] *http://europa.eu.int/eur-lex/pri/en/oj/dat/2002/l_031/l_03120020201en00010024.pdf*

Food and Dietary Supplements

About Food Supplementation

The field of food supplementation is particularly sensitive and heterogeneous in its concepts, perception, and, consequently, definitions. Those advocating the use of natural foodstuffs consider any addition to food as a modification, if not adulteration, of the European tradition of sophisticated cooking, food diversity, and gourmet pleasures. People who consume a daily, simple but balanced diet based on few manufactured products seek reassurance that in so doing they meet their daily needs. The few foodstuffs they consume should therefore provide all required nutrients. In such an approach, supplements are clearly meant to maintain health.

Terminology reflects the two different approaches. On one hand are the terms "food supplement" and "enrichment"; on the other, "dietary supplement" and "fortification" or "nutrification".

A food supplement is a nutrient added to food in which it would otherwise be lacking and which the overall population would not consume in sufficient amounts to meet their needs. Adding folate to bread or iodine to drinking water is part of fortification strategies in many countries to prevent spina bifida and goitre, respectively. The practice also applies to situations where food choices are so limited that healthcare deciders anxious to remain on the safe side prefer to enrich single basic foodstuffs rather than promote food diversification.

Dietary supplements are products rather than natural food, consisting of a number of essential nutrients often in combinations (polyvitamins are a typical example when presented like drugs in syrup or pill form), but in amounts close to and not exceeding nutritional recommendations.

Common Definitions of Food and Dietary Supplements

"'Dietary supplement' refers to products made of one or more of the essential nutrients, such as vitamins, minerals, and proteins."

"A product taken orally containing one or more ingredients intended to supplement one's diet and not considered food."

"Products that are used to improve a person's health. They can include vitamins, herbs, minerals, and botanical products."

"A food supplement is, typically, a nutrient added to a foodstuff which would otherwise not contain that nutrient. In general, the term is restricted to those additives which are deemed to be positive for health, growth, or well-being."

European Union Definitions of Food and Dietary Supplements[10]

In EU legislation, food supplements can, clearly, only be vitamins or minerals. The European Commission considers food supplements as:

"Concentrated sources of nutrients or other substances with a nutritional or physiological effect whose purpose is to supplement the normal diet. They are marketed in dosage form *i.e.* as pills, tablets, capsules, liquids in measured doses, etc."

The EU requires that supplements be demonstrated to be safe, both in quantity and quality. Consequently only those supplements

[10] *http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32002L0046:EN:HTML*

that have been proven to be safe may be sold without prescription. In Europe it is also an established view that food supplements should not be labelled like drug claims, although they can bear health claims.

United States of America: Definitions of Food and Dietary Supplements

In US legislation, dietary supplements can be more than vitamins or minerals. The Federal Food, Drug and Cosmetic Act, section 201, and Dietary Supplement Health and Education Act (DSHEA) of 1994 consider that the term "dietary supplement" means:

(a) A product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients, namely:

1. vitamin
2. mineral
3. a herb or other botanical
4. an amino acid
5. dietary substance for use by man to supplement the diet by increasing the total dietary intake
6. concentrate, metabolite, constituent, extract, or combination of any ingredients described in (1), (2), (3), (4), or (5)

(b) Is intended for ingestion in pill, capsule, tablet, or liquid form;

(c) Is not represented for use as a conventional food or as the sole item of a meal or diet;

(d) Is labelled as a "dietary supplement";

(e) Includes products such as an approved new drug, certified antibiotic, or licensed biologic that was marketed as a dietary supplement or food before approval, certification, or license.

The DSHEA considers dietary supplements as foods not drugs.

Summary Definitions of Food and Dietary Supplements

Products used to improve a person's health. They can include vitamins, herbs, minerals and any botanical products.

Products that contain one or more ingredients (such as vitamins, minerals and herbs) intended to supplement the diet, intended for human use, in the form of a tablet, capsule, powder, or another preparation **that is not a conventional food**.

Comment on Definitions of Food and Dietary Supplements

The concept of "supplement" implies another concept – that of "nutrition". Whereas foods and their additives relate mainly to "aliment" or "nutriture" in the sense of foodstuff, the idea of food supplement suggests the need to reach a balance between different food components. This, in turn, suggests the idea of breaking down foodstuffs into more simple components and introduces the concept of nutrients and the science of bromatology. Defining specific nutritional and bromatological needs and recommending specific intakes accordingly are the core of nutritional science. Further, the concept of "dietary recommendation" is closely connected to health, if not its sole objective. ■

Functional Foods

There is no consensus on any exact definition of "functional food". The term can include foods like cereals, breads, and beverages, which are fortified with vitamins, herbs and nutraceuticals. The US Institute of Medicine defines functional foods as "those foods that encompass potentially healthful products, including any modified food or ingredient that may provide a health benefit beyond the traditional nutrients it contains."

Common Sense Definitions of Functional Foods

"Foods or dietary components that may provide a health benefit beyond basic nutrition, such as chocolate, inulin/oligofructose, nuts, berries and soy."

