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OBESITY AND LIPOPHALIA

PATRICK MALLAN, M.D.

Physician to the Radcliffe Infirmary, Oxford

IT is impossible to do more than give a "bird's eye view" of this large subject within the space of an hour, yet it is one that merits consideration by all those engaged in the practice of medicine for, far from being a merely cosmetic problem, gross overweight is a lethal factor and is the commonest cause of "loading" in cases of Life Insurance.

Some 75% of definitely obese people show physical defects, the most common being those of cardiac or renal type. Taken over a large series of cases, the mortality rate is approximately two and a half times as great in the obese individual as in one of normal weight, or of spare build. Hypertension for example is markedly increased in fat persons; and it is interesting to note that during periods of treatment for weight reduction the blood pressure almost always shows a definite drop. Glycosuria, too, is approximately seven and a half times more common in the obese than in the normal person.

For these reasons the obese state is to be regarded as one in which many of the functions of homeostasis appear to break down; and the physiological processes which regulate heat, water, salt, and carbohydrate metabolism, and the cardiovascular system, all tend to become more or less involved. All cases of obesity therefore should be treated as cases of illness, or potential illness, and it should be borne in mind that after the age of 30 the risk becomes progressive with increasing age and/or increasing weight.

The aetiology of the condition is not really clear. Certainly, there is no evidence that obesity is an occupational hazard, or that it arises commonly from purely environmental causes. On the other hand there is a mass of sound evidence all of which confirms the view that there is a strong marked hereditary factor in the majority of cases. Thus the term "familial" obesity is one well suited to define the vast majority of fat persons whom one is called upon to treat. In a series of cases investigated by the speaker, 640 out of 726 showed marked obesity in the family or person of one or both parents. In such families, however, it is extremely common to find people who are markedly thin, but as a general rule perfectly healthy, i.e. it is not environmental obesity. The conclusion to

be drawn is that the regulating mechanism in certain families is disturbed or defective so that blood relations show signs either of over or under correction in respect of their weight, and sometimes of other homeostatic functions. A close comparison can be made between this last observation and those families in which thyroid disorders occur in varying forms, leading either to over function or under function of thyroid secretion in consanguineous relations. Macrosomia adiposa congenitalis (Christiansen), and Danforth's famous series of fat mice serve to confirm the view that weight disorders have a strong hereditary tendency. The latter observer demonstrated features of familial obesity which were strictly comparable to those met with in man. Thus, fatness was more usually found in females: it developed subsequent to maturity: there was lowered fertility: there were no gross endocrine changes: and the gene was an apparnt dominant which, as in man, was usually transmitted through the female line; though as pointed out by Siemens in the case of endocrine diseases, the genetics are highly complex, and not always easy closely to define.

Obesity must of course represent an excess of intake over output (Newburgh et al), but it is a mistake to regard overweight purely as represented by fat alone: for although (in pituitary obesity for example) the established state may show that the excess is represented solely by fat, there are certain types of overweight where the excess is to a large extent represented by salt and water; and it would appear very likely that all types of obesity, during periods when they are under treatment, tend to retain salt and water to an undue degree. The conception of Seltz-Wasser-Fettsucht which has been fully recognized and investigated in central Europe should always be borne in mind in considering the obese state, especially by the clinician who is attempting to treat these cases.

Accepting the fact that output is too low for the intake, it is nevertheless clinically manifest that certain persons can constantly and with impunity take in calories excessive to their requirements, whereas others cannot do so. The intake level at which obesity starts to show itself depends on the individual hereditary integrity of the weight regulating machine.

The divergence from the normal in weight homeostasis which will produce a marked degree of weight change in one direction or the other is minute. Thus, it is not surprising that the innumerable experiments designed to check the calorie exchanges in obese patients have proved abortive: and in addition many of the experiments done are not only mathematically but physiologically unsound. The chief trouble, of course, is that the formulae used presuppose a certain S.P.G. for the human body as determined by certain peripheral linear measurements; and that when the proportion between fat and muscle is grossly disturbed, the S.P.G. must be falsely calculated. Acute experiments are clearly without any real worth, and long term experiments during a period of weight gain or

loss are, in the human being, impracticable. (The speaker then briefly outlined the problem of the pathological intermediate metabolic processes occurring in fat persons.)

It is a near certainty that obesity begins because the weight regulating machine controlled by the hypthalamus, but with many subordinate generals in the shape of the endocrine glands, and tissue factors, breaks down, and so can no longer preserve the integrity of calorie and water control. At the same time, it must be stressed that if one looks on the post mortem table, or alternatively during life to find some endocrine disorder, one is constantly thwarted. Nor, moreover, do biochemical examinations of the body fluids in fat people reveal any gross abnormality except for a marked tendency to store salt and water.

Is there then any workable explanation?

The hormonal level at which tissues react, i.e. the tissue threshold to stimuli is probably controlled by local tissue conditions, as for example the pH in the periphery local tissue enzymes, oxidases et cetera, and by many factors that are for the moment quite obscure. That is to say that there is a constant balancing of anabolic and catabolic changes in the periphery, that are not necessarily a direct manifestation of a central state. It is, for example, well known that drugs which depress tissue oxidation are capable of acting in the reverse fashion and producing endocrine changes at the centre, i.e. the stimulation of thyroxin secretion.

