THE GEORGE BIDDER LECTURES

The Society for Experimental Biology, with the generous support of the Company of Biologists Ltd., have instituted a series of formal public lectures to be given by distinguished members of the Society, and subsequently to be published, as appropriate to their theme, in either the Journal of Experimental Biology, or the Journal of Experimental Botany. The series is named after Dr George Bidder, who played an important role in the founding of both the Company and the Society.

A. P. M. LOCKWOOD, Hon. Zool. Sec.
N. SUNDERLAND, Hon. Bot. Sec.
Society for Experimental Biology

The second George Bidder Lecture, London:

TISSUE CULTURE AND ITS CONTRIBUTION TO BIOLOGY AND MEDICINE

H. B. FELL
Department of Pathology, University of Cambridge

(Received 15 February 1972)

INTRODUCTION

I feel deeply honoured at being invited to give the George Bidder Lecture this year. I was asked to talk about tissue culture; as it happens this is a not inappropriate subject for the present occasion, because Dr Bidder was one of the original benefactors of the Cambridge Research Hospital, which later was renamed the Strangeways Research Laboratory in honour of its founder and became the chief centre for tissue culture in this country. When the Hospital was built in 1911, Dr Bidder thought that it ought to have more land and so with characteristic generosity provided the necessary funds for the purchase of another acre. I cannot tell you how grateful we have been for that extra land as the Laboratory has developed and expanded through the years, and how much we appreciate Dr Bidder's foresight and kindness.

It is just over sixty years since tissue culture first appeared on the biological horizon. In the first George Bidder lecture, my predecessor, Sir Vincent Wigglesworth (1971), quoted the following passage from one of his early publications: 'Lip service is often paid to the importance of pure science as an aid to practice. But even the loudest advocates sometimes fail to make out a convincing case. That is because it is rare for the results of research in pure science to have an immediate practical application. It is only when the intervening links are interposed that the connexion becomes apparent.' As I shall hope to show in my lecture today, the progress of tissue culture provides a striking illustration of the truth of these words. It also demonstrates very clearly how much we have to rely on chance rather than on deliberate planning for major advances.
in biological knowledge. This is because of the apalling complexity of living matter which makes it impossible to predict what we are likely to find in a given area of investigation – we can only plunge in hopefully and keep our eyes wide open for the unexpected which, as every research worker knows, is so often far more important than the expected result.

**HISTORY**

The origin of tissue culture was itself a matter of chance, and was really a fall-out from a neurological study.

In the early years of this century the formation of nerve fibres was a highly controversial topic. It was not known whether the fibres grew out from the nerve cells in the central nervous system and ganglia, or whether they were secreted by the cells of the tissues through which the nerve fibres were destined to pass. When one considers that in man a nerve fibre may be several feet in length, one can hardly wonder that people found it hard to believe that such an enormous structure was merely the extension of a single cell.

The great American biologist Ross Harrison (1907, 1910) became interested in this problem and he solved it by some very simple experiments. He explanted a fragment of nerve cord from a frog tadpole into a drop of frog’s lymph on a coverslip; he inverted the coverslip and sealed it to a hollow-ground slide to form a hanging-drop culture. Then he watched the bit of cord under a microscope. In a few hours nerve fibres began to sprout from the nerve cells in the cord and pushed their way through the lymph with the aid of delicate undulating membranes at the tip of the growing fibre. So here was a conclusive answer to the question of whether nerve fibres arose as outgrowths of nerve cells – obviously they did, and this result virtually put an end to the controversy.

Not only nerve fibres but also individual cells emerged from the explanted cord, so we can justly regard Harrison’s preparations as the first tissue cultures. Harrison himself did not pursue the matter further, because he changed jobs just then and lacked the facilities for such work in his new department.