"Food that provides health benefits beyond energy and essential nutrients."

"Foods that contain physiologically active compounds that provide health benefits beyond basic nutrition."

"Food or food ingredient that has been shown to affect specific functions or systems in the body. Functional foods play an important role in disease prevention."

"Any fresh or processed food claimed to have a health-promoting and/or disease-preventing property beyond the basic function of supplying nutrients."

"An added ingredient to a product that is beneficial to health. For example, orange juice is fortified with calcium to maintain healthy bones."

Comment on Definitions of Functional Foods

Moving away from the food and additive domains which modestly aim at achieving or maintaining satisfactory health, the concept of functional food appears to lead in the novel, modern direction of improving performance and/or prolonging quality of life through targeted recommendations and active food or food ingredients, which can include living organisms like bacteria.

Such innovative use of foodstuffs for the benefit of health functionalities has to contend with both positive and negative interactions between, for instance, high levels of nutrients (which act almost pharmacologically) needed to achieve a certain effect on the target (organ or metabolism), but likely to cause some undesired effects on others. High calcium diets which are good for the bones cannot, for instance, be separated from high protein intakes, potentially harmful to the kidneys, unless specific foods are manufactured to that end. The gap between foods and drugs narrows when functional foods are, like drugs, manufactured and consumed in quantities (or doses) designed to achieve an effect that can be functional or pharmacological – a subtle difference that is not always easy to discern.

Going further, the exploration of the nutritional benefits of living organisms (like saprophytic bacteria) is an area of inquiry into the advantages and possible risks of symbiotic life often, but not always, in a way not found in nature. ■

Health Claims

Health claims on food labels are claims by food manufacturers that there is a relationship between health and the consumption of an ingredient or product, or that consumption of a product can reduce the risk of developing a specific disease or condition.

European Union Health Claims[10]

An increasing number of foods labelled and advertised in the Community bear nutrition and health claims. In order to ensure a high level of protection for consumers and to facilitate their choice, products put on the market, including imported products, should be safe and adequately labelled. A varied and balanced diet is a prerequisite for good health and single products have a relative importance in the context of the total diet.

The European Parliament Regulation (1924/2006) on nutrition and food health claims defines:

- A nutrition claim as any claim which states, suggests or implies that a food has particular beneficial nutritional properties due to energy, nutrients or other substances.
- A health claim as any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health.
- A reduction of disease risk claim means any health claim that states, suggests or implies that the consumption of a food category, a food or one of its constituents significantly reduces a risk factor in the development of a human disease.

The regulation on nutrition and food health claim lays down harmonised rules for the use of health or nutritional claims (such as "low fat", "high fibre" and "helps lower cholesterol") on foodstuffs based on nutrient profiles.

The regulation also ensures that any claim made on a food label in the EU is clear, accurate and scientifically substantiated. In doing so, it enables consumers to make informed and meaningful choices when it comes to food and drinks.

United States Health Claims[11]

In the United States, the Food and Drug Administration (FDA) regulates health claims in the public interest (21 Code of Federal Regulations §101.14). In 2003 the FDA announced plans to allow the manufacturers of food products sold in the United States to make health claims on food labels supported by less than conclusive evidence. Whereas claims previously required "significant scientific consensus", they are now characterized according to degrees of certainty:

- There is significant scientific agreement.
- Although there is some scientific evidence supporting [the claim], the evidence is not conclusive.
- Some scientific evidence suggests [the claim]. However, the FDA has determined that this evidence is limited and not conclusive.
- Very limited and preliminary scientific

[10] *http://ec.europa.eu/food/food/labellingnutrition/claims/index_en.htm*

[11] *http://members.ift.org/NR/rdonlyres/69E560C7-9AEB-4DBF-8409-F5921FFEA4E2/0/HealthClaims.pdf*

research suggests [the claim]. The FDA concludes that there is little scientific evidence supporting this claim.

This ranking of qualified health claims has been criticized as having opened the door to ill-founded claims.

The Dietary Supplement Health and Education Act provides for claims on supplement labels that describe the effect of a product on the structure or function of the body if they are not disease claims. If the claim diagnoses, cures, mitigates, treats, or prevents a disease, the product is considered a drug. Table 1 lists a number of examples of authorised structure/function claims.

Table 1.

Examples of permissible structure/function claims

Permissible "Structure / Function Claims"	Impermissible "Disease Claims"
Helps to maintain cholesterol levels that are already within the normal range [a]	Lowers cholesterol
Helps support cartilage and joint function	Inhibits platelet aggregation [b]
maintains healthy lung function	Prevents bone fragility in post-menopausal women
Improves absentmindedness	Maintains normal bone density in post-menopausal women
Relieves stress and frustration	Maintains healthy lungs in smokers
	Prevents irregular heartbeat
	Relieves alcohol intoxication
	Use as part of your diet when taking insulin to help maintain a healthy blood sugar level
	Promotes general well being during the cold and flu season, and dietary support during the cold and flu season

[a] FDA also states references to "healthy" cholesterol "may be misleading to consumers", since the phrase is now frequently used to refer to high density lipoproteins (FDA, 2000a).
[b] In the proposed rule, FDA has indicated that this claim would not be considered an implied disease claim.