Viewed in this light, one may justly conclude that fat is deposited in the tissues *because* there is a local or general fat avidity. On this assumption, patients who take excess food and retain salt and water do so only because the intake is devoted to two purposes: the first being the ordinary combustion processes of the body, taking place under conditions where economy is impossible to maintain, due to a heavy coat of fat; and secondly because owing to the raised lipophilia many calories are deviated from their normal purpose and conserved in the form of inert fat. A vicious circle is thus started, with a progressive diminution of functional efficiency throughout the whole organism. (*Note*: A side light is thrown on local lipophilia by the several cases reported in which tissue transplantations done from a fat area to another part of the body have shown local lipophiliac tendencies in the grafted region.)

In the light of the most recent work on adreno-cortical function and similar mechanisms, the concept of local tissue pathology as a basic aetiological factor in many diseases seems more than probable. Local or general chemical changes occurring in the periphery which as far as fat metabolism is concerned may be termed for convenience a "tissue lipophilia", will if increased, and especially if acting in conjunction with a poorly conditioned hereditary mechanism for weight regulation, cause an increase in the body weight under environmental conditions in which the normal person would maintain his weight constant. Admittedly this

theory is not as yet susceptible of full experimental proof; but since we are unable to detect macro or micro anatomical changes in the hypthalamus or endocrines in familial obesity it would on the facts before us appear a workable concept. It is submitted therefore that more or less gross changes in the tissues cause an over strain of the hypothalamic endocrine mechanism which in its breakdown fails not only to control weight but produces, as was said at the outset, other failures in homeostasis; so that the obese person becomes truly sick because other functions of physiological regulation are disrupted in a general breakdown.

DR. WILLIAM BEAUMONT, PHYSIOLOGIST 'AU NATUREL'*

JAMES WARDEN, '50

"TRUTH, like beauty, is 'when unadorned, adorned the most', and in prosecuting these experiments and inquiries, I believe I have been guided by its light." These are the words of a man who would not compromise with his conscience, who, as Osler said, 'lived up to and fulfilled the ideals with which he set out'. These are the words of a man who, on the basis of one well studied case, was able to radically change the course of medical thought in the field of gastroenterology. These are the words of Dr. William Beaumont, who without university or college training, represents the truly self-educated man, curious and eager to learn.

If ancestry have any effect on a man's life, William Beaumont's ancestors are significant. For centuries, the name of De Beaumont had appeared in the annals of French, Norman and English history. In 1635, a certain adventurous William Beaumont sailed from Great Britain and settled in the little New England village of Saybrook. Later the family moved to Lebanon, Connecticut, and here, on November 21st, 1785, was born William Beaumont, third of the name in America. His father was a successful farmer and an active politician, being a staunch Democrat. The family were of the Congregationalist religion and William was compelled to go to church so regularly that in his later life, he explained his non-attendance by the statement that "as a boy I made up for a lifetime."

There are no available records of his scholastic ability as a youngster. He attended a school in Lebanon which was probably no better than others at that time. His education was no better than that of other lads of his day. As to his boyhood tendencies, courage and fearlessness were always predominant qualities. His impaired hearing was the result of a dare between him and some of his playmates as to who could stand closest to a cannon that was being fired. William won, but in later years his hearing became so bad that people had to shout into a huge ear trumpet in order that he might hear them.

In the winter of 1806-7, when he was twenty-two, William left home to seek his fortune and, as we shall see, to meet his destiny. His outfit, we are told, consisted of a horse and cutter, a barrel of cider, and $100 of hard-earned money. Travelling northward through Massachusetts and Vermont, he arrived at the little village of Champlain, New York, where he decided to settle, at least for a time. He soon gained the people's confidence and for the next three years was the teacher at the village school. It was at this time that he evidently determined to be a doctor and during these three years, he learned the fundamentals by studying the medical books from the library of Dr. Seth Pomeroy. Also, at this time, in a letter

*Read at a meeting of the Osler Society, University of Western Ontario Medical School, London, Ontario, December 7, 1949.

to his younger brother, Abel, he gave the following advice in rather flowery, but expressive, language:

"Let virtue, truth and honesty be your planetary guide; temperance, justice, fortitude and prudence your cardinal points;faith, hope and charity your horizon; philanthropy, benevolence, friendship and philosophy your atmosphere, and the elements of life will be smooth, transparent, and pleasant, gently gliding over your imagination like the eastern morning breeze across the swelling field of wheat."

In 1810 he went to St. Alban's, Vermont, and entered the office of Dr. Benjamin Chandler, who taught Beaumont for two years. In one of Beaumont's notebooks, there are recorded some of his experiences during his apprenticeship, along with case records, formulae, prescriptions and quotations, two of which are given here. These are: "Of all the lessons which a young man entering upon the profession of medicine needs to learn, this is perhaps the first—that he should resist the fascination of doctrines and hypotheses 'til he have won the privilege of such studies by honest labour and faithful pursuit of real and useful knowledge" and "the mind that can amuse itself with the love-sick trash of most modern composition of novel reading seeks enjoyment beneath the level of a rational being."