But his results soon attracted the attention of others. At the Rockefeller Institute in New York, Burrows (1910) and Carrel & Burrows (1910) succeeded in growing the tissues of warm-blooded animals. Using the original hanging-drop method, they found that if they explanted a fragment of embryonic chick heart into a drop of blood plasma, cells wandered out of the tissue and the heart continued to beat for a few days; then the culture died. If, however, a saline extract of embryonic tissues was added to the plasma (Carrel, 1913) the cultures could be maintained in a state of active growth for long periods. Carrel also developed a method for cultivating cells on a larger scale in small flasks (Carrel, 1923), which was a much more convenient procedure than the hanging-drop technique. The tissue fragments were embedded in a thin layer of clotted plasma above which was a fluid phase, usually of embryo extract, which was withdrawn and replaced every few days. When the clot became overpopulated pieces were removed and used to seed new flasks. This marked the beginning of what is now known as cell culture.

In 1914 a second and for many years a far less popular branch of tissue culture made its first tentative appearance as a result of a chance observation by David Thomson.
Tissue culture and its contribution to biology and medicine

In that year he published a paper (1914a) in which he reported two distinct types of growth in culture which he termed 'controlled' and 'uncontrolled' respectively (1914b). He found that if he explanted a toe or a feather rudiment from an embryonic chick the rudiment continued to enlarge as a whole, much as it did in the embryo; by Thomson's definition this was 'controlled' growth. At the same time unorganized cells emigrated from the cut surfaces of the explants in the usual way by 'uncontrolled' growth. Thomson did not fully appreciate the importance of his observation and did not continue the work, which was in fact the first step in the development of the technique of organ culture, which I shall be talking about later in my lecture.

CELL CULTURE

Individual cells

Thanks to the old hanging-drop method and to various techniques that have been derived from it, it is possible to study living cells kept at body temperature, under the highest magnifications of the light microscope. This has greatly increased our knowledge of certain aspects of cell behaviour.

What Thomson (1914) called the 'uncontrolled' growth of cells from the cut edge of a tissue fragment explanted in a hanging-drop culture is a fascinating sight under the microscope (see Strangeways, 1924). After a few hours' incubation, delicate translucent tongues of protoplasm begin to protrude from the explant - these are the cells beginning to crawl out of the tissue. Gradually each cell hauls itself clear of the parent explant and adventurously wanders off into the surrounding medium. Finally a broad halo of actively dividing cells is formed around the original fragment. The cells are in constant slow movement; they are continually changing their shape, and their organelles move about in the cytoplasm. Essentially the same process takes place in the body during wound healing.

I want to mention two of the many important observations that were made on these simple hanging-drop cultures. I have selected these particular studies because they are very much to the fore at the present time.

Pinocytosis. The first is Warren Lewis's discovery in 1931 of the phenomenon known as 'pinocytosis' or drinking by cells. In that year Lewis wrote: 'certain cells in our cultures, especially the macrophages, take in globules of fluid from the surrounding medium . . . By pinocytosis the cells are able to take in substances which cannot diffuse into them or be taken into them by ordinary phagocytosis of semi-solid particles.' When a cell is drinking, ruffles of delicate undulating membranes keep appearing and disappearing at different points on its surface. The clefts between these membranes are, of course, filled with fluid from the culture medium, so that one might say that the cell is drinking soup. The membranes forming the sides of the cleft fuse and so trap the fluid in a vesicle enclosed by a piece of cell membrane. These membrane-bound vesicles stream into the interior of the cell where they rapidly shrink and vanish. Probably all cells can engulf fluid in this way, but in some types the process takes place at a submicroscopic level and can only be detected by electron microscopy.

More than twenty years were to elapse before the true significance of this important finding became apparent, as the result of a chance observation by de Duve and his colleagues (de Duve et al. 1955; for review see de Duve, 1969) at the University of
Louvain. In the course of some fractionation studies on a normal rat liver, undertaken with an entirely different object, they found that a number of digestive enzymes were located in a bound form in certain cytoplasmic granules which de Duve named lysosomes. Subsequent research in many different laboratories showed that these bodies represented the cell’s digestive system, and also demonstrated their relationship to Lewis’s pinocytotic vacuoles.

