THOMAS GRAHAM

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Although Thomas Graham might seem to have little connection with our specialty, his discoveries, especially in physical chemistry, of which he has been called the father, have a direct bearing on fundamental intra- and extracellular processes, as well as on respiratory physiology, anaesthesia and resuscitation.

Education

Thomas Graham was born on 21 December 1805, at 55 St Andrew's Square, Glasgow. His father was a prosperous merchant and fabric manufacturer, who ensured that his son had a good education. Thomas attended Glasgow Grammar School (later the High School) and, at the age of 13, which then was apparently not unusual, entered Glasgow University. He studied classics, and also chemistry and natural philosophy, or science, graduating MA in April 1824.[1] His father wanted him to follow many of his forebears and become a minister in the Church of Scotland. Thomas, however, had decided on a career in chemistry, and with the connivance of his mother persuaded his father that the best divinity teaching was to be had in Edinburgh. There he enrolled, but in the Faculty of Medicine, not Divinity. Subsequently, his father discovered the subterfuge and disowned him, but he continued to receive help secretly from his mother.[2]

After a thorough training from some of the leading Scottish chemists, Graham returned to Glasgow in 1828, and began to earn his living by extramural teaching, and by contributing articles to a local magazine on the applications of science in everyday life. At the same time he continued with the research he had begun in Edinburgh. In August 1830, on the strength of a preliminary paper on the diffusion of gases, he was elected a member of the Faculty of Physicians and Surgeons of Glasgow. This qualified him to become a university teacher, and in September 1830 he was elected Professor of Chemistry at Anderson's (now Strathclyde) University. This brought about a reconciliation with his father. One of his students of this period described him as having uncombed red hair and a quiet, stiff, hesitant manner. It seems he was never a good lecturer.

International renown

In 1831 Graham presented his definitive paper on the law which is now named after him, his law of diffusion of gases. In 1833 he concluded an important piece of research into the three known phosphoric acids, which established the principle of polybasicity. This work brought him to the attention of the great Justus von Liebig, who sought him out while visiting Edinburgh in 1834 for the meeting of the recently formed British Association for the Advancement of Science, in which Graham was a very active participant. In the summer of

1836 Graham spent three months touring the Continent, and met a number of leading scientists, including Dumas and Gay-Lussac in France, Magnus and Mitscherlich in Germany, and again Liebig, with whom he established a lasting friendship.

In December 1836 he was elected Fellow of the Royal Society, his proposers being the two most eminent scientists in the country, Dalton and Faraday. This confirmed his position as a chemist of international stature and, in June 1837, he was appointed to the Chair of Chemistry at University College, London. He took up residence at 4 Gordon Square, and lived there for the rest of his life. At University College he was engaged in teaching chemistry, mainly to medical students. During the next 18 years he taught some 2,700, lecturing three times a week. Among these was Joseph Lister, who was very much influenced by Graham, and often referred to him appreciatively in later life. According to one source, it was Graham and Sharpey (Professor of Physiology at University College), who persuaded Lister to go to Edinburgh to train in surgery, with Syme.[3] He was Dean of the Medical School during 1842-44, and again from 1850 to 1852.

Graham continued to be active in the affairs of the British Association and the Royal Society, and in 1841, in a move to promote the professional standing of career scientists, he was one of the founders of the Chemical Society, and was its first President. At first the new society was accommodated at the Royal Society of Arts, but soon moved into another part of Burlington House, Piccadilly, where it is still.

Government adviser

Five years after Graham's appointment to the chair at University College, his textbook *Elements of Chemistry* was published. In the same year, 1842, he became involved in the work at the new Government Laboratory, later known as the Department of the Government Chemist. The original purpose of the Laboratory was not in any way for the benefit of the public or their environment, but to protect the revenue from fraud. Duty was levied on imported beer, wine and tobacco, and if re-exported duty could be reclaimed. The main purpose of the Government Laboratory in its early days was to ensure that dilution or adulteration had not taken place between import and export so that, for example, one ton of imported tobacco was not miraculously multiplied into two tons of exported tobacco by the addition of non-tobacco leaves, salt, sand and nitre.[4]

The laboratory staff consisted initially of one Excise officer, who was a self-taught chemist, so much of the work was farmed out. During the first year Graham analysed more than 100 samples of tobacco, and gave evidence in several trials. He compiled a list of some 25 common adulterants of tobacco, including sugar, molasses, coltsfoot, rhubarb, oak, elm and plane leaves, salt, potassium nitrate, alum, peat moss, oatmeal, and various dyes. In 1844, Graham was called to give evidence to a Select Committee on the Tobacco Trade, and he become recognised as an adviser on chemical matters to the government.

