BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 22 1961

WILLIAM HARVEY'S LESSONS FOR TO-DAY*

BY

JOHN McMICHAEL, M.D., F.R.C.P., F.R.C.P.Ed., F.R.S.

Professor of Medicine, University of London, Postgraduate Medical School of London

It is a great honour to stand here in the school in which William Harvey spent his boyhood and to be privileged to recall the magnitude of his great achievement before an assembly of our profession.

Looking back over the history of human civilization, the archaeologists have unearthed its beginnings in transient discontinuous flashes of precise scientific observation and creative artistic beauty in man's remote history in Sumeria, Crete, the Nile valley and delta, culminating in the rational culture of classical Greece in the Athens of Pericles. These near-Eastern and Mediterranean cultures fed into Rome, whose conquests of the known world imposed the first enduring civilization. When the edifice of the Roman Empire collapsed in the fifth century, Europe sank back into the Dark Ages with a growth of barbarism and tribal war. In the succeeding thousand years development of knowledge was practically impossible through the long centuries of miserable insecurity and the distractions imposed by conflict and poverty. Tribal organization and succeeding feudalism were hardly conducive to the development of organized nationhood, and in fact the only stimulus to national consciousness was usually foreign invasion. It was little wonder, then, that the preservation of knowledge became monastic, as the Church afforded the only shelter for scholars.

An Age of Ferment

Under the wing of the papacy, knowledge was preserved, but over long centuries it became as fixed and static as the theological dogma with which it was cloistered. The search for new knowledge was languid until about the year 1500, when the age of ferment began. The invention of printing and the flight of scholars from Constantinople with their manuscripts brought the spirit of philosophical inquiry of the Greeks back into Western Europe. Prince Henry the Navigator had made possible the long voyages to India and the New World. The spread of knowledge and the realization of its power were factors which started people questioning the omniscience of Mother Church and, along with other influences, led to the revolt of the Reformation. Through the bloody religious struggles of the sixteenth century, the period of the Inquisition and the Counter Reformation, freedom of thought was often vigorously repressed, and Servetus, who first suggested that blood might flow through the lungs, was burned at the stake for this and other heresies in 1553.

*Address given at the Annual Clinical Meeting of the British Medical Association, Canterbury, April 14, 1961.

only one generation before the birth of William Harvey. In this century of storm and stress the University of Padua, in the Republic of the wealthy City of Venice, had grown to be the most famous medical centre in the world. Here independent lines of thought could be pursued; here existed a liberal outlook which sought international teaching talent; and here religious persecution seemed to have no place. The intellectual ferment in this little city was truly remarkable. Vesalius, born in Belgium, completed his new and accurate work on anatomy in 1542, showing the true connexions of the venae cavae to the heart. These connexions had even been inaccurately depicted by the great Leonardo, perhaps in deference to Galenical doctrine. On the anatomy of the heart, Vesalius finally stated: "I do not see how even the smallest amount of blood could pass from the right ventricle to the left through the septum." The questioning of Galen's doctrine had begun.

Vesalius's successor was Realdo Colombo, who on anatomical grounds predicated a pathway for blood from the right heart to the left through the lungs. Colombo in turn was succeeded by Fallopius, who attacked Galen's teachings even more decisively than Vesalius. The next Professor of Anatomy was Fabricius, famous for his studies on the valves of the veins, and whose famous diagram of the bulging knots in the veins of the congested forearm was actually used in Harvey's book. Fabricius was professor in Padua when Harvey arrived, and at the same time Galileo was Professor of Natural Philosophy, teaching a cosmology opposed to ecclesiastical dogma. Only when Galileo left Padua did he fall into the hands of the Inquisition. Thus Padua shone forth as an island of freedom of thought and of shining intellectual endeavour in a Europe torn by savage religious bigotry, prejudice, and repression.

When Harvey returned to England he was a contemporary of Shakespeare, then at the height of his powers: the President of the Royal College of Physicians in 1600 was William Gilbert, whose studies *De Magnete* had gone the length of revealing the phenomena of electromagnetic induction. Francis Bacon was working out his inductive method in philosophy, enjoining the patient assembly of facts. While Bacon was himself curiously ignorant of science, Harvey's pursuit of the problem of the circulation is the supreme and first outstanding example of inductive reasoning in physiology. Harvey assembled an overwhelming mass of facts from animals, from man, from anatomy, from

embryology, and, adding to his facts a quantitative physical argument, he made his thesis incontrovertible. He demonstrated that blood circulated and that it must pass through the lungs from the right heart to the left, and yet he never saw the capillary channels through the lung, which had to wait for the application of Malpighi's elementary microscope shortly after his death. In a conversation which Harvey had with the Hon. Robert Boyle not long before his death in 1557 he said that the starting-point of his thoughts was Fabricius's observation of the venous valves permitting only unidirectional flow.

