crept into a paper (in the *Geographical Journal*, vol. ix, p. 410, 1922) by the late Mr. Mallory. He mentioned that he had been told by the Professor of English Literature at Oxford that the physiologists had proved in a pressure-reducing chamber that it was impossible to climb to the top of Mount Everest without oxygen. There was evidently some misunderstanding about this statement. The experiments referred to were possibly those made on unacclimatized persons by Kellas, Kennaway, and myself. The Oxford physiologists who have concerned themselves with the subject have never regarded the ascent of Mount Everest as impossible, on physiological grounds, without oxygen, or supposed for a moment that any experiments hitherto made in steel chambers indicated such an impossibility; but it is quite evident that the less complete the acclimatization, the more benefit will be obtained from oxygen. In this connexion it would be interesting to try whether acclimatization at the highest camps could not be hastened by administering small doses of an acid salt or of ammonium chloride, so as to get rid of the alkalosis more rapidly than in the natural slow way.

The Acclimatization Phenomena as a Whole.

When we regard as a whole the phenomena of acclimatization to a low atmospheric pressure we see at once that when acclimatization is complete the organism is still in a physiologically different state from what it was before exposure to the low pressure. The breathing is greatly increased; the concentration of the blood in haemoglobin and red corpuscles is also increased, as well as the blood volume; the blood plasma is altered in composition; the blood-forming bone-marrow is increased; and if we could detect them we should probably find histological changes in the lung epithelium. All these changes, and probably many more which are not yet discovered, centre, quite evidently, round what may metaphorically be called an attempt to keep the oxygen pressure, and simultaneously the hydrogen-ion concentration, about and within the living tissues constant. But the attempt is not completely successful: a slight deficiency in both oxygen pressure and hydrogen-ion concentration remains over, and doubtless becomes more appreciable the greater the altitude. This deficiency is necessary as the stimulus for maintaining the state of adaptation. The primary stimulus is the deficiency in oxygen pressure, and the hydrogen-ion deficiency is secondary to this. If we ask why the hydrogen-ion deficiency at least should not be fully compensated, the probable answer is that this would involve such a loss of sodium, and perhaps potassium, as is resisted.

Although from its very nature the process of acclimatization cannot be theoretically complete, yet it has the unmistakable effect of keeping the oxygen pressure within the body approximately constant without more than slight disturbance of other important factors in environment. The carrying out of this involves both functional and structural changes. These changes are intelligible and predictable on the assumption that life tends to assert and maintain structure, activity, and environment in a normal and definitely co-ordinated manner. Without this assumption biology is to my mind nothing but a jumble of disconnected and unintelligible observations. It was a true physiological sense that led Ludwig and Bohr to suspect the existence of oxygen secretion by the lungs, and that led Claude Bernard to his great generalization about the active maintenance of the constancy of the internal environment. The everyday reactions of living organisms to change in environment seem to me not in any way different in kind from the reactions during acclimatization to higher altitudes, and I cannot myself see that physiology is ever likely to get anywhere worth getting to unless it makes the fundamental assumption just referred to.

This assumption differentiates it completely from mere applied physics and chemistry. Biological reality is something which our present physical and chemical conceptions fail to represent and can never come near representing until they have been profoundly modified. This modification may come in the future, but meanwhile biology must regard itself as an independent science. It is also an exact science, since it is everywhere dealing with and revealing

exact regulation and co-ordination. Nothing gives us, perhaps, a clearer and more comprehensive idea of this regulation than thorough study of the phenomena of acclimatization to higher altitudes. That study must, however, be based on exact quantitative results and coherent reasoning; and if in this paper I have had to point out incoherency in the reasoning of scientific friends who in other directions have made most valuable contributions to physiology, I hope that both you and they will understand that any other course would be inconsistent with scientific honesty on my part.

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The Vicary Lecture

ON

RICHARD OWEN AS CONSERVATOR.

GIVEN IN THE THEATRE OF

THE ROYAL COLLEGE OF SURGEONS OF ENGLAND,
NOVEMBER 12TH, 1924,

BY

SIR ARTHUR KEITH, M.D., F.R.S.,
CONSERVATOR OF THE MUSEUM.

(Abstract.)