At first the pinocytotic vacuoles contain only the ingested material, but as they pass into the cytoplasm they fuse with the primary lysosomes, which tip their package of enzymes into the vacuoles, and the contents are then digested. These basic observations have opened up a vast new field of work in different branches of cell biology and pathology (see Lysosomes in Biology and Pathology, 1969).

Contact inhibition. The second discovery that I wish to consider is Michael Abercrombie’s observation (Abercrombie & Heaysman, 1954; for review see Abercrombie, 1970) of what he termed ‘contact inhibition’. He found that when a cell is moving over a glass coverslip on a course that causes it to collide with another cell, it does not crawl over the other cell, but merely ceases to move. Amongst fibroblasts and epithelial cells this inhibition of motion seems to be brought about by a spasm of contraction at the site of contact, which Abercrombie suggests is set off by some signal from the cell contacted. An important difference between normal and malignant cells came to light in this work (Abercrombie, Heaysman & Karthauser, 1957), in that malignant cells have much less capacity for contact inhibition than their normal prototypes. Thus Abercrombie found that sarcoma cells would move readily across fibroblasts in a mixed culture. The situation, however, is complex, and different cell types give different responses to contact. The subject has attracted a lot of attention and is still being investigated.

Cell fusion. Of recent years, I think that the most remarkable and fundamental research on cell cultures is that on cell hybridization. I remember my first introduction to this extraordinary phenomenon. Some years ago I was attending a meeting of the European Tissue Culture Club, at which Dr Barski of Paris described how someone in his laboratory had – I think accidentally – produced a mixed culture of two cell lines with recognizable differences between their chromosomes. When the two types of cells were grown together, hybrid cells eventually appeared which contained the chromosomal complement of both parent lines. Personally I thought the evidence presented in this preliminary account was very convincing, but the idea was so startling that other members of the audience were sceptical. However, the observations of Barski, Sorieul & Cornefert (1961) were repeated and confirmed by other workers in various parts of the world. (For reviews see Harris et al. 1966; Littlefield & Goldstein, 1970.)

In these early experiments only a very small proportion of cells in a mixed culture fused, and not all cell types were capable of spontaneous hybridization. A vitally important technical advance was made by Professor Henry Harris of Oxford (Harris, 1965; Harris & Watkins, 1965). In 1958 Okada had shown that when the Sendai virus was added to a culture of Ehrlich tumour cells it caused widespread cell fusion. Using the inactivated Sendai virus, Harris made use of this fact to induce hybridization of cells on a large scale; not only cells of widely different types but even cells of different species could readily be made to fuse. In this way a completely new field of cell
Tissue culture and its contribution to biology and medicine

biology has been opened up which now extends into cancer research (for review see Harris, 1971), cell physiology, genetics (for review see Davidson, 1971), immunology and biochemistry. Many fascinating and imaginative studies have been made on various aspects of cell hybridization, and there is no doubt that at the present time this is one of the most active growing points of cell culture.

The individuality of cells

I want now to mention an interesting philosophical implication of cell culture.

In 1924 Strangeways wrote: 'The behaviour of the cells in \textit{in vitro} cultures seems to indicate that each individual cell should rightly be regarded as an independent unicellular animal. Although somatic cells have existed in a state of close interdependence and functional association for untold generations of individuals, yet, as shown by tissue culture, they are capable of active amoeboid movement, of reproduction by division, and of growth and reconstruction into normal daughter cells whilst existing in a free-living condition apart from the body.'

This view was not generally shared, for the reason that hitherto all attempts to grow single cells in culture had failed, whereas a single unicellular organism readily forms a colony. So it was argued that somatic cells were just as mutually dependent in a culture as they were in the body. However, the failure to obtain a colony from a single somatic cell proved to be due, not to an inherent incapacity of an isolated cell to multiply, but merely to inadequate technique.