Comments on Health Claim Definitions

The principles of nutritional recommendation, supposing they concern advice about balanced nutrition favouring good health, imply the concept of health claim. General nutritional strategies involve advising people and healthcare professionals about food consumption, nutritional habits, agricultural strategies, prevention policy, etc. in context such as age groups, environment, and affordability. This necessarily entails advice on specific products and data supporting it – in other words a product- or nutrient-related claim. Whilst a recommendation (issued by a health authority) often focuses on a nutrient, a health claim usually emphasises a product and one or more of its (nutritional) components. Such a distinction is, however, purely formal, since both types of claim contain the same message – *e.g.* "one gram per day of calcium is recommended for adolescents to build robust bone mass" versus "product X contains calcium that prevents bone fragility in later life".

Furthermore, in both instances scientific evidence is required. For general recommendations, the evidence is mostly generated by epidemiological studies or investigations into metabolic imbalance, whereas products use well executed but targeted trials to substantiate their specific health benefits.

Health claims help the consumers answer the question: What food should I eat? They enable consumers to think about how they can meet their nutritional requirements and no longer concern themselves with general, nutrient-related recommendations.

A word of caution, however, about the risks of jumping from a sole recommended nutrient to a nutrient-rich food or manufactured product, whose other components may have a nutritional impact. This, however, is precisely what dietetics is about. Education and the improvement of people's eating habit starts with nutritional information about a product's content (labelling) and continues with guidelines as to its use (health claims), with such advice often considering populations at risk. This approach is, not surprisingly, similar to drug labelling or indications specifically targeting a population at risk of developing (prevention) or having developed (treatment) a particular condition. There are, however, only subtle differences between: "Food X or Product Y contains calcium that prevents bone fragility in post-menopausal women" and "oestrogens help prevent bone fractures in post-menopausal osteoporosis".

The quantitative dimension cannot, of course, be ignored. In other words: "How much of the food should I eat to benefit from the health effect?" Again, this criterion corresponds to the dosing regimen for drugs.

In summary, health claims labelled on food or drugs (see below) deal with similar matters (what to use, how much, and what for) in rather different target populations (healthy versus sick), but with considerable overlap (primary and secondary preventions). ■

Medicinal Products and Drugs

There is no single, precise definition of "drugs", as the term has different meanings in medicine, government regulations, and colloquial usage, where it often denotes illicit, recreational substances.

Good Common Sense Definitions of Medicinal Products and Drugs

- "Substance used to treat an illness, relieve a symptom, or modify a chemical process in the body for a specific purpose."
- "A substance used as or in medicine."
- "A chemical substance that affects a biological process."
- "A drug, broadly speaking, is any chemical substance that, when absorbed into the body of a living organism, alters normal bodily function."
- "Any substance presented for treating, curing, or preventing disease in human beings or in animals."
- "Any substance that enters the human body and can change either the function or structure of the human organism." (This broad definition includes practically all foreign materials – even food, vitamins, plants, snake venom, air pollution, and pesticides.)

Scientific Definitions of Medicinal Products and Drugs

- "Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient"
- "A substance intended for use in the diagnosis, treatment, mitigation, cure or prevention of disease in human beings or animals and a substance, other than food, intended to affect the structure or any function of the body of a human being or animal".
- "An agent that affects a biological process. Specifically, a molecule whose molecular structure can be correlated with its pharmacological activity."
- "Any substance or preparation containing any substance, manufactured, sold or represented for use in:

(i) the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical or mental state or the symptoms thereof, in humans, animals or fowl,

(ii) restoring, correcting or modifying functions in humans, animals or fowl."
- "A chemical substance used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being."

European Union Legal Definition of Medicinal Products and Drugs1

Directive 2001/83/EC relating to medicinal products for human use proposes these definitions:

Medicinal product:

- "Any substance, or combination of substances, presented for treating disease in human beings."
- "Any substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings is likewise considered a medicinal product."

Substance:

Any matter irrespective of origin which may be:

human, *e.g.* human blood and human blood products

animal, *e.g.* micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products

vegetable, *e.g.* micro-organisms, plants, parts of plants, vegetable secretions, extracts

chemical, *e.g.* elements, naturally occurring chemical materials and chemical products obtained by chemical change or synthesis.

United States Legal Definition of Medicinal Products and Drugs

The Federal Food, Drug and Cosmetic Act, section 201, considers as a "drug" (1) any substance recognized in the official pharmacopoeia or formulary of the nation, (2) any substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or other animals, (3) any article, other than food, intended to affect the structure or any function of the body of humans or other animal (4) any article, other than food, intended to affect the structure or any function of the body of humans or other animals.

Comments on Definitions of Medicinal Products and Drugs

Good common sense medical definitions of drugs mostly refer to the relief of a symptom, usually the first signs of disease, like fever, swelling, or pain. Patients, on the other hand, seek the alleviation of unpleasant effects or discomfort caused by illness.