In the Vicary Lecture of last year* I gave an account of the dramatic proceedings which culminated in the confession by Sir Everard Home that he had burnt the Hunterian manuscripts. These proceedings were enacted in this College during the summer of 1824—just a century ago. The Board of Curators, six members of the Council of the College, to whom the management of the museum was delegated, then met to consider afresh the problem of describing and cataloguing John Hunter's specimens—some 17,000 in number. The Board sent for its conservator, William Clift, and told him to proceed with the preparation of catalogues forthwith.

William Clift.

Let us see how William Clift was situated. He was then 50 years of age; from Hunter's death in 1793 until the summer of 1824 he had, in reality, been servant to Sir Everard Home; all he knew he had picked up for himself; time after time he had made fruitless attempts under Sir Everard Home to carry out the task just imposed upon him. His daily duty of meeting parties at the door of the College and conducting them round the floor-space and galleries of the museum—a single great room, which had been built for the display of Hunter's treasures—was altogether a joyful task for him. But when it came to stepping into John Hunter's shoes and explaining and interpreting to all the world the harvest of the greatest medical genius of the eighteenth century—a much abler man than the faithful, modest William Clift might well have shrunk back. He set to work in his old way, pen in hand, and in his fairest script copied from such Hunterian documents as he had saved, and from other sources, such extracts as threw light on the collections under his charge. The Board met from time to time and examined these extracts, but by the end of 1826 it had become apparent to John Abernethy, surgeon to St. Bartholomew's Hospital, and at this time President of the College, the truest and most helpful friend William Clift ever had, that further skilled assistance must be given if a catalogue were to be forthcoming.

* See BRITISH MEDICAL JOURNAL, 1923, vol. ii, p. 1127. The sources from which I have drawn information for this lecture are the same as given there, with the addition in the present instance of *The Life of Richard Owen*, by the Rev. Richard Owen, 1834.

The required assistance, as we must suppose Abernethy knew, was close at hand. In the autumn of 1826, when catalogue production was becoming urgent, Mr. Richard Owen, having become a member of the College at the age of 22, put up his plate in Cook's Court, Carey Street (within a stone's throw of the museum), to practise his profession—mostly among young lawyers. Little more than two years had elapsed since he had finished his apprenticeship to a surgeon in Lancaster, in which town he was born and bred. One year he had spent in Edinburgh winning the golden opinion of that most enlightened anatomist Dr. John Barclay. The second year he spent at St. Bartholomew's. Abernethy at once took him on as a prosector, and found that Barclay's strong letter of recommendation in nowise exaggerated Owen's ability. From Barclay young Owen had learned to appreciate Hunter as well as the more modern anatomical schools of France represented by Cuvier and Cuvier's rivals—the philosophic anatomists. In Edinburgh Owen had taken the initiative in founding a Hunterian Society. As a student at St. Bartholomew's he wrote two papers on surgical subjects—one on a case of aneurysm of the gluteal artery, the other on a case of encysted calculus of the bladder. Taking all these circumstances into account one cannot help thinking that Abernethy had something to do with the selection of the site at which Owen sought to establish himself in practice during the autumn of 1826.

Clift and Owen.

When the Board of Curators met in February, 1827, Richard Owen was asked to attend. He was engaged to assist Mr. Clift, his emoluments being £30 a quarter, with permission to attend to his practice in the intervals of his duties. Thus William Clift and Richard Owen were brought together, one of the strangest partnerships to be found anywhere in the annals of medicine or science. They were contrasted types. Clift was a small man, only a little over 5 ft.; Owen stood 6 ft. in his stocking soles. Years later Carlyle described him as "the tall man with the great glittering eyes," for his eyes were great and full, and Clift's were small and sunken. Clift was born of humble people; he was happier as servant than as master. Owen came of a good family; his father was a West Indian merchant who fell on evil times. Owen was born to command; he claimed equality with the best. Clift was the meticulous gatherer of small facts; Owen, we shall see, dealt with big things; he could imagine, create, and discover; he was a statesman; he could conceive and execute. But Clift and Owen had this in common—partisanship: they raised common enmities with ease and maintained them with vigour. Thus it came about that Richard Owen was engaged to assist William Clift to prepare catalogues, but in the course of events, as one could have foreseen, it soon came about that the roles were reversed, and later still Owen dispensed with the conservator's assistance altogether.