After his service with Dr. Chandler, Beaumont was granted a license to practise medicine from the Third Medical Society of the State of Vermont. Shortly after, he entered the United States Army as a Surgeon's Mate and served in the war of 1812. He was present at the attack on Little York, which is now known as Toronto. A diary extract of April 27, 1813, the day of this attack, is interesting: "Sailed into harbour and came to anchor a little below the British Garrison." After a description of the battle in which the British were forced to retire, but not before blowing up their magazine containing 300 pounds of gunpowder, Beaumont continues: "Over 300 were wounded and about 60 killed on the spot. by stones of all dimensions falling, like a shower of hail, in the midst of our men. A most distressing scene ensues in the hospital. Nothing is heard but the agonizing groans and supplications of the wounded and the dying. The surgeons wade in blood. cutting off arms and legs and trepanning heads while the poor sufferers cry 'O, my God! Doctor, relieve me from this misery! I cannot live!' It was enough to touch the veriest heart of steel and move the most relentless savage. Imagine the shocking scene, when fellow beings lie mashed and mangled—legs and arms broken and sundered—heads and bodies bruised and mutilated to disfigurement! My deepest sympathies were aroused—I cut and slashed for thirty-six hours without food or sleep!"

Beaumont also served in the battle of Plattsburgh in 1814. Two years later, after the war was over, he settled in Plattsburgh. In his first year here, he and another doctor were in partnership and they also set up a combined drug and grocery store. In a year's time, Beaumont gave this

up and confined himself entirely to practising medicine. His practice was not much of a success for, a few years later, he sold everything negotiable, satisfied his creditors and re-entered the army.

In 1820, he was sent to Fort Mackinac which is located on an island in the Straits of Mackinac which join Lakes Huron and Michigan. The remains of the old fort still stand and there is also a memorial erected in honor of Beaumont. He returned to Plattsburgh in 1821 to marry Mrs. Deborah Platt, a widow and the daughter of the town's most prominent citizen and innkeeper. The young married couple settled easily into the routine life of the Fort, entirely unaware that very soon a rare opportunity would present itself to Dr. Beaumont as the chance for him to benefit all mankind and to achieve world-wide recognition.

Listen to an eyewitness account of the events of the morning of June 6, 1822. "On this morning, a young French Canadian, Alexis St. Martin, was standing in the Company's store where one of the party was holding a shotgun which was accidentally discharged, the whole charge entering St. Martin's body. The muzzle was not even three feet from him. The wadding entered as well as pieces of his clothing. His shirt took fire, he fell, as we supposed, dead. Dr. Beaumont, the surgeon of the post, was immediately sent for and reached the wounded man in a very short time, probably three minutes. After the doctor had extracted part of the shot, together with pieces of clothing, and dressed his wound carefully, he left him remarking, 'The man cannot live 36 hours, I will come and see him by and by.' "

Beaumont himself describes the event: "I considered my attempts to save his life useless, but I have always considered it a duty to use every means in my power to preserve life when called to administer relief. The wound was received just under the left breast. A large portion of the side was blown off, the ribs fractured, and openings made into the cavities of the chest and abdomen, through which protruded portions of the lungs and stomach, much lacerated and burnt, exhibiting altogether an appalling and hopeless case. The diaphragm was lacerated and a perforation made directly into the cavity of the stomach, through which food was escaping at the time I was called to his relief."

After debriding the wound and replacing the lungs and stomach as much as possible, he applied a carbonated fermenting poultice made of flour, hot water, charcoal and yeast, which was changed every 8-12 hours. The parts were constantly bathed with a solution of ammonium chloride in spirits and vinegar. He also gave internal doses of camphorated ammonia water.

At the end of about ten months, the wound was partially healed. However, Alexis was miserable, helpless, and destitute and the Fort authorities were going to ship him back to Lower Canada, as Quebec was then called. Beaumont took Alexis into his home and for the next two years, fed and clothed him, bathed and dressed his wound at least once a day,

until finally St. Martin became able to walk and help himself a little.

In May, 1825, nearly three years after the accident, Beaumont began his experiments. His army duties took him to Niagara and to Plattsburgh and it was here that his experiments were interrupted by the sudden departure of St. Martin, who returned to Canada, married and had two children.

News of Alexis did not reach Beaumont until 1825. He induced him to return and performed a second set of experiments which terminated in March, 1831, again due to St Martin's departure for Canada. That Alexis was a man of great physical strength and vigour is illustrated by the fact that he took his family in an open canoe "via the Mississippi, passing by St. Louis, ascended the Ohio River, then crossed the State of Ohio to the lakes, and descended Lakes Erie and Ontario and the St. Lawrence river to Montreal, where they arrived in June."

