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HUMANISM, HISTORY, AND NATURAL SCIENCE IN MEDICINE*

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The Linacre Lectureship, to which the Master and Fellows of St. John's College have done me the honour to call me, is, I believe, the oldest medical lecture foundation in this country. It has a tradition all its own in that it was one of the academic activities that survived the greedy spoliations of this University by Henry the Eighth that Latimer was to deplore in 1550, and again because its founder, Thomas Linacre, has a great place in our history, not only as a physician and the translator of the works of Galen from their original tongue but also as the principal restorer of the knowledge of Greek in this country.

In this work of restoration he was one of that small group of English humanists which included Grocyn, Lily, Colet, and Thomas More, who shed such lustre upon English learning in their time; one of whom, Thomas More, was to catch the imagination of all Christendom in his day as the living embodiment of all that was best in Christian Humanism; an ideal by which he lived and, in the manner of his death, endorsed.

What perspectives of opportunity, therefore, this lecture must conjure up in the heart and mind of anyone possessed of imagination and called upon to take his place in the long sequence of Linacre lecturers.

It would be vain for me to hope to rise to the height of this opportunity. I can but do my best to set out in their relevance to medicine three themes which come naturally to the mind in the contemplation of Linacre's life and circle. They are Humanism, History, and Natural Science.

For my shortcomings in a journey that will take me beyond the confines of medicine, as we ordinarily think of it, I ask your charity. And if I venture upon this task, it is not with the hope of completing it, but out of the conviction that to rebuild a bridge between medicine and the humanities is a pressing need; that this building can be done only from the side of medicine; and that someone must make a start if medicine is not to lapse into a mere congeries of techniques, to fail in coherence on its theoretical side, and to suffer the loss of its traditional values. Linacre was a bridge-builder between the ancient world of Hellas and Tudor England. It is not unfitting, therefore,

that the Linacre lecturer of to-day should, in however humble a fashion, seek also to be a bridge-builder.

I shall not be derogating from Linacre's just place in history when I submit that perhaps his chief claim to enduring renown amongst us was his reintroduction of Greek to England. He was already an accomplished Greek scholar when, almost by chance as it might seem, he turned aside in his Italian journey to visit Padua, then a foremost centre of medical learning and of philosophy. There with a remarkable celerity he graduated as a doctor of medicine. Upon his return to England the Universities of Cambridge and Oxford hastened to confer upon him the like degree, with an easy liberality that must excite the puzzled envy of the present generation.

I am not enough of a historian to know precisely what could have been the course of the studies so speedily accomplished, but we learn that he defended his thesis with skill and applause against all comers, that within a few years of his return to his native land he had been appointed physician to that formidable patient King Henry the Eighth, and had embarked upon his famous translations of Galen, about which, were I strictly faithful to the provisions of his foundation, I should now be discoursing to you. One of his last acts was to found these lectures, expressing in his Deed of Gift the wish that they should "redound to the glory of God, the true art of medicine, the relief of the fallen, and the increase of the realm." I take leave to say, even in this bleak age of the spirit in which we live, that no nobler ideal of the vocation of the true physician could be proposed.

In a Harveian Oration before the Royal College of Physicians in 1948 I ventured to submit the claim of medicine to a place as of right within the body of the natural sciences. It is not my purpose to-day to reiterate this claim, but rather to propose to you that in its nature and aim medicine transcends the natural sciences; that medicine has in it an element also that properly belongs to the discipline of historical science, and that, ranging high above these, it has, at its best, qualities of humanism that the natural sciences, at least, can scarcely claim. Humanism, History, and Natural Science therefore are, I submit, the elements which medicine, worthily conceived and practised, integrates, or seeks to integrate, into a harmonious whole.

*The Linacre Lecture delivered to the Master and Fellows of St. John's College, Cambridge, on May 6.

Humanism

In his attractive seventeenth-century phraseology Hobbes reminds us that "the Light of Humane minds is Perspicuous Words, but by exact definitions first snuffed, and purged from ambiguity," and there can be few terms in respect of which this process is more necessary than the one now in question—namely, Humanism. Aristotle provided the first apology for an intellectual and secular humanism in his *Ethics*. Boethius, in his *Consolations of Philosophy*, gave us an early and familiar apology for a truly Christian humanism; and since his day, and particularly during the Italian Renaissance from the time of Petrarch onwards, ideals of humanism, secular and Christian, have been many.