In 1948 the American workers Sanford, Earle & Likely succeeded in establishing cultures from single cells, known as clone cultures, by a very ingenious technique. The isolated cell was sucked into a very fine capillary tube containing what was called 'conditioned medium'; this was medium that had been taken from a conventional type of culture in which a large population of cells had been growing. The piece of tube that enclosed the cell and its conditioned medium was broken off and placed in a big culture dish containing ordinary nutritive medium. The single cell multiplied actively in its protective tube, and soon the large family of daughter cells began to crawl out of their nursery into the larger world of the big dish. There they flourished and established a large, rapidly growing colony. Nowadays clone cultures are widely used, but as we shall see, they can be obtained by a much simpler method than that adopted for these pioneer experiments.

Modern cell culture

I want now to indicate briefly how cell cultures are made and used at the present time.

When we consider the staggering complexity of cells' normal environment in the body, I think it is very surprising that they can be cultivated \textit{in vitro} at all, and that they survive the ruthless treatment they receive at the hands of the cell culturist. In a normal tissue, cells are held together by intercellular material which they secrete and they are arranged in very elaborate patterns in different tissues. To make a cell culture, the first thing we do is to destroy completely the normal architecture of the tissue by digesting away the intercellular material and reducing the tissue to a suspension of single cells. The cells are then seeded on the floor of a Petri dish or on the walls of a flask or bottle containing nutritive medium. Soon they spread out on
the glass and begin to multiply. Every few days the old medium is sucked off and replaced by fresh, and when the population reaches a certain density the cells are detached from the glass by digestion, again reduced to a suspension of single cells and re-seeded in a fresh vessel. This cycle is repeated week after week, month after month, often for years on end.

To maintain cultures in this way, certain environmental conditions are required. 

*Food.* Obviously, a suitable nutritive medium must be provided. And here we are in a difficulty, because we do not know very much about the cells' nutritive medium *in vivo.*

In the body, the cell is nourished by intercellular fluid supplied by the bloodstream and derived from blood serum. But before the serum reaches the cells it is filtered through the walls of the capillary blood vessels. The fine structure of the capillaries is not identical in all organs, so the filtrate received by the cells probably varies in different parts of the body. Moreover, every organ contains cells of many different types, and there is no telling what products these various cell types contribute to the intercellular fluid. We have no means of obtaining precise information about the composition of this intercellular fluid, because it is technically impossible to obtain it in a pure state.

A great many synthetic media have been devised and are extremely valuable, but it is a tiresome fact that, apart from a few specially 'trained' cell strains, all cells require the addition of a little blood serum - perhaps less than 5% - for prolonged growth and survival. No one knows why. It is not enough to add the known components of serum; it seems clear that there must be substances present in complete serum, probably in minute quantities, which have not yet been identified, but which are essential for the cell's welfare.

Imperfect though these media still are, they have made it possible to use cell cultures to investigate the physiology of growth at the biochemical level, and much important information in this field has now been obtained. The original media, of which saline extract of embryonic tissues was an essential component, were far too complex for this purpose, and rendered this otherwise ideal material almost useless for the biochemical study of growth.

The technique of seeding cultures with a dilute suspension of single cells provided a very efficient way of obtaining clone cultures. This procedure was originally developed by Puck and his colleagues (Puck & Marcus, 1955). Originally they used what was called a feeder layer. This was a sheet of cells in culture which had received a dose of irradiation that was sufficient to inhibit cell division permanently but did not prevent metabolic activity. A dilute suspension of the cells from which clones were desired was added to the feeder layer, and individual cells then proliferated to form a clone colony each of which could be isolated and transferred to another culture vessel. Later it was discovered that clones could be obtained from many permanent strains of cell cultures without a feeder layer. Only a proportion of the cells in a culture are capable of producing clones. Such clone colonies can be isolated and subcultured, and provide a rather more uniform population for experimental purposes than the genetically mixed cultures from which they were derived.
Malignancy

As I said earlier in my lecture, in a cell culture cells are placed in a very abnormal environmental situation, and it is surprising that they can adapt themselves to these altered conditions as well as they do. There is evidence that one factor in their successful survival is the fact that their chromosomal constitution usually changes during growth *in vitro*.