"The man with the lid on his stomach" returned to Beaumont once more and from November, 1832 to November, 1833, there was a third experimental series. Of interest is a contract drawn up by Beaumont in 1833 which bound Alexis to "serve, abide, and continue with the said William Beaumont, wherever he shall go or travel or reside, etc. . . . . that he, the said Alexis will at all times . . . . assist and promote by all means in his power such philosophical and medical experiments as the said William shall direct or cause to be made on or in the stomach of him, the said Alexis." For his co-operation, Alexis was to receive board and lodging and $150 a year. That Beaumont was willing to do anything in order to continue his experiments is indicated by the fact that his own salary at that time was only $45 a month and two meals a day!

After 1834, Beaumont was never again able to induce Alexis to return. He sent his son after him in 1846, and in 1852 offered him $500 and complete support for him and his family, but "old, fistulous Alexis" as Beaumont called him, decided to keep his stomach for himself, and would not return. However, he did travel around exhibiting his wound to medical societies, schools and to anybody who would pay to see it. He died at the age of 83 in absolute poverty, but having survived Dr. Beaumont by twenty-seven years. Sir William Osler, then a teacher in physiology at McGill, was keen to conduct a post-mortem examination but Alexis's relatives weren't. They allowed the body to decompose in hot weather for a few days and placed it in a grave eight feet deep, guarded by armed French-Canadians. Needless to say, Dr. Osler did not perform the autopsy.

Dr. Beaumont was sent to St. Louis in 1834. Five years later, he was ordered to Florida by an unfriendly Surgeon General but he refused to go and threatened to resign. His resignation was accepted but he still continued to fight to stay in St. Louis and also in the army. Finally his army pay was stopped; in no uncertain words, he denounced the "weak, waspish, and wilful head of the Medical Department."

Many times later (and earlier) in his career, he was never at a loss for words to express his disdain for those whom he disliked or whom he thought were poor practitioners of medicine. When invited to attend the first meeting of what is now the American Medical Association, he declined and set forth his reasons in a long letter which contained this statement:

"I believe some 15 or 20, or more, were elected to represent the faculty of this city. Perhaps they will not attend 'in propia persona' but you will doubtless have a specimen of the variety of professional talent and disposition of our medical community; the honourable high-minded and nobly aspiring young minds, radiant with vanity but not deficient in sound sense and professional skill and acquirements; the invidious, jealous, and obsolescent minds; the egregiously egotistical and ignorant blockheads and dunces; some mean and vindictive, and others on a descending scale even down to the very bottom of baseness and rascality!"

In March 1853, he suffered a fall while descending some steps. A few weeks later a carbuncle appeared on his neck; he died on April 25th. His wife lived seventeen years longer. They are buried side by side in Bellfontaine Cemetery, St. Louis.

To return to his experiments, we should realize that they were performed with practically no equipment, in a wild and rugged country, and on a subject who was quite often very unco-operative and hungover. We might also refer to the knowledge of the physiology of digestion prior to 1932. It is best summed up by William Hunter's succinct remark:

"Some physiologists will have it, that the stomach is a mill, others that it is a fermenting vat, others again that it is a stew pan, but in my view of the matter, it is neither a mill, a fermenting vat, nor a stew pan, but a stomach, gentleman, a stomach!"

There is a painting by Dean Cornwell entitled "Beaumont and St. Martin" which depicts Alexis lying on a couch in a rough-hewn log cabin while Beaumont is draining the gastric juice from the fistula into a small bottle by means of a long rubber tube. It aptly demonstrates the conditions under which the experiments were carried out. Yet, in Beaumont's records he noted the time, the weather, the direction and strength of the wind, the mood in which Alexis was in, and any other detail that might have any possible bearing on the experiment and its results. Here then was a true scientist, making the best of an opporunity, seeing things as they were, and recording correctly what he saw.

According to Sir William Osler, the following may be regarded as the most important of the results of Beaumont's observations:

1. The accuracy and completeness of description of the gastric juice itself.
2. The confirmation of the observation of Prout that the important acid of the gastric juice was the muriatic, or hydrochloric.

3. The recognition of the fact that the essential elements of the gastric juice and the mucus were separate secretions.
4. The establishment by direct observation of the profound influence of mental disturbances on the secretion of the gastric juice and on digestion.
5. A more accurate and fuller comparative study of the digestion in the stomach and outside the body.
6. The refutation of many erroneous opinions relating to gastric digestion, and the establishment of a number of minor points of great importance, such as the rapid disappearance of water from the stomach, through the pylorus.
7. The first comprehensive and thorough study of the motions of the stomach.
8. A study of digestibility of different articles of diet in the stomach.

In the light of modern gastric research, his more important contributions, according to Rosen, are:

1. His observations on the influence of the psyche on gastric secretion.
2. The significance of his work for the problems of nervous dyspepsia and gastritis
3. His studies on the influence of intemperance and unwholesome diet on digestion.

There are many other "inferences" drawn by Beaumont from his work in fact, fifty-one in all. They were all published in a book in 1833, which could then be bought for approximately $2.00 and an original edition of which would now cost well over a hundred dollars.