The advantage of having a trained staff of government chemists was soon obvious, and during January 1845 fifteen excise students started training in Graham's department at University College. This arrangement continued until 1858, by which time it was felt that the Government Laboratory was sufficiently well staffed to undertake its own training.

Graham became involved in the analysis of other products, such as pepper, which was dutiable until 1866, which he found to be adulterated with sago, ground rice, powdered slate, and quartz. He also examined coffee, which tended to contain ground roast peas, beans and orange pips, burnt sugar, and iron oxide. He investigated methods of purifying coal gas, and became an expert witness on chemical patents. In several enquiries he worked in a team with two other eminent chemists, Theophilus Redwood and A W Hofmann whose name became known to anaesthetists in the early 1980s for Hofmann's degradation of atracurium. Hofmann was one of Liebig's brightest pupils, and had been hand-picked by a committee headed by Prince Albert, to set up and lead the newly established Royal College of Chemistry in Hanover Square.

The first investigation the team undertook was into the alleged adulteration of beer by strychnine, and the second was into the purity of London's water supply, stimulated by the cholera epidemic of 1849.[5] The problem here was that no-one knew what it was in water that was harmful. Spa waters, which were thought to be health giving, had been analysed since the mid-seventeenth century, so it was thought that a certain mineral content was desirable in any drinking water. There was, however, what might be described as a gut feeling that the presence of organic matter undergoing active putrefaction was not a good thing. Initially, the level of nitrates was used as an index of putrefaction, and subsequently the reduction in oxygen content, estimated by the discoloration of potassium permanganate. Unfortunately, because of the absence of any standards, the report was indeterminate, and disappointing to the sanitary reformers. *

Master of the Mint

In 1851, Graham was a member of the scientific selection committee for the Great Exhibition, and at about the same time he was asked by the Master of the Mint, the great astronomer Sir John Herschel, to advise on the assaying of gold bullion that was being supplied to it, much of which had been found unsuitable for the minting of coins. When Herschel resigned in 1855, Graham was appointed to succeed him, relinquishing his chair at University College.[6] The post was no sinecure: Graham was given the task of reducing waste, and improving the quality of coins. His main achievement was to introduce the more durable bronze that we still

* It is tempting to imagine that these chemists might well have been in touch with John Snow. This possibility is reinforced by the fact that Snow obtained some of his anaesthetic agents, notably his supply of amylene, from John Bullock, a pupil of Liebig, who had a chemist's shop in Hanover Street, and was a friend and patron of Hofmann.

use today, to replace the copper coins which wore very badly. The Mint made a substantial profit from the recovery of the copper.

Graham's researches

Among Graham's researches there were three topics of special interest to anaesthetists - the diffusion of gases; osmosis, dialysis and the diffusion of liquids; and inhibition of the oxidation of phosphorus by certain vapours. For the earlier phases of his diffusion experiments, conducted about 1829, Graham enclosed gases in large test tubes with the outlet tubes oriented so as to avoid the effect of gravity. The contents of the tubes were analysed after four hours. The definitive experiments were conducted some 3 years later, with tubes of ½ inch diameter and 6 inches to 14 inches long, sealed at one end by a plug of plaster of Paris 1/5 inch thick, and inverted over mercury. With a tube 6 inches long filled with hydrogen, the whole contents escaped within 20 minutes, as shown by the rise of the mercury to the top of the tube. Subsequently, the mercury level started to fall, as air diffused into the tube. Applying Dalton's law of partial pressures, he reasoned that the external air was a vacuum as far as the hydrogen was concerned, and the tube a vacuum to the air. He experimented with a number of other gases, including carbon dioxide, oxygen, nitrogen, ammonia and nitrous oxide, showing that they diffused at different rates, which were inversely proportional to the square root of their densities.