Harvey's discovery was of little practical use in the clinical medicine of his day. This great scientific triumph was worked out without thought or even hope of any material benefits. Harvey was one of those exemplary men who love knowledge for its own sake and who carry out their researches to satisfy their own intellectual curiosity and in the never-ending pursuit of understanding of phenomena otherwise inexplicable.

The Teachings of Galen

Galen is usually made the scapegoat responsible for the prevailing medical ignorance of the Middle Ages. In defence of Galen, however, it must be remembered that he had been dead for a thousand years, and it was not he who was responsible for the elevation of his teaching to the status of fixed doctrine. Galen, after all, did the best he could with the available observations of his time. It was known that if a man's windpipe was compressed he would die, and therefore something called "vital spirits" entered the body by this route. On dissection of the body at death, the arteries were often found empty or nearly empty of blood. Therefore Galen considered that only a little blood got through to the left heart and arteries, clearly mixed with the air which entered through the lungs. Veins, on the other hand, were filled with blood, and in the absence of other detailed observations unknown to Galen an ebb-and-flow was possibly quite reasonable. Galen did his best with his factual observations, and if his successors had been as assiduous as he in the study of anatomy over the succeeding centuries more truth might well have emerged. It took many long centuries before men felt themselves sufficiently free to pursue inquiry and to descend from the lofty philosophizing of the mediaeval schoolmen to the work of new observation and new dissection. It does not require a very acute ear to perceive the echoes of this long-standing conflict between pedantic scholasticism and scientific endeavour going on to-day in our universities and even in Whitehall.

Harvey's Lessons for To-day

The first lesson from Harvey, then, is "no authoritarianism." All our work, all our endeavours, all our observations, and especially our interpretations, must be subjected to continual critical scrutiny, to persistent reassessment by new techniques, so that we may constantly revise the very bases on which our professional practice is founded and thus maintain our status as a learned profession. New ideas are for the most part developed in the course of actual experimental investigation or inquiry. Some people complain nowadays that medicine has become too much of an applied technology. We admit that its technical complexity is beyond the scope of any one man to

master, but these techniques are merely methods of making our observations more precise and more extensive to the point of accurate quantitative measurements of an ever-increasing range of physiological functions on which we reach our diagnostic conclusions and practical therapeutic judgments on a basis of detail undreamed of by our predecessors. The advancing science of medicine with its modern technological equipment keeps us continuously exposed to irreducible and stubborn facts on which our theory must be built and the rationale of our practice reviewed.

Harvey had to face incredulity, opposition, and even the scorn of some of his otherwise distinguished contemporaries. In answering them he was firm, patient, and remarkably restrained. Progressive ideas are seldom given a cordial reception. Simpson introducing anaesthesia had to face odium, and Semmelweis, who reduced puerperal sepsis, was driven to despair and death by his jealous colleagues. Primitive religious beliefs and superstitions can still oppose the beneficent work of medicine, and only a generation ago the political frenzy of Nazi Germany wrecked medicine in its universities to a degree from which it has scarcely yet recovered. Our society, which we may call "enlightened," is still not wholly rational, even in matters intimately touching the welfare of its individuals.

Harvey's example of patient endeavour, the slow accumulation of relevant information, and the continuity of deep thought over a quarter of a century before he made his publication is another lesson for to-day. Harvey's work needs no revision. His observations and the deductions drawn from them are faultless. Charles Darwin was of similar temperament. He took twenty years to piece together the conclusions and the consequent change in biological thought drawn from his observations during the voyage of the *Beagle*. To-day the application of electronic machines in the laboratory has brought us into the age of push-button research. Data are collected, tabulated, passed through adding machines and computers, sanctified by statistical symbolism, and thrown at us, sometimes with little evidence that they have ever been subjected to any mental digestion by a trained medical intellect. We cannot compare the flimsy tissues of these communications with the impressive depth and volume of biological knowledge which Harvey assembled so massively and yet presented so concisely in support of his great argument. In spite of our electronic equipment there is no easy way and no simple way to tackle the vast problems of human life and its disorders. Observational data are meaningful only when subjected to deep and informed thinking. Wisdom is proportional to the breadth of knowledge brought to bear on the situation.