As of course you know, the cells of every species of animal and plant have a characteristic number of chromosomes, which *in vivo* varies very little. But cells grown for a long time in the unnatural environment of a cell culture often undergo abnormal division and in the process acquire more than the normal number of chromosomes. Such cells become remarkably well adapted to life in culture, and can be grown *in vitro* for years, perhaps indefinitely.

However, this is not true of all cells. It has been possible to establish strains of cells in which the number of chromosomes remains normal. Such cultures continue to flourish and proliferate, sometimes for as long as a year. Then growth gradually dwindles to nothing and the cells die. A remarkable example of this is provided by the work of Hayflick & Moorhead (1961), who studied the behaviour of 25 different strains of human cells. In every strain the characteristic number of chromosomes remained unaltered, and after a long period of active growth eventually the cultures always died. No way of reversing the degenerative changes has been found, and Hayflick and Moorhead suggest that the phenomenon may represent a built-in senescence at the cellular level, but not everyone accepts this view. This capacity of the altered cell lines to grow indefinitely *in vitro* will suggest to many of you a possible connexion with the problem of malignancy. Such a connexion does in fact exist, and it is not uncommon for such cultures to become malignant, so that when grafted into an animal of the same species, the cells give rise to a transplantable tumour. This was first observed almost simultaneously by Firor & Gey (1945) at Johns Hopkins University and by Earle and his collaborators (1943) at the American National Institutes of Health. It has been confirmed many times since then.

Virology

When Ross Harrison made his classical observations on the outgrowth of nerve fibres, he little thought that this work was destined to develop into a method that would revolutionize the science of virology and lead to the production of a vaccine to protect people against poliomyelitis. This is one of the most remarkable examples of the truth of Sir Vincent Wigglesworth's contention that the results of research in pure science seldom have an immediate practical application, because the intervening links have not yet been obtained.

For many years virologists had been frustrated by the fact that viruses, unlike bacteria, cannot be grown in an artificial medium *in vitro*. This is because viruses are intracellular parasites, and are completely dependent upon living cells for protection, nourishment and the ability to multiply. The advent of tissue culture, and especially the development of methods for making cell cultures on a very large scale, removed this barrier and resulted in spectacular progress in all aspects of virology.

The first step in the application of tissue culture to the prevention of poliomyelitis
was made in 1949, when Enders, Weller and Robbins showed that the poliomyelitis virus could be grown in cultures of normal human embryonic cells. In 1954 Dulbecco and Vogt succeeded in cultivating poliomyelitis virus in cell cultures of monkey kidney. Once the virus had been successfully propagated in culture, the preparation of a vaccine against the disease became possible. This was achieved by Jonas Salk and his colleagues (Salk, 1954), who grew the virus in cultures of monkey kidney and then inactivated it with dilute formaldehyde. When injected into children and young adults, vaccine prepared from such cultures induced the formation of antibodies against polio and afforded good protection against the disease.

**Organ Cultures**

With rare exceptions, cells grown in a cell culture soon cease to exercise the specialized functions that they performed in the body. All that the cells of an established cell line can do is survive and multiply. This is not surprising. In its normal habitat – the body – the cell forms part of an intricately structured society in which it lives and works in close collaboration with other cells of many different types and specialized for many different functions. Torn from its natural environment and isolated from its usual colleagues, the cell in a cell culture is forced to adopt a far simpler way of life than that to which it is accustomed *in vivo*, and usually abandons all its normal functions except those required for survival and reproduction.

So when we want to study organized, functional tissues *in vitro* cell cultures are no good. Instead we use the organ-culture technique that I have already mentioned. This method, of which there are now many different forms, is designed to encourage cells either to form or to maintain a tissue of normal architecture, and to preserve the normal structural and functional relationship between different cell types.