Scientific definitions focus more on underlying causes and tend to define drugs according to the mechanism by which their action alleviates visible symptoms.

Legal definitions in the EU (those of the US are confusing) tend only to refer to the purpose of a substance, *i.e.* treatment of disease. This way of thinking seems more in line with a restrictive view that the practice of medicine should be under control, as should the pharmaceutical industry.

An interesting concept relates to "novel and advanced therapies", or "new drugs" as they are known in the US, which have been defined in very recent legislation.

These therapies replace drugs or medicines by biologicals that address root causes (*e.g.* gene repression of deleterious oncogenes) or suppress and prevent symptoms rather than only alleviating them by intervening earlier on the mechanism of disease. Enzyme replacement therapy does not cure, but prevents symptoms by substituting defective enzymes. Such medicines are no longer drugs but recombinant biologicals similar to their natural protein counterparts.

The current trend in medical science is to develop replacement therapies by producing cells, insertion genes, engineered tissues, etc. In this sense, scientific progress moves closer to the concept of using helper systems (adjuvants) and live production systems such as bacterial machinery to synthesize large recombinant molecules, culture media to produce autologous cells, and viral vectors to insert genes that correct deficient ones. This approach has many similarities with the development of "external media" designed to insert and incorporate into the gut living symbiotic micro-organisms in order to producing beneficial (and often complex) substances, *e.g.* for the immune system.

Where does the frontier lie between food used in desensitisation (some recognized allergenic substrates are attached to and carried by bacterial extracts that present antigens to the appropriate gut T-cells in order to facilitate and re-induce tolerance) and the continuous interaction occurring naturally in the intestinal lumen between food components, physiological flora, and the local immune system? Clearly the answer does not lie in considering whether vitamin D is a nutrient or a hormone, a food or a drug. The understanding of complex biological systems forces us to reconsider boundaries with an open mind. Though clear-cut demarcations facilitate the work of lawyers and inspectors, they are of little value to scientists, obstructing more than anything the understanding of living organisms and their interactions.

Categorisations are useful mostly for educational purposes, helping consumers to decide. They have to make numerous choices, not only finding out what is beneficial to their health, but also considering when to switch from self-care to the search for wider medical advice or support. ■

Health and Disease

Definitions of Health, Well-being, Wellness

The definition issued by the World Health Organisation (WHO) in 1948, and unchanged since, is brief and comprehensive: "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."

The following definitions of health, however, consider it as much a state of well-being or wellness as a condition free of disease.

- "A healthy state of well-being free from disease."
- "The state of being free of physical or psychological disease, illness, or malfunction."
- "The overall condition of an organism at a given time in regard to soundness of body or mind and freedom from disease or abnormality."
- "A state of being that occurs in varying degrees of wellness and illness ranging from optimal health to death. Determinants of health include the internal and external environments, availability of personal, social, and cultural resources, and lifestyle."
- "The general condition of the body and mind; the condition of being free from sickness or disease."
- "A state of well being deprived of any illness or injury."
- "Physical fitness is good bodily health, and is the result of regular exercise, proper diet and nutrition, and proper rest for physical recovery."

Definitions of Disease, Discomfort, Illness, Sickness, Injury

- "An impairment of health or a condition of abnormal functioning."
- "A disease is an abnormal condition of an organism that impairs bodily functions, associated with specific symptoms and signs."
- "Any departure from health; a particular destructive process in an organ or organism with a specific cause and symptoms."
- "An abnormal condition of the body or mind that causes discomfort or dysfunction; distinct from injury insofar as the latter is usually instantaneously acquired."
- "A process that is a hazard or injurious to health and/or longevity."
- "Illness or sickness often characterized by typical problems (symptoms) and physical findings (signs)."
- "Disease can be defined as a derangement in the function of the whole body of the host or any of its parts."

Scientific Definitions of Disease

- "Any malfunctioning of host cells and tissues that results from continuous irritation by a pathogenic agent or environmental factor and leads to development of symptoms."
- "The condition in which a disease is only detectable by special tests and there are no apparent symptoms and signs."
- "A general term describing a morbid condition which can be defined by objective, physical signs (*e.g.* hypertension), subjective symptoms or mental phobias, disorder of function (*e.g.* biochemical abnormality), or disorders of structure (anatomic or pathological change)."
- "Disease is an unhealthy condition caused by infection, diet, living conditions, or inheritance."

Comments on Definitions of Health and Disease

As often, difficult concepts are defined using their opposites: health is the absence of any illness, whereas disease is a disruption of the healthy state. Turning in circles is a classic ploy when seeking to express in concrete terms an abstract concept based mostly on perception and feeling. Everyone knows what it is but nobody can say it in simple words.