Harvey's exposition was clear and concise, made in the precise and universally understandable scientific language of his day. The logic of his presentation was clearly understood by all who were capable of reading. One of to-day's great problems in science and medicine is that of communication. Small groups of specialists speak their private language, and the presentation of a new paper is often clouded about by incomprehensible technicalities. Two recent distinguished medical presidents of the Royal Society, Lord Adrian and Sir Henry Dale, have always been exemplary in their presentation of new ideas to their colleagues. They invariably caught and sustained the interest of their

audience. They cut out all the esoteric technicalities of their complex experimental methods and presented results in lucid comprehensible English and in a manner both clear to their peers and inspiring to their younger colleagues. All this involves taking extra trouble in the final presentation of the results of research. The spoken paper should only bring out the highlights of new research endeavour. The technicalities can be read in the specialist journals by those few who wish to continue the work. The simple technique of rehearsing a paper before colleagues from allied disciplines can improve its comprehensibility.

Present Urge for Publication

We seem to be passing into an increasing dilemma of rapid and overwhelming publication. Most of our young men feel that they are engaging in a race, and the hurry for priority often compels premature publication. In judgment for promotion, too, numbers of papers may occasionally impress, especially where the judges are unable to spare the time to assess their quality. The grant-giving bodies supporting research are also apt to demand "results." It would require a considerable change of heart all round to alter these attitudes. The function of meetings of our learned societies should be critical commentary at various stages of research, and a list of demonstrations and orally presented communications culminating in one good paper should impress selection boards by signifying commendable restraint on quantity in favour of quality of publication. If the patrons of research could encourage more long-term investigation and depend on direct or indirect personal contact with the investigators for reaching their judgments we might conceivably achieve a state of affairs in which completed and conclusive work of the highest quality only was printed in our journals.

Research and Finance

Research is a tender plant and unless cultivated with care and sympathy it is apt to wither and die. It grows with difficulty, and discouragement can kill its early growth: life is easier for those who do not utter disturbing thoughts. The antagonism to inquiry which pervaded most scholarly circles in Harvey's day could be overcome only by great strength of character and fortitude of mind. Harvey pursued his inquiries privately and consistently, but his dedication of his book to King Charles II, who was wise enough to make him his physician, though somewhat obsequious, was possibly determined by the need to ensure royal protection, as he possibly remembered the fate of Servetus only 70 years previously. The research worker can pursue his endeavours only if he is in a position to have access to the tools for his task, libraries to consult, the company of sympathetic colleagues, and financial support. Inherited wealth and privileged positions helped such men as Darwin and Cavendish. The Rev. Stephen Hales sublet his pastoral duties while John Hunter toiled as a private teacher.

It is only in the last 100 years or so that the universities have in fact played an important part in the development of research activities, as has been brought out by Sir Eric Ashby in his recent book, *Technology and the Academics*. The decline of personal wealth by taxation has thrown the whole onus of support of research on to the national resources of the Exchequer and some of the giant industries which are

farseeing enough to notice that they are likely to benefit from the cultivation of talent. It is to them we must turn for the patronage of our ever-increasing scientific endeavour. The Treasury grant via the Privy Council to the Medical Research Council represents about one-half of one per cent. of the total amount spent in the support of the Health Service. Considering the opportunities which lie before us, it is exceedingly doubtful if this represents an adequate investment. The fault may not lie with the Medical Research Council, which can only respond to demand, but rather with the attitude of mind of our stringent Treasury, inclined to see little economic gain in biological research and even worried by the possibility of increasing National Health Service costs from medical investigative endeavour. We should never cease to counter the fallacies of such ill-informed ideas.

The defeat of tuberculosis in our young adult population has probably added hundreds of thousands of working man-years to our productive and economic capacity. It has saved a vast expenditure on the old type of sanatorium treatment and virtually abolished the necessity for pulmonary surgery by the simplified efficiency of modern methods of attack on the tubercle bacillus. But it is impossible to compute in cash the value of the abolition of tuberculosis as a cause of human misery, family distress, and impoverishment. Even on a commercial level we should also remember that this country may have lost hundreds of millions of pounds by failure to exploit the discovery of penicillin. An unbalanced effort to develop the physical, chemical, and engineering sciences at the expense of biology and medicine is unrealistic, as refinements of these sciences make new starting-points for medicine. Medicine and biology cannot lag behind the rest of general science, of which they form an integral part: and, after all, human welfare is the most important objective of all our endeavours, be they political or scientific.