These experiments were not serendipidous, but arose from some brilliant reasoning. It was by then accepted that the pressure exerted by a gas in a container was a manifestation of the force with which the atoms bombarded its walls. Graham argued that since equal volumes of oxygen and hydrogen at the same temperature exert the same pressure, then the force exerted by the atoms of each gas must be equal. But oxygen is 16 times heavier than hydrogen; therefore, since force = mass x acceleration, the hydrogen atoms must be moving much faster than the oxygen atoms. Hence they could be expected to escape more quickly, which is what he demonstrated.

Graham went on to apply his observations on diffusion to the mechanics of respiration, arguing that while the whole capacity of the lungs is some 300 cubic inches, the volume of a single breath is only about 20 cubic inches. This breath will fill only the windpipe and its larger branches, so that the contents of the ultimate reaches of the lungs might be expected only to advance and recede with each breath. But, he argued, this oxygen diffuses in, and carbon dioxide moves out, and since the latter is denser than the former, 81 parts of carbon dioxide are replaced by 95 parts of oxygen. This mechanism, according to Graham, provided for the full and permanent inflation of the ultimate air cells of the lungs.

As a further demonstration of gaseous diffusion, he placed an animal bladder half full of coal gas in a receiver of carbon dioxide. After 12 hours so much carbon dioxide had diffused into the bladder that it was full to bursting point. This demonstration provided supporting evidence in the debate about whether gases could cross animal membranes. Later, he showed that indiarubber selectively absorbed nitrogen, leaving an oxygen-enriched atmosphere in a bag originally full of air. Anaesthetists, of course, are well acquainted with these phenomena, seen, for example, in the passage of nitrous oxide into tracheal cuffs.

His textbook, *Elements of Chemistry*, published by Ballière in 1842, was a massive volume of almost 1100 pages. The first 240 were devoted to the basic sciences: heat, light, evaporation, diffusion, distillation, atomic theory and chemical affinity. He then proceeded through the chemistry of non-metals, metals, organic compounds and, finally, the chemistry of plants and animals. He introduced the linear balanced chemical equation in the form we are familiar with today.[7] What would have been of interest to John Snow was a very full discussion of heat, the boiling point of liquids, the influence of atmospheric pressure on the boiling point, hygrometry, dew point, wet-and-dry bulb thermometry, and a formula for calculating vapour pressure in air. Unfortunately, this is difficult to test today, because the temperatures are given in degrees Raumur, and the pressures in Parisian lines. This book became the standard text and was soon translated into German and other European languages, and was very influential for a number of years.

In 1846, Graham reported experiments on the differential diffusion of gases from a mixture. Almost one century later this work formed the basis of the method used during World War 2 to separate the fissile isotope of uranium, U^{235} from the ordinary and much more abundant U^{238}. In his Bakerian Lecture to the Royal Society in 1850 Graham considered whether the spread of salts through a solution was similar to diffusion. In 1861 he broke new ground in a paper presented to the Royal Society. He pointed out that, as regards diffusibility, some solutions, in an analogy with gases, might be regarded as volatile, and others as fixed. The volatile solutions were able to crystallise. The fixed were not, and were slow in the extreme to diffuse. Examples of these were starches, dextrin, gums, caramel, gelatine, and certain animal and vegetable extracts. Since glue was the commonest preparation of gelatine, he proposed (from kolla, the Greek word for glue) to designate such compounds as colloids. Substances of the other type would be classed as crystalloids. He suggested that: 'the distinction is no doubt one of intimate molecular constitution'.