The significance of the man and his work was first recognized in Germany, then in England, then France, and finally, as is the case with most scientific pioneers, in his own country.

Beaumont's contrbution to medical knowledge has stood the test of time for one hundred and fifty years and stimulated gastric research the world over. May I conclude with another quotation from one of his notebooks: "A man of sterling talents and pure integrity is a blessing to any people or country." This was Doctor William Beaumont.

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TREATMENT OF HYPERTHYROIDISM WITH RADIOACTIVE IODINE

FRANK BUTSON, MEDS '50

ONE of the first more or less effective non-operative treatments for hyperthyroidism was the roentgen ray. Mean and Holmes in 1923 pointed out that by this means one-third of their patients were cured, one-third were improved and the other third were unaffected. Following this, iodine by mouth was used as a treatment, in some cases curative and in other cases preparatory for surgery. This was followed by the discovery of Mackenzie and Astwood who found that certain chemical compounds were capable of inhibiting the function of the thyroid gland. Following the investigation of several of these agents, thiouracil and propyl-thiouracil were found to be quite effective clinically. One of the most recent developments in the treatment of hyperthyroidism is the use of radioactive iodine.

History

A radioactive isotope of iodine was first prepared by Fermi and his co-workers in Italy in 1934. Because the thyroid gland absorbs iodine selectively, it seemed to them that the beta rays from the radioactive iodine would have a greater radiation effect than that derived from roentgen rays directed through the skin and overlying tissues. The use of this substance in the study of thyroid physiology was soon undertaken and the results were first reported in 1938. Radioactive iodine was first administered as a therapeutic agent in the treatment of thyrotoxicosis by Hertz and his associates in Boston in 1941. Shortly afterward, Hamilton and Soley at the University of California Hospital commenced treating patients. The results were first published in 1942. The experience of these men has shown that radioiodine may be an effective agent in the treatment of Grave's Disease.

Physical Properties

There are thirteen or more artificial isotopes of iodine, and all of them are radioactive. Today (I^{131}) is used almost exclusively at several centres in America where studies with radioactive iodine are being made. This is made by neutron bombardment of tellurium. It has a half life of eight days. (I^{131}) disintegrates by emitting beta particles and gamma rays to become inert and harmless xenon. The beta particles provide the greater part of the radiation effect while the gamma rays produce little effect before they pass out of the body. The effect of the beta particles is confined almost exclusively to the tissue containing the isotope, since beta particles travel at the most only a few millimetres in tissue.

Radioiodine is absorbed rapidly from the stomach, and most of a dose usually appears in the circulation within one hour. The thyroid has great affinity for radioiodine, taking it up in the same manner as ordinary stable iodine. The emanations from the radioiodine cause the same

changes in tissue as do radium emanations or roentgen rays, but radioiodine administered orally can deliver a much greater amount of radiation to the thyroid tissue than is possible with roentgen rays or radium. The doses of the latter are limited by radiation damage to the tissues other than the thyroid, particularly the skin. The amount taken up by the gland appears to be related to the size and the state of activity of the gland, more being taken up as the degree of hyperactivity increases.

Animal Experimentation

Prior to the study of radioactive iodine in the treatment of hyperthyroidism in human subjects, its effects were studied on the thyroid tissue of animals. At the University of California Hospital, three hundred microcuries of this isotope per kilogram of body weight were injected subcutaneously into rabbits and dogs. At the end of the tenth day, the rabbit thyroids showed extensive necrosis, hemorrhage and arterial changes. By the twentieth day the glands showed the above plus healing vascular changes, and fibrosis. At the fortieth day the thyroid gland had reduced to approximately one-half its pretreatment size. One rabbit showed some damage to the renal tubules, otherwise the extra thyroid tissues were normal.

Further experiments were carried out to determine the effects of massive doses of radioactive iodine upon tissues surrounding the thyroid gland. It has been found that upwards of forty times the maximal therapeutic dose for the human patients was required to produce serious damage to the continguous structures in mice and rabbits.

Uptake Studies and Excretion

The radiation emanating from the thyroid gland was measured by a Geiger-Miller counter. A count was also taken over the thigh, to test for the radioactive iodine contained in the non-thyroid itssue. This was subtracted from the gland count, thus giving the amount of the isotope present in the gland itself. The count of the standard was also taken. This represented one hundred percent. The count of the thyroid gland was divided by the count of the standard to obtain the percentage uptake of the substance by the thyroid gland.

It has been shown that in the average weight normal gland the uptake of radioactive iodine does not exceed thirty percent. Studies have shown that the uptake is maximal within forty-eight hours after administration. The average uptake in twenty-six patients studied by Dr. Prinzmetal and his co-workers at Los Angeles was sixty-two percent before treatment of any type was given. After treatment with radioiodine the average uptake was twenty-seven percent. Studies by Dr. Soley and his associates at the University of California Hospital showed the average uptake before treatment to be sixty-one percent, whereas in the treated patients the average was sixteen percent. There were forty-six patients in this group.