A Commonwealth of Medicine

Finally, Harvey was an internationalist who gathered his knowledge from the ideas of great men in the developing universities of Europe. His knowledge also was given to the world. Only a few weeks ago we read the inspiring address of Sir Douglas Robb appealing for a Commonwealth outlook in medicine. Our Commonwealth of Nations is no longer held together by the strong arm of military and naval power but rather by the benign enduring influence of the Crown and by the slender but powerful threads of cultural influence and an example of scientific integrity. The best doctor exercises by his ethical example an enormous influence in society everywhere. Hundreds of young men and women from Asia and Africa are flocking to Britain, repeating in our modern world Harvey's pilgrimage to Padua. We must make them welcome. We must help them, and we must go out to sustain and encourage their efforts in their own countries. Fortunately our Government has contributed a substantial sum recently to promote the interchange of Commonwealth students and postgraduates, but a great deal more is still needed to ensure that our visitors get an appropriate welcome and are suitably housed in residential colleges and hostels. We should create more opportunities for high standard work in the peripheral as well as in the teaching hospitals in order to familiarize our visitors with our special methods of approach to the problems of the

sick. The more effort we put into our work in teaching these visiting doctors—and, after all, we can only teach by example—the more we are likely to retain the respect of the leaders of the emergent nations of Africa and Asia.

We have achieved in this country, by a very substantial expenditure, a high standard of health and life expectancy. It costs less than 5% of our national income, or about £12 per head per annum. We must approach with sympathy and understanding the problems of the poorer countries in which the expenditure may hardly be as many shillings per head, and where obviously it will be many decades before they can apply our standards widely. We must be sympathetic to their efforts to adapt to the new knowledge. We must show them how to translate the results of research (which they themselves may not yet be able to pursue) into effective practical action. The sustained British tradition of shrewd and detailed bedside history-taking and clinical examination, backed by appropriately selected laboratory checks, is our greatest strength in transmitting "know-how," for we can frequently demonstrate that, by precise and accurate clinical observation, costly and extensive laboratory investigations may be merely confirmatory and often unnecessary for practical decisions. These working rules of bedside practice which we discern by careful study and research are available for the guidance of all. I believe that our standards of medical practice in this country stand at the highest ethical level in the world, and our ability to set an example of professional integrity combined with high scientific endeavour is a factor favouring British cultural leadership in medicine. William Harvey himself would have envied our opportunities to follow the example of the leadership of Padua in our own troubled century.

SENILE TYPE BODY-WATER CHANGES IN DEGENERATIVE DISEASES OF THE CENTRAL NERVOUS SYSTEM IN MIDDLE-AGED SUBJECTS*

BY

E. WOODFORD-WILLIAMS, M.D., B.Sc., M.R.C.P.

AND

D. WEBSTER, B.Sc.

From the Department of Geriatric Medicine, the General Hospital, Sunderland

In an investigation of body-water distribution in aged normal subjects we showed that the lean body mass (L.B.M.) and the intracellular water (I.C.W.) diminished as age advanced, the ratio extracellular water to total body water remaining constant (Olbrich, Woodford-Williams, and Attwood, 1958). This finding was thought to be a true sign of ageing, as the proportion of extracellular water increased if somatic disease intervened. Certain degenerative diseases of the central nervous system (C.N.S.) occurring in middle age cause changes in the body characteristic of old age, such as presenile dementias (Huntington's chorea, Alzheimer's disease, and Pick's disease) and post-encephalitic Parkinsonism.

*This study was supported by grants from the Nuffield Foundation and the Scientific and Research Subcommittee of the Newcastle Regional Hospital Board.