Leaving these two men to pursue their vocations in the museum throughout the year of Owen's appointment (1827), we turn aside to note certain events which happened outside their daily routine and which had a very important bearing on the history of the museum. The conservator's house looked out on the trees of Lincoln's Inn Fields; its back staircase served the gallery of the museum as well as the conservator's bedrooms. In September, 1827, the inmates of this house were the conservator, his wife, and their two children—William Home Clift, a young man of 26, and Caroline Amelia Clift, aged 25. Young Home Clift was to be his father's successor. His father had trained him in museum ways, and at present he was struggling very ineffectively at the compilation of catalogues. He was light, gay, and fond of company, a source of anxiety to his father. It was otherwise with Caroline; she had inherited her father's slight build of body and could pull his heart-strings as she would. Years afterwards Caroline Fox described her as "a very perfect little fact in the great history of the world."

Caroline Clift.

It so happened on a September day in this year that little Caroline mounted some steps to put a bell-pull to rights, overbalanced, and fell. Her brother fetched Richard Owen

from the museum to render first aid. The tall young surgeon with "the great glittering eyes" speedily proceeded to fall in love with his patient—"the perfect little fact." It was a brief wooing; by Christmas-time he had presented her with a carved tortoise-shell comb, a volume of Cowper's poems, and an engagement ring. He was 23 and she was 25. She knew well that she had linked her fortunes with those of a man destined to greatness. This apparently insignificant affair of the bell-pull, we can now see, turned out to be a critical event in the history of the museum; it not only gave Richard Owen a perfect wife, but it secured for the Hunterian Collection the services of the one man then in England who had the ability and energy to grapple with its problems.

Two years later, although still in practice, Owen was regarded as a permanent member of the museum staff and paid at the rate of £150 a year. But even in 1829 such an income was altogether insufficient to set up house on. Hence early in 1830 we find Owen in Birmingham in search of a house-surgeoncy. From there he wrote a letter to Caroline which permits us to see what kind of man and lover he was. "You know not," he writes, "how rapidly I have succeeded in gaining golden opinions from all sorts of men in this place. You have lent me your attractions and have prompted me in all my interviews." He saw no prospect of an early marriage by settling in Birmingham; his heart, he wrote, longed for the "happy Fields." The true lover at the end of this letter exclaims, "The die is cast; you shall be with me ever and guide and prompt and see my exertions." He returned from Birmingham in this mood, and within twelve months the College was in possession of its first batch of catalogues—for which it had waited wellnigh thirty years.

We find entries in William Clift's private notebook which show us that Owen did not return to his rooms in Cook's Court but became an inmate of the conservator's household. He paid £15 a quarter for board and lodgings and young Clift paid the same. But there was this difference: Owen settled his account promptly on pay day, whereas the scapegrace Clift was always behindhand and had usually to borrow part of his belated payment to meet present needs; Richard, however, borrowed only when setting out to see his mother in Lancaster—which he did every year, and often had to ask for an advance to bring him back to work. In September, 1832, these entries in William Clift's private notebook suddenly cease. When we turn to his diary we find the explanation. "On the evening of this day (September 11th, 1832) a most unfortunate and fatal accident occurred to my dear son; in alighting from a cabriolet near the lower end of Chancery Lane at about 10 o'clock p.m." . . . September 17th: "This morning about half-past-three my poor son breathed his last." The cab accident comes into the history of our museum, for it left the ultimate succession to the conservatorship open to Richard Owen.

The amount of work which Owen got through after his return from Birmingham, the researches he carried out, and the discoveries he made, leave one in wonderment; with the death of William Home Clift in 1832 they became almost incredible. But his Herculean efforts did not impress the Board of Curators—for a reason I shall explain presently. In 1833 Owen protested; he complained to the Board that he was worse paid than the meanest country apothecary and that he had to carry on his work in a draughty thoroughfare. The Board raised his salary to £200 a year and gave him a more comfortable workplace. In 1834 the museum had to be rebuilt and extended. All the responsibilities of the change fell on Owen. In the following year, 1835, when the building alterations were completed, quarters were provided for Owen, now the assistant conservator, behind the museum, with a door opening on Portugal Street, on which "Mr. Owen" had his name inscribed, for he still regarded himself as a surgeon waiting for practice. In this year, 1835, his salary was raised to £300 a year, which apparently justified him in embarking on marriage. Early in the morning of his thirty-first birthday, July 20th, he and Caroline Clift drove to St. Pancras Church, where they brought an eight years' engagement to an end by a happy marriage and a brief honeymoon. And then back to catalogues! Here, however, I must note a little but significant entry in William Clift's cashbook. He drew from the bank

500 golden sovereigns at this time; 30 he put in one bag for the bride, 30 in another for the bridegroom, and 440 went to their bank account. John Hunter's apprentice was proud of his son-in-law, and well he might be.