Excretion

There appears to be an approximate balance between the administered radioactive iodine on the one hand, and the sum of the thyroid retention plus the urinary excretion on the other. It was found early that significant amounts of the original dose were to be found only in the first three days specimens of urine. Fecal excretion was found to be so low that it could be considered negligible.

Indication for Use of Radioactive Iodine

1. As a diagnostic procedure to differentiate thyrotoxicosis from similar clinical conditions, especially anxiety neurosis and thyroiditis.
2. Patients with multiple recurrences of thyrotoxicosis after previous adequate surgical removal of the thyroid tissue.
3. Patients with severe congestive heart failure complicating an underlying thyrotoxicosis and thus a poor surgical risk.
4. Conditions of extreme emotional instability or frank psychosis complicating thyrotoxicosis.
5. Patients with an unusually severe toxicity, difficult to control by antithyroid drugs or by the administration of stable iodine.

Treatment of Hyperthyroidism

Although radioactive iodine was used in the treatment of thyrotoxicosis as early as 1941, detailed reports did not appear until five years later. The number of patients treated is still comparatively small, and time available for followup studies has been limited. Before the usefulness of radioactive iodine in the treatment of hyperthyroidism can be fully assessed a much wider experience of its therapeutic value will be required. The isotope has been used in selected cases of toxic diffuse goitre with and without complications. In hyperthyroidism without complications, radioactive iodine appears to be very effective in producing a total remission in a very high percentage of the cases. Such good results cannot be obtained under other circumstances, however. Apparently the poorest results from the use of radioiodine are obtained when it is used in the treatment of toxic nodular goitre and in thyroid malignancy.

Dr. Prinzmetal and his co-workers at Los Angeles reported results from two groups of patients:

1. Those with hyperthyroidism with no complications.
2. Those with hyperthyroidism plus complications.

In the group with no complications there were twenty-six patients. They were previously maintained on a low iodine dietary intake for a period of four to six weeks before the treatment was commenced with radioactive iodine. They were followed for a year or longer; subsequently all but one are now clinically well and the latter is greatly improved. One of the patients relapsed but again responded to the treatment of this isotope.

All patients had an elevated plasma organic iodine level, the average being 11.3 micrograms per hundred cubic centimeters of plasma, the

average following treatment was 6.3 micrograms per hundred cubic centimeters of plasma. The normal values range from four to eight micrograms. Clinically the patients had shown the usual criteria for a remission: weight gain, return of the pulse to normal, disappearance of the tremor, and a decrease in the size of the gland. It was found that a period of from three to four months was required to pass to the euthyroid state in these patients.

The second group of eighteen patients were those with complications accompanying the hyperthyroidism. This group was considered unsuitable for operation on the thyroid gland. The preparatory and followup studies were carried out the same as for the preceding group. Among the surgically unsuitable were:

1. Patients with multiple recurrences of thyrotoxicosis after previous adequate surgical removal of the thyroid tissue. *Eight cases.*
2. Patients with severe congestive heart failure. *Three cases.*
3. Patients with extreme emotional instability or frank psychosis. *Three cases.*
4. Patients with unusually severe toxicity difficult or impossible to control by the use of antithyroid drugs or by the administration of stable iodine. *Three cases.*

In all three cases of congestive heart failure there was a complete response to the therapy with subsidence of toxicity and recovery from failure. One patient with an associated coronary disease later had an acute myocardial infarcation from which she also recovered.

There were two patients with extreme emotional instability and one a case of frank psychosis. These were referred to a psychiatrist and were considered unsuitable for surgical treatment. All these cases made an excellent recovery after the administration of radioactive iodine.

The poorest results were obtained from the extremely toxic group. One patient with a toxic adenoma received a relatively large dose of the isotope without any therapeutic response. This was the only total theropeutic failure in this series. The second patient responded with a slow response after the administration of a very high dose of radioactive iodine. Before treatment in this case the thyroid gland was greatly enlarged and there was a severe degree of hyperthyroidism. The third patient was interesting because of her decided toxicity, her failure to respond to many other forms of treatment, and her slow response to radioactive iodine therapy. At the time of the last examination she had not obtained a complete remission but was decidedly improved. She was troubled only by occasional attacks of palpitation, and was able to hold a position. Thus in this group there was no response, a complete remission, and a partial remission, respectively.

In the group of eight patients who had recurring thyrotoxicosis following surgical treatment, four followed two previous subtotal thyroidectomies, two after four previous operations. Three of these six patients

failed to respond to previous courses of therapy with both the antithyroid drugs and deep radiation over the gland. The other two patients followed one previous operation. One of the patients in this group had developed an auricular fibrillation, a state of malnutrition and had escaped congestive failure only by greatly limiting his activities and by taking frequent doses of inorganic iodine. Excellent results were obtained in all cases; they were restored to the euthyroid state and had remained so for the twelve to eighteen months during which time they were under observation.

In this series there was one case of thyroid malignancy. Good results have been reported. The great majority of patients do not respond, however, because the malignant thyroid tissue only rarely retains iodine in therapeutic quantities. Surgical removal of the metastatic nodule was necessary before results could be obtained with radioactive iodine therapy.