In our own time and country Pater and Housman have expounded their views on the subject, and have written of a humanism in which the cultivation of the mind, of an intellectual excellence, is an end in itself.

But it seems to me that the humanism which a Linacre lecturer must put before you must be the Christian ideal and not the purely secular one, though this undeniably has its own intrinsic excellence. With the narrowest of all conceptions of humanism, that which equates it with a classical education, I am certainly not now concerned. Nor do I adopt any of the definitions given in that impressive shorter dictionary which emanates from another seat of learning than this.

Let me say, more positively, to what I do refer by the term "humanism." The Christian world inherited from the ancient world an idea and an ideal of culture which had three aspects: a speculative aspect, the ideal of truth, *veritas*; a moral aspect, the ideal of virtue, *virtus*; and an oratorical and literary aspect, *eloquentia*. And, since we are the agents of thought, speech, and action, this ideal may properly be called humanism.

Here is a humanism that strives for intellectual excellence, on the speculative side for the perfection of the lower reason which is ordered knowledge, *scientia*, and for that of the higher reason which is wisdom, *sapientia*, by which we are enabled to place knowledge in the whole framework of life; while, on the moral side, it includes practical wisdom—that is, prudence. Aristotle in his *Ethics* points out that science deals with things that are of necessity and with universals, while prudence deals with the affairs of men and not with universals only but with particulars. Thus it demands experience.

In the application of science to the practice of medicine the physician needs practical as well as speculative wisdom. He must be governed in his actions by a wise regard for the whole welfare of each patient individually. This regard is the peculiar, the essential, act of the virtue called prudence, which transcends natural science and comes within the category of moral excellence—ethics.

Finally, a complete humanism demands also the literary quality of eloquence: lucidity and conciseness of language and the skilled use of analogy and metaphor, which is what the mediaevals spoke of as rhetoric.

This is the humanism we see so beautifully exemplified in the life of Linacre's youngest and most famous pupil, Sir Thomas More, the patron saint of humanism. To whomsoever may not have read them I recommend the biography of More, and the smaller volume upon More's place in English literature and history, written with such insight by the late Professor R. W. Chambers, himself a rare humanist; works which have done so much to clear away those mists of provincialism and prejudice that have blinded the eyes of so many writers on More.

More's humanism had an eager zest for the things of the mind and a fine sense of proportion—"nothing too much"; a clear sense of the limitations of the State when viewed against the natural rights of the human person, and the courage to resist tyranny in the State; a clear and unfailing vision of what lay beyond finite values; and the grace to look beyond these to the hope of a greater experience in another sphere of existence. Here, then, is the humanism I should like you to associate with your thought of Linacre and of the practice of medicine. It is all implicit in the terms of this lecture foundation, drawn up by him in his last years and already quoted.

This occasion therefore seems to me one singularly appropriate for an exposition of medicine, not primarily as a theoretical and practical activity within the realm of natural science, but as an activity whose full scope and final end transcend natural science. With this confession of faith I turn to my second theme—namely, the relation of medicine to historical science.

Relation of Medicine to Historical Science

Medicine to-day carries the wounds of much ruthless administrative planning, but what she most needs is some intellectual organization from within, and as part of this it is important that we should ourselves undertake some analysis of her relations to the disciplines under which her activities are subsumed.

In a recently published book, *The Concept of Mind*, the Waynflete Professor of Metaphysical Philosophy in the University of Oxford, Professor Gilbert Ryle, writes that medicine is but "the name of a somewhat arbitrary consortium of more or less loosely connected enquiries and techniques, a consortium that neither has, nor needs, a logically trim statement of programme."

This is surely an erroneous notion of the nature and methods of medicine, lacking both in historical sense and in philosophical comprehension. Yet it is significant that such a definition should find serious utterance, and that in Professor Ryle's mind—if indeed I may apply this term to the neutral dispositions of an avowedly anti-intellectualist philosopher—medicine is, as it were, comparable to a travelling country dealer's horse and van, wandering the countryside from farmhouse to cottage, with its odd assortment of wares, chosen in a spirit of opportunism, casually thrown together and having no other relationship than that of contiguity.