Cataloguing the Museum.

I must now turn back and briefly trace the course of events in the museum from the time Owen was engaged as assistant to the conservator until his marriage. From the minute-books of the Board of Curators we find an ever-recurring call for catalogues. The conservator always responds "coming," but never comes. When Owen returned from Birmingham matters rapidly changed—catalogues were prepared in rapid succession. In the spring of 1831 six volumes had been written, printed, and published; six sections of John Hunter's collection had at last been supplied with catalogues—namely: (1) Morbid specimens in spirits; (2) Morbid specimens in a dried state; (3) Human and comparative osteology; (4) Natural history preparations; (5) Monsters; (6) Vascular and miscellaneous preparations. The two largest and most important sections still remained untouched—namely, the physiological series, about four thousand preparations, by which Hunter had sought to illustrate the manner in which the functions of the animal body are carried on in all forms of living things—movement, circulation, respiration, digestion, reproduction, development, and growth. Even more difficult to handle was his collection of fossils—enigmas to the men of Hunter's time, but not to him.

The Board ordered Owen to prepare a catalogue of the physiological series. It was estimated that it would occupy him for three years. Part I, which covered the preparations illustrating the modes in which locomotion and digestion were carried out in the animal kingdom, occupied two years. While cataloguing this single section of the physiological series Owen found it necessary to dissect two hundred animals in order to identify Hunter's preparations and to complete the founder's formulated design. He became the most active Fellow of the recently founded Zoological Society; somehow he scraped the money together to become a life member. He claimed and obtained the first call on all the animals which died in the gardens of the Zoological Society. He gave such vivid and full accounts of his dissections as had never before appeared in England. A single example, chosen from scores at our disposal, will serve to illustrate the quality of his genius. A member of the College, Mr. George Bennett, brought home from the Pacific in 1831, and presented to the museum, a specimen of the pearly nautilus—a "living fossil," almost the first to reach Europe. In 1832 the Board entrusted it to Owen and requested him to dissect it and prepare a description for publication. He spent five months on it, and, although imperfectly preserved, he unravelled its exact structure, and fathomed its relations to all other living cephalopods as well as the relations of these to one another; he applied to it Hunter's methods, and noted how its bodily functions had been carried out during life. He was his own dissector and his own draughtsman—a finished workman in both capacities. The monograph was published by the Council at a cost of £365. It drew unstinted praise from every source except that from which Owen had expected most—his own Board. Clift thought "Owen was much to be pitied"; Sir Anthony Carlisle, a member of the Council of the College, bluntly said that "his pearls had been cast before swine"!

Conflicts with the Board.

On reading the minutes of the Board of Curators at this time one is made conscious of a feeling of antagonism between the members of the Board and its servants Clift and Owen—an antagonism which flared up into open strife in 1841 and reached a climax in 1842. In the spring of 1841 Owen finished the fifth and last volume of the catalogue of Hunter's physiological series. The preparation of this catalogue occupied him ten years, during which time he passed from being an obscure member of his College to being acclaimed "the first anatomist of the age." Honours were being showered on him by learned societies at home and abroad. The ladder by which he reached greatness was made by Hunter, but it was just because Owen understood

Hunter's aim and design and knew how to make the steps secure that success came to him. As he proceeded from volume to volume of this catalogue he encountered innumerable problems which required laborious research and uncommon insight for their solution. In the ten years spent on it he contributed to learned societies 157 papers—all of them abiding additions to knowledge, many of them opening up great uncharted territories of animal life. Besides these he wrote ten volumes in the form of catalogues or treatises. Every year, from 1837 onwards, he gave in the theatre of the College twenty-four Hunterian lectures, in which he expounded fresh observations and generalizations gleaned in the course of his work in the museum and in the Zoological Gardens. One marvels at what he accomplished; and how he managed to get so much out of his body, his brain, and his purse. For the scientific societies to which he belonged were expensive; he was fond of society, of the theatre, of music, of dining out, and of famous men. Yet his income was his salary of £300 with £50 additional for lectures, for soon after his marriage he abandoned all thought of gaining money from practice. Caroline Owen must have managed well.