Dr. Soley and his associates at the University of California Hospital administered radioactive iodine:

1. To study the efficiency of (I^{131}) as an agent to destroy hyperfunctioning thyroid glands subtotally.
2. To study the uptake of iodine by the thyroid gland before and after the symptoms of hyperfunction had been relieved.

They reported the findings in forty-six cases. All of these cases had undoubted hyperfunctioning, diffuse, moderately enlarged thyroid glands. A patient was considered to have responded satisfactorily to treatment by radioactive iodine if within approximately four months the signs and symptoms of thyrotoxicosis had disappeared, the thyroid gland had returned to the normal size, the B.M.R., the level of serum protein iodine and other laboratory findings were within normal limits.

Forty-two of the above forty-six patients responded satisfactorily to treatment. The four remaining patients failed to satisfy the criteria for a satisfactory response, because the interval between the beginning of therapy and the return to normality was prolonged. These four patients had larger goiters, a more severe degree of hyperthyroidism, and required larger doses of radioactive iodine. These slow responses may be accounted for in the main by a too conservative dose schedule initially, and the inability to secure large enough quantities of the isotope at the beginning of treatment.

Some interesting clinical and laboratory observations were made on these patients. Tenderness was noted in the region of the thyroid gland within twenty-four to seventy-two hours after the administration of the isotope. This was noted spontaneously by some patients, only on palpation by others. The tenderness was most evident when a single dose of at least two thousand microcuries was given. During the period of tenderness of the thyroid, the sedimentation rate was increased to as high as thirty-five millimeters per hour, also the protein-bound iodine of the blood rose temporarily. These findings were sometimes associated with

a return of the signs and symptoms of the thyrotoxicosis between the fourth and the tenth day. Within two to four weeks after radioiodine was administered, the thyroid became softer than it was previously, and the size of the gland began to diminish gradually.

Measurements with a Hertel ophthalmometer were made in order to record changes in the prominence of the eyes before and after the treatment with radioactive iodine. The results showed that sixty-six percent of the patients showed no increase in the degree of exomphthalmos, twenty-five percent showed a definite but minimal increase, and eight percent showed a marked increase. According to the experience of this group of observers, the exophthalmos occurs less frequently than in the patients treated surgically, or with the antithyroid drugs, and more frequently than in the patients treated with external radiation therapy.

Dose Required for Adequate Results

Definition of a millicurie:— that amount of material which produces 3.7×10^7 disintegrations per second.

Disagreement still exists among groups of workers regarding the dose to be used, and the advisability of a single dose rather than smaller more frequent doses. At the present time, the total dosage required by any patient is a matter of clinical judgment.

Dr. Prinzmetal and his co-workers administered total doses of 1.5-14.5 millicuries of radioactive iodine. For the uncomplicated cases the average dose was 4.4 millicuries. For congestive heart failure very good results were obtained from a dose of 2.5 millicuries. For extreme toxicity doses as high as 11 millicuries were used with no therapeutic response, 13 millicuries produced a partial response, and 14 millicuries produced a total remission but a slow response. Four millicuries produced an adequate remission of symptoms in cases of recurring thyrotoxicosis following surgical treatment.

Dr. Soley and his associates started with small doses of 250 microcuries of radioactive iodine given at weekly intervals, but later used a more adequate single dose of 1000 to 4000 microcuries and repeated as necessary up to a total dose of 10,411 microcuries. The above-mentioned results were obtained from these procedures. Thus it appears that doses of 1-4 millicuries are apparently adequate for the treatment of mild to moderate cases of hyperthyroidism, whereas 10 to 14 millicuries are necessary for severe hyperthyroidism.

Advantages

1. Thyroid surgery reports the lowest mortality rate in the post operative period of 0.5%. There have been no deaths reported as a direct result of the therapeutic use of radioactive iodine.

2. Radioactive iodine can be administered to the ambulatory patient without loss of time from work. As compared with antithyroid drugs, the patient does not need daily medication nor is he as likely to be subjected

to the risk of granulocytopoenia. Even with propylthiourical reactions are reported in 1.6% of the patients.

3. The administration of radioactive iodine is not followed by such complications as hypoparathyroidism, severe thyroid storms, post operative pneumonia, laryngeal paralysis, and the emotional strain of a major surgical operation.

4. So far evidence points to a decreased incidence of progressive exophthalmos with radioactive iodine therapy as compared with its incidence with surgical or medical treatment.

Disadvantages

1. The dosage of radioactive iodine is not accurately known, as a result in some cases many months of treatment are necessary before there is a remission. In other cases too much radioactive iodine is administered with a resulting hypothyroidism. With further experience it should be possible to more accurately gauge the dosage so that the number of inadequately or overtreated patients will be reduced.

2. There are certain unknown dangers to the handlers of the isotope and the people being treated by it. Although no complications have been seen in the literature, there is a theoretical possibility of such happening, an example being thyroid malignancy.

3. With surgical treatment the histological changes of the gland can be appraised accurately. The pathological changes can only be surmised without removal of the gland.