Yet, however apt the analogy, the light of common sense shows us that even the travelling dealer has a unity of method and purpose, capable of and needing that trim logical statement of programme that Professor Ryle denies to medicine, either as a possession or as a requirement. Yet it has seemed worth while to cite this pronouncement because it hints at what may, even now, be thought of medicine by many others, even within its own ranks, who have not given serious thought to its history and problems. Who can doubt that the mushroom growth of specialisms, especially therapeutic specialisms, in medicine is tending to its disintegration as a body of ordered knowledge taught by men alert to lift their minds out of the mass of detail? This state of affairs is justification enough for an attempt to subsume medicine under the notions of history and natural science, for now, more than ever, some logical principles must be impressed upon those who will influence thought and practice in the medicine of the future.

In discussing in what sense medicine may be said to come within the discipline of historical science I shall submit,

also, that what is known as psychological medicine belongs primarily to this discipline and not to that of natural science. In doing so, I begin to tread upon dangerous ground, knowing full well that many rhetorical land-mines may be expected to go up noisily and dustily in my track as I proceed upon my hazardous way. Nevertheless, someone must clear the ground if it is to be made fertile soil for the growth of clear and coherent notions in psychological medicine.

Those who are acquainted with Collingwood's stimulating work entitled *The Idea of History*, or with Whitehead's *Modes of Thought*, where the same thesis is briefly expounded, will know something of the argument I shall try to develop, but to many within the ranks of medicine this will be unfamiliar and it is to them primarily that I address my thesis.

History in Medicine

We are prone to take it for granted that our activities in medicine are all to be subsumed under the heading of scientific theory and practice on the one hand, and that of purely empirical and traditional arts on the other. However, in the primary and essential process of eliciting what we call the history of an illness, our activities do not come within any of these categories. We are in fact seeking to collect a record of past events that for us are not sense data, but things that have happened not under our eyes; things that, more often than not, we cannot submit to any process of scientific verification. This record we proceed to subject to a process of critical thought. From its items we select, discard, and assemble in the light of our previous experience; and the final product of our activity is the sublimation of a certain kind of evidence from one source and of a critical study of it from another. Also, since the evidence we thus collect includes not only events that have happened to the patient but, in addition, actions that he has performed, there appears a new element not encountered in natural science—namely, human action. Between a simple event and a human action a distinction has to be made. In short, what we call "the history" in clinical medicine is not a mere chronicle of events, subjected to no analysis or interpretation, but it is a true exercise in historical method, as I shall seek to define this. This is not yet to assert that we are historians in the sense commonly understood by historians, but that we are using their method, which is not the method of natural science.

Distinction Between Natural and Historical Science

Let me briefly elaborate the distinction that I wish to make between natural and historical science, but although I begin from Collingwood's conception of history I shall allow myself the liberty of differing somewhat from him in his application of this conception to psychological factors in medicine.

The prime method of natural science is the observation of events, the flux of which forms a moving spectacle before us, with such verifications and repetitions of this observation as sound factual conclusions may demand. Under the term "observation" I include the method of controlled experiment which Bacon has spoken of as "putting nature to the question." Having observed these events as particulars, we then seek to determine the patterns and sequences into which they fall, and from these to make the generalizations that we speak of as laws of nature. The historian, on the other hand, is not concerned with events which he perceives, nor does he seek to make generalizations, abstractions, or to propound universals. He is concerned with human actions that lie in the past, though they may

have their consequences in the present, which have not the quality of sense data as these are understood in natural science. His evidence is the written and archaeological record, to which he applies a critical judgment based on his experience, using those processes of selection and assembly that I have spoken of as of the essence of clinical history taking. To his final conclusion there go the same two elements that we have seen in the clinical history. In both historical science, as the historical expert conceives this, and in taking a clinical history there is a subject-object composition.

Now the historian regards his task as concerned not with simple events as such, but with events as determined by, and expressive of, human thought—that is, with human actions—and his quest is to uncover the motive forces which, for him, are the inside of the event. Events are not spectacles which he observes and seeks to classify, but something that he seeks to go behind so that he may uncover the human thoughts and motives, conscious and unconscious, that they express.