In 1839 the Board of Curators was reconstituted and became the Museum Committee. Three members of this committee require our attention—Mr. Robert Keate, surgeon to St. George's, Mr. George James Guthrie, surgeon to Westminster Hospital, and Mr. John P. Vincent, surgeon to St. Bartholomew's. Their patience with Mr. Owen was wellnigh exhausted by 1840. The committee informed him that it was dissatisfied with the way he was spending his time, particularly as regards the study of fossils. Owen defended the collection and study of fossils and declared he worked solely for the credit of the College. Mr. Darwin had presented to the College the remarkable fossils he had gathered in South America while on board the *Beagle*, and Owen had described them. "When," asked Mr. Guthrie, "had Mr. Owen obtained permission to do such a thing?" Mr. Keate, who was then president, told him "he must give his full time to the museum or resign." The committee threatened to stop lectures and all forms of research until catalogues were completed. The painting of a picture of a chimpanzee, which Owen was having made for the museum, was left on his hands because it had not been sanctioned. The attendants in the museum were ordered to report directly to the committee every week, not through their officers. Mr. Guthrie went into the museum and altered the arrangement of the specimens.

The climax came on January 25th, 1842. A special meeting of the Museum Committee, with certain additional representatives from the Council of the College, was summoned to consider Owen's position. Clift and Owen waited by the door; Owen was called in. The president of the College, Mr. Guthrie, informed him that there was grave dissatisfaction in the Council concerning the manner in which he performed his duties. Owen expressed his regret if he had given cause for offence and was conciliatory. He was then asked if he would take over the duties of conservator with the proviso that he would publish nothing without having first obtained the permission of the Council. Owen expressed his willingness to take over the duties of conservator with one exception—namely, the daily task of conducting parties round the museum. This difficulty was overcome; William Clift, who was to become senior conservator, wished to retain the conduct of parties. Poor William Clift was merely a spectator in these proceedings! He was given £400 a year for life. He vacated the conservator's official residence and his son-in-law moved into it. And here we must leave Owen as he enters the second period of his conservatorship; it was to last fourteen years—until 1856, when he became superintendent of the Natural History Department of the British Museum. Suffice it to say that it was even busier, more brilliant, and more turbulent than his first period.

A Clash of Ideals.

What was the cause of these conflicts between Owen and his committee? He was proud, imperious, overbearing, and, it must be owned, selfish and jealous, especially towards his rivals and juniors. His committee may be accused of shortsightedness. Although these opposing qualities may have

contributed to the quarrel, yet the real cause of the conflict lies elsewhere. The truth is that Owen had yoked John Hunter's chariot to Cuvier's steeds, and his committee, if it did not know exactly what had happened, did see that the chariot was moving in a wrong direction as far as surgery and medicine were concerned. Hunter pursued his studies and built up his museum to throw light on man—on the nature of his disorders and diseases, and on the manner in which the functions and actions of his body are accomplished. He knew well that the collections he had assembled might be employed for two other purposes. His dissections might be used, not for the study of function, but for the classification of all living things into natural groups and orders. He knew that his great collections of fossils opened vistas into past ages of the world. John Hunter turned his back on such aims, but two years after his death Cuvier set to work. He built up anatomical collections just for the two purposes which Hunter refused to entertain, and by his genius and industry enthralled the world by his discoveries during the first three decades of the nineteenth century. At first Owen's sympathies were with Hunter's

original aims, but they soon became dissipated under the brilliance of Cuvier's sun. When Cuvier visited our museum in 1830, two years before his death, he fired young Owen with his aims and zeal. We must remember that in Owen's time the Natural History Departments of the British Museum were in abeyance, and Owen set out to make our museum supply a national deficiency. He intended to make it the home for the classification of all forms of animal life—for the separation of the animal kingdom into natural groups according to structure. More particularly he intended that the museum should become the headquarters for the interpretation of past worlds of life. If we are to understand the continual friction recorded in our minutes throughout Owen's time, we have to keep in mind the clash of ideals—the ideal the Museum Committee had in view, and the ideal which Owen nursed as if it were his religion. The committee was for ever trying to get Owen to go its way, and he was for ever breaking off to follow his own path. It was in Cuvier's world that Owen lived, not John Hunter's. If we are to study structure and function as a service to medicine we must go "back to Hunter."

British Medical Association.

PROCEEDINGS OF SECTIONS AT THE ANNUAL MEETING, BRADFORD, 1924.