The WHO definition of 1948 makes a point of excluding this symmetry by stating that health is not simply the absence of disease. But it does not specify what else health is. ■

Conclusion

It is universally acknowledged that a continuum runs from full health to severe disease and from pure food to therapeutic drugs. However, some distinctions are necessary if partial health is to be distinguished from mild sickness and if the same foodstuff is to be differentiated when consumed as nutrient or remedy. In other words, perception depends on the nature of use. Are low-cholesterol diets (like vegetarian regimes) for the prevention of long-term arterial damage, low-calorie diets against obesity, and protein-phenylalanine restricted diets for the prevention of neurological deterioration of phenylketonuria to be considered as special eating habits, medical diets, or therapeutic regimen? There are no single or consensual answers. A "well-balanced diet" does not refer to its content (who knows for sure of what it should consist of?) but rather to its purpose – namely that it is supposed to offer a nice, long life.

Similarly, when people affected by coeliac disease avoid a "natural" food component like gluten, when the fructose-intolerant steer clear of fructose, when members of a family with inherited hypercholesterolemia do not eat saturated fat, and when people with metabolic disorders linked to impaired enzymes eat certain nutrients, the perception is that they are following a "medical" diet, similar in effect to a drug. Doctors prescribe such regimens to "patients" affected by symptoms as part of wider treatments which include medication (*e.g.* nitrogen chelating agents or statins).

Yet when healthy subjects are not yet patients (suffering from symptoms), changes in their feeding habits are perceived less as a diet than as an improvement in their regimen – *e.g.* low cholesterol diets are healthy and recommended to the whole family even when only one sibling suffers from hypercholesterolemia.

Preventative attitudes hardly enter the field of medicine. Vaccines, for example, are not perceived by the general public as drugs (although they fall under that definition by law) and as such their adverse effects are sorely resented. This leads in some extreme attitudes to wholesale rejection, with all vaccines considered to make the healthy sick. Any administered substances, even foods, that make people ill are called poisons. The same substance can therefore be considered very differently, depending on a person's health status (sick or healthy) and on both the nature (preventative or curative) and latency (immediate or long term) of the effect.

Glucose and its polymers (starch, etc.) are the largest constituent elements in daily foodstuffs. Glucose given orally to a hypoglycaemic neonate is a therapeutic regimen; when infused intravenously, it is considered a medicinal product. Conversely, glucose levels are limited in the diets of diabetics, considered toxic when they rise steeply and suddenly in the blood (acidoketosis and coma), or as deleterious when they are lightly but chronically enhanced and contribute directly to the diabetic's renal, neurological, ophthalmologic complications. Lastly, it is absolutely prohibited to subjects suffering from the rare metabolic disease of glucose-galactose intolerance.

Different stakeholders will therefore use different classifications, retaining those that are most meaningful to their daily lives. Consumers will prefer to stay in the secure field of health; patients will not be in a situation to deny their underlying illness, seeing potential food consumption habits as part of their therapy; healthcare professionals will have to deal specifically with disease; and lawmakers will tend to (over-) regulate "food and drugs", emphasising safety issues (precautionary principle) and the importance of inspection.

In such a context, all definitions are useful: they clarify consumer understanding, they are prescriptive for patients, legally binding on Health Care Professionals and the food and pharma industries, and serve as legal reference for courts.

Definitions at a Glance

- **Food:** "What living things eat."
- **Food Additives:** "Substances that are added to foods to prevent spoilage, improve appearance, enhance the flavour or texture, or increase the nutritional value."
- **Food Supplement:** "Food supplement is, typically, a nutrient added to a foodstuff which would otherwise not contain that nutrient."
- **Dietary Supplement:** "A product taken orally containing one or more ingredients intended to supplement one's diet and are not considered food."
- **Functional Food:** "Any fresh or processed food claimed to have a health-promoting and/or disease-preventing property beyond the basic function of supplying nutrients."
- **Health Claim:** "Health claim means any claim that suggests that a relationship exists between a food or one of its constituents and health."
- **Drug or Medicinal Product:** "A substance used in medicine for treating, curing, or preventing disease in human beings."
- **Health:** "The state of being free of physical or psychological disease, illness, or malfunction."
- **Disease:** "An abnormal condition of an organism that impairs bodily functions, associated with specific symptoms and signs."

Conclusion

by Ken Kincaid

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"Food and drugs for health and for the prevention and treatment of disease" is both the title of this book and its central tenet. That is not to say that each contribution is a position paper in its own right. All seven authors accept that both food and drugs can be used to maintain health, prevent and even treat disease. They have chosen, however, to address from very different angles the various implications thrown up by their shared belief.

Our first task in endeavouring to gather the disparate strands of thought that make up the rich fabric of this book relates to its topicality. A sign of the times, it explores the breakdown of the rigid separation between food and drugs, *i.e.* pharmaceutical products used for medicinal purposes. (Professor Brasseur proposes numerous definitions of "drugs" in VI.) In the sweeping historical canvas that opens the book Professor Bourlioux describes how (essentially plant-based) foodstuffs were originally used for medicinal purposes as early as 2000 BC. The Far East, particularly Traditional Chinese Medicine, perpetuates those practices, while the West gradually came to regard food, on one hand, as a source of enjoyment or sustenance and drugs, on the other entirely separate hand, as what we must take when we are ill.