Collingwood gives a simple example that may make this distinction clearer to those who are not familiar with it. He says, "When a scientist asks, 'Why did that piece of litmus paper turn pink?' he means, 'On what occasions do pieces of litmus paper turn pink?' When a historian asks, 'Why did Brutus stab Caesar?' he means, 'What did Brutus think which made him decide to stab Caesar?' The cause of the event for him means the thought in the mind of the person by whose agency the event came about; and this is not something other than the event, it is the inside of the event itself."

It is the function of the natural scientist to ask the first kind of question, but that of the historian to ask the second kind; and, having asked it, he does not proceed to formulate general laws or to indulge in predictions, and in this also he differs from the natural scientist.

The True Historical Method

We come now to consider the relevance of all this to medicine. It is clear that the historian does not regard sequences or patterns of simple events as part of the historical process as he conceives this. Therefore, much of what we elicit and interpret in the taking of a "clinical history" is not history in this general sense, though, I submit, the method we have used is in fact the true historical method.

Yet, as every physician knows from his experience, the elements of "event" and of "human action" do enter into the development and behaviour of bodily illness: there is action and reaction between mind and body, and both contribute to the sum which is presented for elucidation. This is true not only of what I shall continue to call the "history" of the illness, it is true also of the clinical picture presented to our direct observation. I submit, therefore, that even in the apparently and exclusively somatic illness we cannot confine ourselves wholly to the methods of natural science but must take account also of the historical method. Further, owing to the common incompleteness of the data of observation presented to us, we have to read them in the context of the clinical history. Thus the methods of natural and of historical science are closely interwoven in our activities.

Every physician, and especially every teacher of medicine, knows that what is called "history taking" is a task calling for experience and critical thinking, and that it cannot be learned with the ease to which the techniques of clinical examination often lend themselves. This is in

accord with what, following Collingwood, we have said of the nature of historical evidence, and of its criticism, selection, and assembly in the writing of history : a complex intellectual exercise in which the evidence is given life and meaning by the historian's own contribution of thought and knowledge. Therefore, we need not be surprised that the young student so often gives us those flat and incoherent chronicles, thickly sown with irrelevances, that are too frequently allowed to pass muster as medical histories.

History and Psychology

It is when we come to consider psychological medicine, and what we may term psychologically determined illness, that the analogy between medicine and history leaps to the eye. Here, I submit, we are truly within the realm of historical science as the historian strictly defines it. Psychology, or the science of human nature, as our eighteenth-century philosophers were wont to call it, has since their time sought assiduously to establish itself as a discipline within the field of the natural sciences, and has claimed to use their methods.

In the case of psychological medicine, or psychopathology, this claim has been eloquently stated by Bernard Hart in his Goulstonian Lectures of 1926. He regards the data of the psychologist in medicine as strictly comparable in character to those of natural science, and goes on to say that a scientific concept "must explain the observed facts, and must be capable of verification by repeated reference to experience and experiment." These postulates he clearly believes to be fulfilled in psychological medicine. Yet surely the aim of psychological medicine is the discerning and unravelling of the mental processes, conscious and unconscious, that lie behind the "observed facts," which are in their origin and nature merely derivative phenomena and of infinite variability and unpredictability. The essential data in psychology, as we find it in medicine, are the mental processes behind the façade of the so-called "observed facts." It is surely a *non sequitur* to invoke the canons of natural science in this situation. The postulates propounded by Hart are not, and cannot be, fulfilled by psychological medicine, and it is meaningless to speak of "verification by repeated reference to experience and experiment" in this connexion. Elsewhere in the lecture he says that "the introduction of purpose removes psychology from the mechanistic sciences, but this does not justify its removal from the whole field of science." Here Hart seems almost trembling on the brink of awareness that psychology does not belong to natural science. However, he goes on to place it with biology. Yet the word "purpose" is not unequivocal, for teleology in biology is not the "purpose" that determines human actions. Such are the pitfalls of linguistics.

It is of course virtually impossible to generalize about psychology as we find it in medicine to-day, because it has no unity of method or of concept, and it continues to be regarded by its exponents as "scientific" in so loose and undefined a way that the adjective has no clear connotation. Nevertheless, countless expositions make it certain that it is natural science which the psychologist has in mind when he uses the term.