Details of Findings in the Three Groups

Case	Age	Height (cm.)	Weight (kg.)	E.C.W. (litres)	T.B.W. (litres)	E.C.W. T.B.W.	E.C.W. Body Weight (%)	T.B.W. Body Weight (%)	L.B.M.* (kg.)
Normal Subjects 40-59 Years									
32	49	166	68.2	11.6	44.5	0.26	17.0	65.2	62.0
33	49	160	49.1	11.2	36.0	0.31	22.8	73.3	50.0
33A	48	178	72.3	17.3	44.0	0.39	23.9	61.0	62.0
23	41	173	59.5	11.1	42.2	0.26	18.8	70.9	60.0
24	41	173	65.9	14.5	39.9	0.36	22.0	60.5	56.2
25	43	161	58.6	10.0	41.6	0.24	17.1	71.0	58.0
26	45	164	54.5	10.6	40.8	0.26	19.6	74.8	57.0
27	48	161	54.1	9.9	38.6	0.25	18.3	71.3	54.0
28	48	169	68.2	11.8	50.4	0.23	17.3	73.9	70.0
29	48	169	44.1	9.7	44.1	0.22	15.3	68.8	62.0
30	49	178	62.3	9.9	41.9	0.24	15.9	67.2	59.0
31	49	168	60.9	10.2	43.2	0.24	16.7	70.9	60.0
34	50	180	72.7	9.1	44.2	0.20	12.5	60.8	62.0
35	50	168	57.3	10.6	37.3	0.28	18.5	65.1	52.0
36	51	164	49.5	12.1	37.5	0.32	24.4	75.8	52.8
37	52	165	63.2	10.5	45.3	0.30	16.6	71.5	63.0
39	57	168	68.2	12.8	37.7	0.34	18.8	55.3	53.0
40	58	170	52.7	11.0	37.0	0.30	20.9	70.2	52.0
41	58	178	70.0	12.0	43.1	0.28	17.1	61.4	60.0
42	59	170	63.6	13.2	38.2	0.25	20.8	60.2	53.9
43	59	168	64.4	15.7	40.6	0.32	24.4	77.0	69.8
38A	54	152	58.2	13.0	41.3	0.32	22.3	70.9	58.0
Mean	50	168	60.7	11.7	41.7	0.28	19.0	68.0	58.4
Subjects with Degenerative Diseases of the C.N.S. (Pathological Group)—40-59 Years									
H	48	158	53.2	9.8	35.2	0.28	18.4	66.2	48.2
L	49	178	70.5	12.7	35.1	0.36	18.0	49.7	48.1
M	41	154	53.0	12.2	30.9	0.40	23.0	58.3	42.3
N	49	171	68.8	12.3	39.5	0.31	17.9	57.4	54.1
F	57	172	44.5	13.7	22.3	0.61	30.8	50.1	30.6
J	59	170	47.5	8.9	30.2	0.30	18.9	63.8	41.4
K	57	176	57.7	12.4	32.1	0.39	21.4	55.6	44.0
Mean	51	168	55.0	11.7	32.1	0.38	21.2	57.3	44.0
Normal Subjects—80-89 Years									
68	81	170	58.0	10.4	32.6	0.31	17.9	56.2	45.9
69	82	164	57.3	13.4	31.4	0.42	23.4	54.8	44.2
70	82	164	56.4	12.8	29.7	0.43	22.7	52.7	41.8
71	83	163	62.3	15.3	31.5	0.47	24.6	50.5	44.4
72	83	165	62.3	10.0	29.1	0.34	19.1	55.6	41.0
73	84	170	73.6	12.8	42.0	0.30	17.4	57.1	59.2
74	84	160	61.4	14.8	33.5	0.44	24.1	54.6	47.2
75	85	175	61.4	14.4	34.5	0.41	23.4	56.2	48.6
76	86	173	61.8	11.3	29.5	0.38	18.3	47.7	41.6
77	86	163	50.2	12.3	28.9	0.42	24.5	57.6	40.7
Mean	84	167	59.5	12.7	32.3	0.39	21.5	54.3	45.5

* Lean body mass = T.B.W. 0.73 kg.

Post-encephalitic Parkinsonism, for example, shows a posture imitating that seen in old age with head and neck craned forward, and a slight flexion of elbows, wrists, hips, and knees. To-day some neurologists (Stevenson, 1959) would agree with Gowers (1902) and classify these conditions as abiotrophies.

Histological changes also have been found in the brain in the above and other degenerative diseases of the C.N.S. which resemble closely those found in old age. There is, for instance, the accumulation of lipochrome in the cytoplasm of nuclear masses such as the inferior olives, thalamus, and dorsal ganglia (Altschul, 1938), and the deposition of lipofuscin very early in these diseases in the thalamus, a most constant finding in the aged. The presence of lipofuscin in the thalamus has been thought to account for the emotional lability of old age. Malfunction and atrophy of the internal secretory glands has also been attributed to similar changes in the nerve cells of the dorsal nucleus of the vagus in the medulla and of the hypothalamic nuclei (Wolf, 1959).

To determine whether these phenomena of premature ageing in subjects suffering from these degenerative diseases of the C.N.S. are also accompanied by characteristic changes in body water we have measured the distribution of total body water and extracellular water