Professor Bourlioux situates the beginnings of the great divide between food and drugs in Europe in the 12th century, which saw the rise of distillation. Over the centuries the gap widened – from the Cartesian separation of mind and matter and the rise of mechanistic biology in the 17th century, through the rationalism of the Enlightenment, to synthetic chemistry and the pharmaceutical industry. "The result," concludes Bourlioux, "is that science has come to consider drugs in isolation." And sealed their separation from food and embedded it in minds. Today, however, the wheel is coming full circle. There are signs that the mindsets and practices of healthcare professionals and consumers alike are changing.

Paradigm Shift

Writing from a physician's viewpoint, Professor Cummings describes how his profession has come to think seriously about health, as well as disease: "The observation that blood cholesterol was a major, measurable risk factor and that dietary saturated fat contributed to its control was a turning point for our understanding of the role of diet in health, beyond the simple provision of nutrients for energy, growth and the maintenance of function.

Enquiry into this relationship has since spread into all aspects of health, and diet is now seen as a key lifestyle contributor to many diseases."

In "Blurred Borders", Professor Brasseur considers the demise of the large, high-protein meal, which he terms "the *zakuski* diet" and Professor Schipper refers to as the "bingeing" legacy of the sacrificial feast. Where such foodways were once signs of ruddy health and wealth, evidenced-based science has shown that they are in fact factors in a lifestyle that can contribute to chronic conditions like renal disease, hypertension, and heart disease. Lifestyle, of course, encompasses more than diet alone. Sunlight and exercise are more important factors than diet in bone health and the prevention of osteoporosis, for example.

Consumers are increasingly accepting and becoming interested in the close links between lifestyle and health and disease. They are accepting responsibility for their own health and that of their families. As life expectancy grows they are no longer resigned to "neither dying nor recovering", but keen to stay healthy, enjoy quality of life, and forestall disease. And advances in nutritional science and food technology are empowering them.

On the policy side governments and healthcare authorities are anxious to reduce burgeoning health costs and limit the toll of chronic and age-related disease. They are encouraging new healthcare models, where individual self-care and conventional medical treatment both have their place. Building on the concept of the balanced diet, "one of the major contributions of nutrition in the twentieth century" (Roberfroid, 2002), there are moves to promote the value of foods like fruit, vegetables and wholegrain cereals, which contain nutrients with health benefit potential that ranges from improving function to reducing the risk of disease. The European Food Information Council reports that since the 1990s some EU countries have sought to facilitate the use of health claims, while in the USA "reduction of risk of disease" claims have been permitted since 1993 for certain foods.

In his thought-provoking study, "The Foods of Longevity", Professor Schipper argues with eloquent erudition that all these changes are signs of an even more profound change taking place in the West – what he calls "a paradigm shift", in which "the notion of the individual and his or her personal experience and conscience [becomes] the very foundation of the human being".

This paradigm shift occurred in Mediterranean world, the Near East, India and China during what the thinker Karl Jaspers termed the "Axial Age", a period during the second half of the first millennium BCE, which saw the rise of the individual and his/her search for immortality. In China this led to the development of a

new religious system, Taoism. The impact on foodways (nutritional habits) was profound: food offerings were no longer made to the gods, but to the body. Food had to be good for the health of the body and self – which are one and indivisible.

The West is now grappling with the same paradigm shift, posits Professor Schipper. The quest for immortality has never been more vigorous or looked so attainable. Genetic engineering, biotechnology, plastic surgery, and nanotechnology contain tantalising prospects of physical youth over biblical lifespans. Signs of profound change are everywhere. People live longer, have fewer children, and think less about their heirs than about their own longer, healthier lives. Smoking has become (literally) a mortal sin, consumers are eating more vegetables and less meat, while macrobiotics, organic farming, and the health food business are now international business concerns. Companies like Fertilia in Germany and Lima in Belgium spring to mind, while in France Groupe DANONE built its business on yogurt, popularised by Nobel medicine laureate Elie Metchnikoff who believed it could help people live to be 150 years old.

Schiffer cites just some of the countless books on miracle diets. The regimens advocated by the likes of Roy Walford and Dr. Atkins would, he says, would strike a chord with Taoists. And to illustrate the Western fascination with Chinese foodways (another sign of the paradigm shift), he mentions Campbell and Campbell's exhaustive *The China Study*, published in 2007, which explores the close ties between nutrition and disease. Writes Schipper: "[The book] also shows that proper nutrition can have a dramatic effect on reducing and reversing ailments." ■

From Prevention to Function

The nub of the "paradigm shift" – the understanding that, just as poor diets can cause conditions like obesity, hypertension and diabetes, so the right nutrition can not just sustain health, it can also prevent and treat disease.

Or can it? Not according to conventional "separatist" medical thinking, because – as Professors Jones and Mackay note in the introductory essay – "prevention is unfortunately not at the core of modern medicine's tenet". The operative word here is "unfortunately", meaning modern medicine should re-engage with prevention, placing its focus on health, not on disease. The chronic, lifestyle-related conditions of contemporary society cannot be managed by synthetic drugs alone.