Of its possible relation to historical science we find no word in the superabundant writings on psychological medicine. Even that most lucid and philosophic critic of Freudian method, psychology, and philosophy, Maritain, in his attempt to assess and orient them, shows no realization of the possibility that much of the difficulty in determining their status would be resolved if they were measured against

the standards and methods of history and not against those of natural science.

Yet how far removed from the methods of natural science are the Freudian psychology and philosophy Maritain indicates in the following verdict : "It is in the techniques of interpretation (that is, of dreams and free association), and especially in the use of symbolism, that Freud and his disciples have been led to the profusion of the arbitrary, of obsessional dogmatism, and of pedantry."

Even in the latest review of the development of psychological medicine by Rickman it is stated that the unravelling of the meaning of dreams is "the main tool of research," and the concepts derived from the use of this tool are spoken of as within the realm of "scientific thought," though what order of science we are not told.

An Illusion

For any who may still cherish the illusion that Freudian psychology has any discoverable relation to natural science in its methods or concepts, a careful reading of Rickman's article, "The Development of Psychological Medicine," should prove an effective remedy.

The fact surely is that the psychologist in medicine is not primarily concerned with events, nor does he use the sense data that are the material of natural science, but his first concern is the application, more or less imperfect, of the historical method to the fragmentary and fugitive records of human thinking and action which he can glimpse in his patient's mental past. It is upon this application that all depends.

The springs of human action which are his quest are not data of observation amenable to experimental control or classification. If they are to be revealed at all it is only by the method of historical thinking in which the inquirer collects his record of evidence, subjects it to critical assessment and selective assembly, and then formulates conclusions that have the duality of origin I have already proposed for the ordinary clinical history.

In this process he aims to understand the mental activities underlying the concrete situation he is studying, and he can do this effectually only by rethinking or reliving these activities in his mind and in the context of his own knowledge. The medical psychologist's problem is a concrete historical one and does not and cannot lead to the formulations of universals, for there is no blue print, no master key, to the springs of human thoughts and actions, applicable to all persons at all times and in all circumstances, and no natural laws for the human mind as natural laws are generally conceived.

We may therefore conclude that the steady endeavour of two centuries to fit psychology within the realm of the natural sciences is based upon a false analogy, to which the very term "human nature" lends colour. This analogy has gravely retarded the growth of a true science of psychology under the aegis of history.

In medicine the easy illusion that they are natural scientists, using the methods of natural science, has not saved medical psychologists from wandering within a labyrinth of conflicting speculations and methods, blown about by every wind of doctrine ; from exotic symbolist systems on the one hand to extremes of anti-intellectualism on the other, and through the latter to a new psychiatry which in effect dementizes mind and seeks to account for its activities in terms of "nerve nets," "reverberating circuits," and "feedback mechanisms" in the cerebral cortex—that is, to provide physiological accounts of mental activities and in so doing to leave no room for psychology.

Wanderings of Psychological Medicine

This constant wavering of psychological theory in medicine between allegory and machinery, and of psychological practice between the exegesis of dreams and what in a barbarous neologism is called "psycho-surgery," does not allow a resting-place for the psychology of the modern psychiatrist within the confines of any known scientific discipline. It has become a chaos of conflicting allegorical systems, of pseudomysticism, and of "hit or miss" mutilations of the brain that have no ascertained scientific basis.

Surely, in such a situation, the claim to come within the realm of natural science is revealed as no more than the overt expression of unconscious yearnings to acquire some sort of academic prestige within the world of ordered knowledge. These wanderings of psychological medicine in the wilderness, not yet ended, always recall to my mind the title of one of Captain Marryat's stories for boys, *Japhet in Search of a Father*.

Yet, despite this profoundly unsatisfactory situation, there are of course sage medical psychologists who do use the historical method in its strictness, though they may not know it for such. When these men do turn to physical methods of treatment they remain fully aware that these have no scientific basis, but are wholly empirical procedures acting in unknown fashion but having the possibilities of pragmatic justification in particular instances. Nevertheless, it is surely clear that the hope of an advance towards coherence and scientific status for psychological medicine would be immeasurably increased if its exponents thought out the nature of their subject and became aware of the scientific discipline to which it should be affiliated—that of historical science.