SECTION OF PATHOLOGY AND BACTERIOLOGY.

Professor C. H. BROWNING, M.D., President.

XANTHOMA AND XANTHOSIS.

BY

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THE importance of the part played by cholesterol and its esters in pathological processes is receiving increasing recognition, an outcome of the large amount of work— anatomical, chemical, and experimental—which has been done on this subject in the last twenty years. The purpose of the present communication is to integrate a number of different pathological states in which the deposition of cholesterol fat is the salient anatomical feature, and to show at the same time how frequent is the occurrence of minor grades of this condition in relation to a large series of pathological processes.

When cholesterol fat is deposited in a cell in crystalline form it causes the cytoplasm to assume a "foamy" appearance in paraffin sections, while a sufficient aggregation of such cells gives rise to an area opaquely yellow to the naked eye. The gross and microscopic appearances are exemplified normally by the outer two-thirds of the adrenal cortex, and in the female by the corpus luteum, especially the corpus luteum of pregnancy in its later stages. Pathologically, foamy cells are, in the main, phagocytic cells of endothelial origin, but there is evidence to show that fibroblasts may become similarly affected, and in the central nervous system a corresponding part is played by the neuroglia.

In a previous communication¹ I have classified local cholesterol-fat deposits into those which are due solely or principally to local tissue changes, and those which are the focal expression of a condition of hypercholesterinaemia. The latter group is much the smaller, its principal constituents being the various forms of cutaneous xanthoma, the "strawberry gall bladder," cholesteatomata of the choroid plexus, and probably certain cases of arterial atheroma. The former group includes a large number of local necrotic and chronic inflammatory lesions of various kinds, and, especially, conditions in which there is retention in the tissues of lipid-rich secretions, extravasations, and exudations. A third group might be added: lesions in which the deposit of cholesterol fat is merely the continuation of a normal function of the cells of the part—for example, adenoma of the adrenal cortex.

The extracellular deposition of crystals of pure, or nearly pure, cholesterol in many of these lesions, and the frequent occurrence of foreign-body giant cells in relation thereto, is described in detail in the paper referred to above. Suffice it to say here that the condition is usually associated with some form of cellular death, and especially with lesions in which large aggregations of foamy cells are themselves becoming, or have already become, disintegrated. Thus we find that whereas small early cholesteatomata of the choroid plexus are composed simply of closely packed aggregations of foamy cells in the meshes of a delicate connective-tissue stroma, the corresponding tumours of larger size are mere encapsuled collections of cholesterol plates, with or without related foreign-body giant cells.

A short account may now be given of some of the more important examples of cholesterol-fat deposit.

A. HYPERCHOLESTERINAEMIC XANTHOSIS.

1. Xanthoma.

This is a cutaneous disorder in which one or more bright yellow plaques or nodules make their appearance on various parts of the body. Several clinical varieties are recognized, according to the site, character, and etiology of the lesion. When it is confined to the eyelids—and this is much the most common form—it is termed "xanthoma palpebrarum"; when it is more widely disseminated "xanthoma multiplex." Sometimes the lesions are flat (xanthoma planum), sometimes nodular (xanthoma tuberosum). In a small proportion of cases, usually of multiplex type, there is an underlying diabetes—hence xanthoma diabetorum. The essential lesion is the same in all—the accumulation in the subepithelial layers of the skin of numerous phagocytic cells laden with esters of cholesterol. These cells are present in great profusion as a rule, and to begin with are most abundant around the smaller blood vessels. In lesions of longer standing, especially those of tuberosum type, there is also much proliferation of fibrous tissue, which leads ultimately to a relative reduction in the number of foamy cells, as well as to diminished vascularity.

The presence of giant cells in cutaneous xanthoma has often been noted. For the most part these are giant foamy cells, in which the nuclei, numbering from two to twelve or so, are situated centrally, and the peripheral cytoplasm is exactly similar to that of the uninucleated forms. Occasionally giant cells of the ordinary foreign body type with deeply eosin-staining non-foamy cytoplasm, and larger and more widely scattered nuclei, are seen. They are most frequent in xanthomas of larger size and longer standing, and are often related, as above described, to extracellular crystals of pure or nearly pure cholesterol which have been formed by disintegration of the foamy cells. There is evidence to show that such cells pass through a "foamy giant-cell" stage.

Cutaneous xanthoma, especially the multiple tuberosum type, is sometimes accompanied by similar lesions affecting