In "Diseases: History, Classification and Definition", Dr. Antoine explores what makes a disease a disease. He considers the once lively debate between the physicians who argued that pathogenic factors were exogenous and those who held that they were endogenous. He resolves the debate thus: "Medicine should be able to use one single approach to explore both sides of the etiological coin. Clinical and biological signs stem from two intricate sets of phenomena. One set comprises the effects induced directly by the pathogenic factor, and the other groups the reaction of the body as it seeks to cope with the invaders."

The dominant chronic diseases of the late 20th and early 21st centuries do not, however, necessarily show signs or symptoms until well after their onset. The shift from homeostasis to diagnosed disease takes place gradually along the health-disease continuum. At some point the disease – be it cirrhosis, cancer, or cardiovascular disease (CVD) – sets in. Yet there are no signs until long, possibly years, afterwards. Leriche's "silence of the organs" is not always an eloquent one.

Similarly, Professor Cummings notes that the proliferation of cholesterol-lowering drugs has led to growing calls "for the designation of a cut-off point at which therapeutic intervention is recommended". He also describes how, in a study he carried out on the bowel habit of healthy subjects in the UK, "there was no clear cut-off point for quantifying the risk of bowel cancer. There was a continuum."

Food and drugs do not merely lie at either end of health-disease continuum. Food is key in primary prevention. Not only through the World Health Organisation's widely acknowledged and implemented guidelines on the use of diet to prevent chronic non-communicable diseases. But also through specific nutrients that target function and may be used in secondary prevention, possibly in combination with drugs.

Dr Antoine rounds off his examination of disease with this paragraph:

"The role of food is to provide nutrition and is a normal part of everyday life. The purpose of drugs is to cure 'abnormal pathogenic' factors and manage their harmful consequences. Human beings will benefit from both – food on a daily basis, and drugs as infrequently as possible."

The wording is telling: "the role of food" and "the purpose of drugs" are both turns of phrase which imply intended, not actual, use. Actually, food has burst its boundaries. As we have already observed, new health challenges like longer life expectancy, larger numbers of elderly people, and spiralling healthcare costs have combined with growing consumer awareness, new food technologies, and advances in nutritional science to give rise to foods that demonstrably enhance physiological functions and reduce the risk of disease. Known as functional foods, they blur the boundaries with drugs. ■

Functional Foods

Only Japan, where the concept of functional food originated in the mid-1980s, offers a legal definition under the acronym FOSHU – Foods for Specified Health Use.

In Europe and North America the term may encompass conventional foods, foods to which components have been added or removed, and dietary supplements. Generally, they are intended to be consumed as part of the normal diet and contain biologically active components which offer the potential of enhanced health or reduced risk of disease. Professor Brasseur proposes the following definition of functional food in "Food or Drug: Definitions and Perspectives": "Food or food ingredient that has been shown to affect specific functions or systems in the body. Functional foods play an important role in disease prevention."

What distinguishes functional foods, then, is that they are foods, or specifically isolated compounds thereof, that have specific, scientifically substantiated (beneficial) effects. Examples are foods that contain specific minerals, vitamins, fatty acids or dietary fibre, foods with added biologically active substances such as phytochemicals or other antioxidants, and probiotics that have live beneficial compounds. Historically the first functional food was lime, recognised in the eighteenth century as preventing and curing scurvy. Others include broccoli, which contains sulforaphane, an antioxidant linked with a reduced risk of a number of cancers, especially lung, stomach, colon and rectal cancers; fatty fish – salmon, mackerel, sardines and tuna – which are rich in omega-3 fatty acids; and kiwifruit, which has antioxidant effects and may also benefit DNA repair enzymes.

Genetics has shown how nutrients affect the body at a molecular level and how dietary components can affect each individual differently. The emphasis in research is thus increasingly on isolating components that enhance well-being and can reduce the risk of disease. The FAO 2007 Report on Functional Foods considers functions and diseases targeted by nutrients.

Gastrointestinal functions, for example, are targeted by foods containing probiotics like lactobacilli or bifidobacteria and by prebiotics like inulin or oligosaccharides. The FAO report also considers CVD and cancer. Diets rich in natural antioxidants has been associated with prevention from and/or treatment of CVD. Epidemiological evidence, has shown that certain types of dietary fibres, certain probiotics, small molecule dietary antioxidants including ascorbic acid, vitamin E, glutathione, various polyphenols, carotenoids and selenium antimutagens may slow progression toward cancer.

But does food, particularly functional food, prevent and even cure disease? The European Commission Concerted Action on Functional Foods programme divides the effects of functional food into two categories: Type A, which improves function, and Type B, which reduces the risk factors of disease. Although "[reducing] the risk of disease" stops short of "prevents disease", prevention – or, at the very least – delaying the possible onset of disease may be inferred. Dairy products, calcium, and vitamin D all help to build bones and may help prevent osteoporosis, for example.