If there be a body of psychological knowledge within the bounds of natural science it is that physiological psychology which has sense data to observe and classify in the forms of nervous and muscular activity which are the physical expression of current mental causes. Of such a physiological psychology there is a distinguished school in this university, but its aims, methods, and results in no way resemble those of the so-called medical psychology which shares with it little but the substantive common to their names.

It would be over-sanguine to look for a ready assent from the psychologist in medicine to a proposition so contrary to all he has hitherto believed regarding the nature of his activities and their place in the body of science. Yet it may be that the moment will arrive in which he is found willing to turn to some epistemological contemplation of his special body of knowledge and theory. The need is surely urgent, for there is a place for a scientific psychology in medicine under the aegis of historical science, a discipline as worthy of our esteem as that of natural science. To seek to remove psychological medicine from the one domain to the other is not to derogate from its status and importance.

Yet the historical method has its own ideals of truth; and the realization of these is not compatible with intellectual submission to fixed symbolic systems in the interpretation of human action. Such lesser loyalties have no place in any scientific discipline, and with their advent there creep in, as attendant evils, myth and pseudomysticism, an obsessional dogmatism, and a sacerdotalism of outlook that have always been the greatest enemies of science.

The medical psychologist must be elective if he is to preserve his intellectual freedom and integrity, and in the interpretation of human records which are the essential data of his study his own knowledge and critical insight must be the dominant instruments.

A Dissent

Before I leave this subject I venture to make one dissent from Collingwood's view of the proper task of psychology. He says: "In realizing its own rationality mind also realizes the presence in itself of elements that are not rational. . . . These irrational elements are the subject matter of psychology. They are the blind forces and activities in us that are part of human life as it consciously experiences itself, but are not parts of the historical process: sensation as distinct from thought, feelings as distinct from conceptions, appetite as distinct from will. Their importance to us consists in the fact that they form the proximate environment in which our reason lives, as our physiological organism is the proximate environment in which they live. They are the basis of our rational life, though no part of it. Our reason discovers them, but in studying them it is not studying itself."

Yet surely reason does not work in an emotional vacuum, and in studying human actions it is impossible to separate, save by the process of abstraction, the emotional from the rational elements in our actions and their motive forces. And if history is the study of the concrete, this abstraction cannot be made save for purposes of discourse and logical analysis. I venture to submit, therefore, that we cannot regard psychology as concerned solely with the irrational in us, or allow that the latter is not involved in the historical process which it is the psychologist's business to study.

Conclusion

I believe, then, that history and natural science are recurrent themes, closely interwoven in medicine, not always recognized by us as such as we pursue our activities, but always present. I believe, too, that we shall think more clearly if we know that this is so.

At least those of us who teach medicine, and bear responsibility for the future of medicine, should have some awareness of the nature of our subject. In his book, *The Idea of the Universe*, Collingwood, whom I have quoted so often, observes that "a man who has never reflected upon the principles of his work has not achieved a grown-up man's attitude towards it; a scientist who has never philosophized about his science can never be more than a second-hand, imitative journeyman scientist. A man who has never enjoyed a certain type of experience cannot reflect upon it."

These thoughts must be my justification for the excursion I have made this afternoon upon territory which the physician will enter with diffidence and tread with circumspection, yet the physician is the man best placed to reflect upon his experience and to philosophize upon it.

This foundation of Linacre's has seemed to me an admirable opportunity for such reflection, and I venture to think that he might not altogether disapprove the intention which informs my lecture, though he might well have thought less highly of its realization.

In conclusion, although the occasion that calls us together is not the only Foundation we owe to Linacre's concern for the advancement of medicine, it is the only one which has been consistently devoted to humanist and academic themes and ends.

To use the brief recurrent occasions which this lecture affords us amidst the press of material preoccupations in order to dwell upon these values and purposes is not mere escapism. It should be refreshment.

Doubtless the cynic will think and say otherwise, but cynicism is too often only the threadbare cloak for timidity in the face of threats to our traditional values. The idealist, as he looks at the world around him, which he has so little

share in moulding, need not feel ashamed if he continues to cherish and to advocate his ideals.