Thomson's report (1914) of what he called ‘controlled’ growth *in vitro*, in which explants of embryonic structures grew as a whole, much as they do in the body, was confirmed by several other workers who showed also that such explants underwent progressive histological development. Oddly enough, for many years these important findings attracted little attention, and with one exception tissue-culture laboratories concentrated their efforts entirely on cell culture. The one exception was the Cambridge Research Hospital, now the Strangeways Research Laboratory, where the subject has been actively pursued and developed for nearly fifty years. Later, organ culture was taken up first by Pieter Gaillard of the University of Leiden and then by Etienne Wolff, now in Paris, and the organ-culture technique in various forms is now in world-wide use.

The scientific objectives of organ culture are quite different from those of cell culture, and unlike cell cultures, organ cultures are only occasionally used for studies on growth. Organ culture might be defined as the cultivation *in vitro* of tissues in a differentiated, functional state similar to that of the organs from which they were derived; usually we only want to maintain a balance between cell death and cell multiplication in such explants, so that the cell population remains stable, as it does *in vivo*. 


Cellular interactions

Of recent years, organ culture has made spectacular contributions to the study of cellular interactions. I will give you two examples of the pioneer work in this field.

Grobstein. The first example concerns the development of the salivary gland.

The normal adult gland contains several different types of cells, which are arranged according to a definite pattern. The saliva is manufactured in a mass of little chambers lined by secretory cells, the secretory chambers discharge the saliva into a tree-like system of branching ducts which lead into the main duct opening into the mouth; the whole structure is held together by connective tissue cells and their intercellular substance. The gland is richly supplied with blood vessels and enclosed by a capsule of fibrous connective tissue.

I want to emphasize the mutual dependence of the various cell types in maintaining the normal functioning of the adult gland. This interdependence of different cell types is also a feature of the normal development of the glandular rudiment in the embryo, as was beautifully demonstrated by Clifford Grobstein (1953) on the foetal gland of the mouse.

In the early embryo the gland first appears as a tiny bud from the epithelium lining the mouth. Below this little bud is an oval mass of cells of a different type, which are destined to form the protective capsule and supporting tissue of the gland. As the epithelial bud lengthens, it invades this underlying mass of cells; at the same time it begins to branch and forms a complex tree of secretory tubules embedded in the mass of connective tissue.

Grobstein separated the little epithelial downgrowth from the underlying tissue, and studied its behaviour in culture under different conditions. When he cultivated the bud by itself, the cells survived but merely spread out into an unorganized sheet with no trace of glandular structure. In other experiments he combined the epithelial rudiment with the connective tissue of the embryonic lung. Again the rudiment failed to develop, and only formed a round nodule embedded in the lung connective tissue. But when Grobstein recombined the epithelial bud with its own salivary gland connective tissue, it immediately began to grow and branch, and formed a glandular tree of remarkably normal appearance.

Moscona. The mechanism whereby embryonic cells contrive to organize themselves into that complex society that we call a tissue is a fascinating problem. As often happens in biological research, such information as we have serves only to shift the mystery to another level.

A remarkable series of investigations by Aaron Moscona, beginning about 1952, opened up a new approach to this question. He began this work at the Strangeways Laboratory.

Moscona proposed to disaggregate the cells of an embryonic organ at a very early stage of development, and then, instead of seeding the naked cells as a cell culture, to allow them to reaggregate and grow them as an organ culture. Would the randomly arranged cells in such an aggregate be able to sort themselves out, and form a tissue like that from which they were derived? One set of experiments that Moscona performed while he was with us was on the kidney rudiment (mesonephros) from 4-day embryonic chicks. He disaggregated the cells in the usual manner, by digesting away
the intercellular material, then placed the loose collection of cells in a hollow-ground slide in a drop of culture medium; in due course they sank to the bottom of the hollow by gravity. Finding themselves once more in close contact with one another, the cells again became stuck together in a fairly solid mass, which Moscona was able to transfer to the surface of a nutritive clot. The little explant was then incubated, and when examined after a few days’ growth it was found to have developed a tubular structure, very like that of the original organ.

A lot of fascinating work has been done in the field of cellular interactions since the original observations that I have quoted.