The 2007 FAO report specifically states that diets rich in antioxidants have been "associated with prevention from and/or treatment of

CVD". In his keenly thought essay, Professor Cummings describes how certain prebiotic carbohydrates have been shown to stimulate the growth of relatively rare health-promoting species of gut flora. "Changing the gut microflora in this way," he writes, "must count as 'correcting or modifying physiological functions', which defines a medicinal product in the European Community (Directive 2001/83/EC)." Cummings goes on to suggest that drugs, notably antibiotics, are unlikely to achieve the changes to gut flora that can apparently be ascribed to prebiotics. An example, he concludes, of a food ingredient "providing a unique benefit to health beyond drugs".

Similarly, rickets can be cured solely by vitamin D, coeliac disease by gluten-free diets, while type-2 diabetes can be controlled by diet (in preference to metformin), and probiotics treat and prevent antibiotic-associated diarrhoea (AAD) so successfully, writes Cummings, that "if there were a drug so effective it would be widely prescribed". Similarly, there are reports of successful experiments with protocols of four nutrients. ■

Fuzzy Frontiers and Overlaps

Instances of food – either diets or specific nutrients – preventing and treating disease are numerous. But along the continuum of "food and drugs for health and for the prevention and treatment of disease" drugs, too, are used for prevention.

Ubiquitous examples are fluoride in water supplies, aspirin to prevent blood clotting and colorectal cancer, while statin is widely used to control cholesterol levels. These drugs can only be effective, however, if those taking them keep to a low-cholesterol, high-fibre diets, and generally healthy lifestyle – just as Traditional Chinese Medicine practitioners, states Professor Schipper never prescribe medication without an accompanying change in diet. And although treatment is long, it is also root-and-branch, with no side effects.

The West saw a controversial development in 2003 in the shape of the "polypill", proposed by two British researchers. They contended that it could cut by 80% the incidence of Western society's two major killer diseases, heart attacks and strokes, if taken by everybody over 55. The pill contained a cocktail of aspirin to prevent blood clots, a statin to lower cholesterol, and agents to lower blood pressure. A group of Dutch scientists countered by advocating a polymeal, consisting of fish, wine, dark chocolate, fruits and vegetables, garlic and almonds. They argued it would be as effective, with none of the side effects.

Although the hullabaloo over the polypill was perhaps more news- than science-worthy, it is nevertheless significant in demonstrating how diet, specific nutrients, and drugs can all be used to the same effect, prompting questions about dividing lines. "Borders between good and bad, beneficial and dangerous, natural and artificial do not exist as such," writes Professor Brasseur in "Blurred Borders".

Indeed, a constant theme of this book has been fuzzy frontiers and overlaps, compounded by the rise of functional foods. As Dr. Antoine puts it: "What is normal and what is not?" Are we ill if we take statins because there is a history of heart disease in the family? Where do we stand on the health-disease continuum? Healthy or unhealthy? What's more, although a drug can reinforce a function or make the body do something it is not ready to do, diet can do the same thing (by cutting out certain kinds of food) as can certain kinds of bioactive nutrients. At what point does a disease begin? Where does the cut-off point lie? Is it always arbitrary? Against this background what are the definitions of food and of drugs?

The need for definition and distinction is wholly legitimate, with "different stakeholders [using] different classifications, retaining those that are most meaningful to their daily lives," writes Professor Brasseur in his contribution on definitions. But, as Professors Jones and MacKay suggest in their introduction, what distinguishes a food from a drug may not be as relevant as when it becomes a drug." Put another way, the answer is not whether, say, an oligosaccharide is a nutrient or a drug, but understanding that it has its place in a shifting, comprehensive healthcare paradigm where individual responsibility for health and drug-based treatments and surgery are part of the same continuum. "The understanding of complex biological systems forces us to reconsider boundaries with an open mind. Though clear-cut demarcations facilitate the

work of lawyers and inspectors, they are of little value to scientists, obstructing more than anything the understanding of living organisms and their interactions," writes Professor Brasseur.

Definition is the meat of regulators – and it is primarily labelling which distinguishes food from drugs, determined by their intended use. Traditional dividing lines between food and drugs should not stand in the way of consumers' access to knowledge. And while a strong regulatory oversight with its insistence on evidence-based proof is essential to ensuring safety, particularly as non-pharmaceutical research into functional food components continues apace, it is important that barriers should not needlessly prevent their development and their contribution to a comprehensive healthcare approach, underpinned by lifestyle and diet and encompassing functional foods, prescription drugs, and surgery.

Let us conclude with Professor Brasseur who writes in *Blurred Borders*: "Rules and limits should be regarded as tools not as delineations of what is right. They should be adaptable and meet the real needs of those who have agreed to use them at and for a certain time. Such an approach enables insight into what is really needed and can be improved upon for the benefit of all." ■

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- Disseminate relevant knowledge on diet and nutrition to professionals such as health care professionals, teachers, journalists as well as to the general public.

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In 2004 was created an international entity in order to develop international activities such as research support, scientific conferences or publications, to enhance collaborations between Danone Institutes and/or their members as well as to promote sharing of experience between Danone Institutes.

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