Other terms coined by Graham are dialysis, osmosis (to replace the old-fashioned osmose), pectin, sol and gel.[8]

The third observation of particular anaesthetic interest is actually the earliest, and is one that John Snow mentions several times. It was well-known that a piece of phosphorus in air is surrounded by white smoke, as a result of the slow oxidation or combustion that it undergoes, and that for the same reason it glows in the dark. In 1829, Graham described how the presence of certain vapours would inhibit this reaction: ethylene, then known as an olefiant gas, in a concentration of 1:450, sulphuric ether 1:150, naphtha vapour 1:1820 and turpentine vapour 1:4444. He described an experiment in which two or three moist sticks of phosphorus are placed in a pint sized jar of air: 'It will fill with white fumes. Introduce a little ether vapour - the fumes will disappear in a few seconds and not reappear, the air becoming quite transparent. Stopper the bottle. The ether will slowly react with oxygen in the air to form acetic acid - this will take a few days, after which the white fumes will reappear. Similarly, ethylene prevents the luminosity of phosphorus in the dark, and will prevent the sparking of hydrogen and oxygen in the eudiometer.'

John Snow used this observation to support his contention that ether and chloroform act by damping down the oxidation process in the body. Snow had shown that oxygen consumption and carbon dioxide output were reduced during anaesthesia. Graham had demonstrated that ether inhibited oxidation in vitro; by extension, Snow argued, this should explain the in vivo observation, too.[9]

Graham died at his home in Gordon Square on 16 September 1869. He had returned a few days previously from a stay at Great Malvern. Possibly he had gone to Dr Gully's hydropathic institution in Malvern for the fashionable water cure. I had difficulty finding where he is buried. To their great chagrin, neither the Royal Society, of which he had been a Vice-President, nor the Royal Society of Chemistry knew. His grave is in the grounds of Glasgow Cathedral. There is a statue of him in George Square. (Figure 1) A volume of his collected works, in which all the researches described will be found, was published some six years after his death.[10]

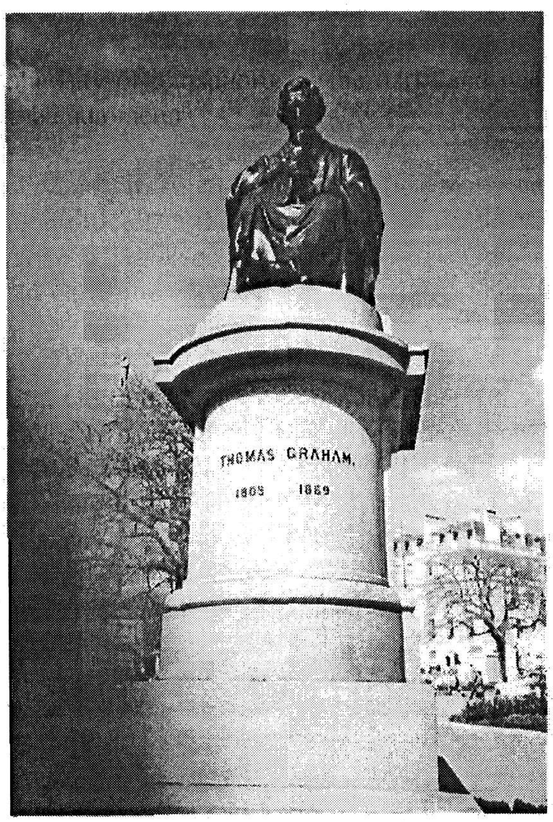

Figure 1. Statue of Thomas Graham, in George Square, Glasgow

Conclusion

Graham was described in one posthumous appreciation as an atomist. Certainly all his observations on diffusion strongly supported both the atomic theory and the kinetic theory of heat. In his *Elements of Chemistry* Graham discusses the older material or caloric, and the newer undulatory, theories of heat. He preferred the latter because, he says: 'the different propeties of heat can be referred to differences in the size of the waves, as differences in colour are accounted for in light'.

In many of his ideas Graham was much in advance of his contemporaries. He was for long a supporter of the move towards the decimalisation of weights and measures, having observed that scientific papers using national systems were rarely translated into other languages. He also advocated the decimalisation of coinage, and also the establishment of an international unit of currency. During his lifetime, chemistry changed from being an experimental science pursued by a few amateurs and itinerant lecturers, into a fully fledged professional occupation in which one could make a career and a living. No-one did more than Graham to help bring this about.

Acknowledgements

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