The effects of biologically active agents

An organ culture is an excellent experimental system in which to study the responses of organized, functional cells to environmental factors. In the body, the cells are exposed to all kinds of humoral influences brought to them by the blood-stream; so it is often impossible to discover what a particular environmental factor is doing to a particular tissue, because the situation is hopelessly confused by complex systemic reactions. These reactions are, of course, automatically excluded from the closed in vitro system provided by an organ culture. So it is a very fortunate thing that the response of tissues to such agents as hormones, vitamins and drugs is often essentially the same in organ culture as it is in the body. This means that we can examine in great detail under closely controlled conditions not only the effects of selected environmental factors on the explant but also – what is equally important – the reciprocal effect of the tissue on its environment; in this way information can be obtained that would be difficult or impossible to get in any other way. That we can now use organ cultures for a wide variety of biochemical studies is due partly to the remarkable development of microchemistry during the past decade, and partly to technical improvements in the organ culture method, for which we are largely indebted to the late Dr O. A. Trowell (1959).

At the present time organ culture is being widely used to study the physiology and pathology of cartilage and bone, especially with reference to diseases of the joints.

In 1929 (Fell & Robison, 1929) we found that when the cartilaginous limb-bone rudiments were dissected from 5½- to 6-day chick embryos and grown as organ cultures, they continued to grow and to develop histologically and anatomically to a remarkable degree. Subsequent work at the Strangeways and other laboratories showed that cartilage and bone give essentially the same response to certain vitamins (e.g. Fell & Mellanby, 1952) and to hormones (e.g. Reynolds, 1968) in organ culture as they give in the intact animal. These and other types of skeletal explants could therefore be used to analyse such effects at the biochemical level in much greater detail than is possible in vivo.

I have mentioned cartilage and bone merely because I myself have worked extensively on these tissues, but similar experiments have been made on explants from many different organs.
Tissue culture and its contribution to biology and medicine

Link between cell culture and organ culture

Nowadays there is not such a sharp division between cell culture and organ culture as there used to be. This is because methods have been developed for maintaining differentiated cells in thin sheets in which the individual living cells can be studied under the microscope. The cultures of nerve cells prepared by Dr Edith Petersen (1950) in Dr Margaret Murray’s laboratory in New York, provide one of the most remarkable examples of this. During cultivation the cells form myelinated nerve fibres and can be maintained in vitro for months without showing any deterioration. Dr Murray and her colleagues are using them in studies on nervous diseases (e.g. Cook et al. 1971) and the mode of action of drugs.

CONCLUSION

In this lecture I have only lightly scratched the surface of this vast subject, but I hope that I have given those of you who are unfamiliar with the field some idea of the main achievements and potentialities of tissue culture.

It is sometimes hoped that tissue-culture experiments can be used to replace animal experiments, but unfortunately this is not practicable. I will try to explain why. Tissue culture methods have been specifically designed for the experimental study of cells; as we have seen, they can provide basic information about cell physiology and behaviour. Moreover, when some biologically active agent such as a hormone, vitamin or drug is found to have the same effect on a tissue in culture as it has on the same tissue in the body, then the direct action of the agent on its target tissue can be analysed in great detail under the simplified, readily controlled conditions provided by a tissue culture.

Now let us consider what a tissue culture cannot tell us. It can tell us nothing about the physiology of an animal’s circulatory or excretory systems; nothing about the physiology of its brain or sense organs; nothing about the complex interactions of the endocrine glands; nothing about the functioning of the lungs or alimentary canal. This means that a chemical compound that might appear quite harmless when tested on a tissue culture, when administered to a patient might produce disastrous side-effects due to systemic reactions that could not be reproduced in the simple in vitro system.

So I am afraid that we must accept the fact that experiments on tissue cultures, valuable though they are, are ancillary to, but rarely if ever a substitute for, experiments in vivo.

REFERENCES


STRANGEWAYS, T. S. P. (1924). *Tissue Culture in Relation to Growth and Differentiation.* Cambridge W. Heffer and Sons Ltd.

Tissue culture and its contribution to biology and medicine