Only such an ideal of humanism as I have sketched, with its emphasis upon practical wisdom, and such reflections upon the nature of our activities as I have so imperfectly put before you, can save the loss of our traditional values and keep us aware of the nature of what we are thinking and doing. Yet, whatever be true of the latter, there can be no doubting that the practice of medicine flourishes most when doctors think most highly of their functions; when they remember that prudence governs the employment of science, and that in the last resort they are concerned with the ultimate particular thing, the human person, whom science by itself is inadequate to comprehend.

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INSULIN-INDUCED SKELETAL ABNORMALITIES IN DEVELOPING CHICKENS*

BY

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According to C. S. Stockard (1912) developmental anomalies of various types and degrees cause "the death of about 23% of the human race before or shortly after the time of birth and handicap(s) a certain proportion of the survivors throughout their lives." During the last few decades the discovery of genetic factors leading to malformations has attracted a great deal of attention, while research in the field of environmental teratogenic factors has lagged behind.

There exists a widespread belief among laymen as well as among physicians that single and multiple congenital malformations are always the result of changes in the germ-plasm—in other words, they are genetically determined and hereditary. I do not, for a moment, minimize the role of genetic factors in the causation of congenital anomalies, but it has been shown in recent years that developmental processes can be altered by environmental disturbances as well as by abnormal genes. It will be of great interest to the geneticist to know that types of congenital malforma-

tions which are sometimes genetically determined, such as microphthalmos, cleft palate, and certain skeletal abnormalities, can be produced in the offspring not only by maternal nutritional deficiencies and by roentgen irradiation, but also, at least in some animals, by the deliberate introduction of certain substances during embryonic growth.

New momentum to this line of thought has been given by the valuable epidemiological observations first made by Gregg in Australia in 1941. Since then evidence has accumulated that the contraction of rubella by the mother early in pregnancy is related to the development of congenital anomalies like cataract, heart disease, and deaf-mutism in the offspring. This has naturally raised the question whether other infectious diseases, particularly those due to a virus, such as mumps, measles, and chicken-pox, may cause similar defects. It may easily be that the more severe infectious diseases contracted during pregnancy are prone to result in abortion or miscarriage, whereas comparatively milder ones like rubella can give rise to congenital anomalies in the foetus without jeopardizing its life.

In 1943, while investigating the role of glycogen granules in hypertrophic cartilage cells during endochondral ossification, I made an accidental observation as a result of which I became interested in the insulin-induced skeletal abnormalities in developing chick embryos. In the course of a series of experiments I introduced 5 units of insulin into hens' eggs at various intervals after the beginning of incubation and noticed that some of the chicks showed x-ray appearances resembling osteogenesis imperfecta in the human, that some had developed abnormalities of the spinal column like spina bifida, with partial or complete suppression of development of some vertebrae, while others showed deformities in the limbs. I have observed that "synthalin," too, can induce certain skeletal deformities when injected in the same way, and an account of these deformities will be given in a separate paper. Unfortunately my investigations were interrupted during the war, and for one reason or another I could not renew my experimental work until I came to Liverpool in October, 1947.

Material and Method

My experiments have been conducted mostly with eggs from brown leghorn matings. I have used a simple apparatus not only for testing the fertility of an egg before injection but also for transilluminating it while drilling a hole into the shell and injecting into the yolk. In this way I have avoided injuring the embryo and the chorionic blood vessels. A fine dental drill held in a small chuck has been used to make a hole in the egg-shell, which has been sterilized with spirit. A tuberculin syringe fitted with the finest hypodermic needle $\frac{1}{4}$ in. (1.9 cm.) long has been found most suitable for making the injections. This length of needle enables one to inject into the yolk.

In my experiments I have used crystalline insulin dissolved in distilled water and made up to a strength of 40 units in each millilitre. The doses given varied from 0.05 to 6 units at different intervals after the beginning of incubation. Calculated on the basis of the human dose, 6 units to a developing chick embryo may appear to be distinctly excessive. But Riddle (1923) and others have shown that birds are highly resistant to insulin and can therefore survive a dose of insulin 30 times as strong as that which would kill a rabbit. Whenever the volume of the solution injected has exceeded 0.05 ml. an additional hole has been drilled into the egg-shell in the region of the

*Based on a paper read at the Liverpool Medical Institution on January 19, 1950.