4. A certain amount of apparatus and well trained personnel are required for the administration of radioactive iodine accurately and safely.

5. Radioactive iodine has been used only since 1941; it is a relatively new form of treatment, thus unforeseen difficulties may occur as in any new form of therapy.

Summary

The isotope of radioiodine used in the treatment of thyrotoxicosis in these series was (I^{131})), which has a half life of eight days. It was administered orally, and appeared in the circulation in large quantities within one hour. Radio iodine produces its effect by emitting beta particles and gamma rays to the thyroid tissue. Extremely large doses were required to produce any effect on the tissues surrounding the thyroid gland. The amount to be taken up appeared to be related to the state of activity of the gland, more being absorbed as the degree of hyperactivity increased. This isotope was very effective in producing total remissions in conditions of hyperthyroidism without complications. This was not the case in other conditions. It appeared to be least effective in cases of toxic nodular goitre and in thyroid malignancy. The total dosage to be administered varied in different patients, and in different clinics. There are certain advanages and disadvantages, which are listed above. Because of the necessity of being administered by trained personnel, it can be admin-

istered only in certain centres in the United States as yet. Although radioactive iodine shows promise as a new therapeutic agent in the treatment of thyrotoxicosis a longer period of followup studies will be required before its value can be accurately assessed. It appears this substance is more effective than antithyroid drugs or stable iodine, but up to the present subtotal thyroidectomy still remains the most effective form of therapy for hyperthyroidism.

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INTRAMEDULLARY NAILING

E. G. Duck, '50

IN 1940 at Fribourg, Germany, G. Kuntscher, a German surgeon introduced a revolutionary technique for treatment of fractures of the long bones. The principle involved introducing a metal shaft into the medullary cavity of the bone being treated. At first the treatment received a great deal of criticism, not only from surgeons but also from physiologists and biochemists who considered this method anti-physiological. However, some orthopaedic surgeons such as Boeler, Ehalt and Soeur, not willing to discard a technique, which in principle exacted the requirements for treatment of fractures, that is reduction, fixation, immobilization and restoration of function, experimented with the now called Kuntscher nail with results that nullified previous criticism, and encouraged other investigators to attempt the treatment to the point where instead of being a revolutionary method of treatment, it is now an accepted and proper procedure to be applied to certain fractures of the long bones. The Kuntscher nail is used quite extensively in the Central European countries, and is now used in Canada and the U.S.A.

Type and Size of Pin Used

Kuntscher originally used a V-shaped pin of V2A stainless steel. Since then other investigators have introduced U-shaped and □-shaped pins (introduced by Street et al in U.S.A.). The main point to bring out here is probably not in the shape of the pin, but in its strength. In treatment of fractures of tibia and femur where a great deal of weight must be borne, this is of prime importance. Venable and Street, in a recent study of metals used in internal fixation, came to the conclusion that Vitallium and machined 18.8 stainless steel plus Molybdenum (S.M.O.) both were excellent metals as far as being inert in tissue was concerned, and also for strength. The S. M. O. being more reliable as to strength is probably the better of the two to be used in this type of nailing. The length of the pin, of course, varies with the length of the bone involved. Since the pin traverses the entire length of the medullary cavity, by measuring the good limb of the patient, an accurate estimate of the length of pin required may be obtained, e.g. Soeur recommends for fracture of femur, measuring from top of greater trochanter to knee joint line and subtract a constant figure. He uses a 4 cms. This is checked by fluoroscope or X-ray as, and after, the pin is introduced. The width of the pin is probably the most difficult to ascertain, and is one of great importance. A pin too thick will split the cortex; too thin, it allows rotation. By placing the X-ray tube 1 metre from the bone, a good estimation as to the width of pin required may be obtained. However, the pin must be introduced before satisfaction as to width can be obtained. Note: The length, width and shape of pin varies with bone involved in the treatmen, e.g. straight pin recommended for femur, curved pin recommended for tibia to facilitate introduction and also in preventing rotation. As the

medullary cavity of tibia enlarges considerably distally, a split pin has been introduced which will flare out in the distal fragment.

Other Equipment Required

A metal guide (not used in tibia) two feet long and strong enough to be hammered, hollow punches and a nail remover are necessary.

Objections to the Technique of Intramedullary Nailing

1. *Destruction of Marrow*: This has very little, if any, effect on R.B.C. and W.B.C. formation and is inconsequential.

2. *Foreign Body*: As yet any deleterious effect produced by the presence of the metal pin in the medullary cavity is to be proven. This is, of course, taking for granted the pin used is of recognized inert material.

3. *Fat Emboli*: The complications of fat emboli occurring must be seriously considered. The Kuntscher Nail when introduced into the medullary cavity displaces from 1-2 teaspoons of intramedullary fat. There are very few cases of fat emboli associated with intramedullary fixation reported in the literature. Kuntscher has reported two and it is questionable whether the fat emboli occurred as a result of treatment of the fracture or from the fracture itself. Some investigators consider the possibility of fat emboli occurring so great as to recommend open reduction with removal of the intramedullary fat at the fracture site.

4. *Risk of Infection*: At any time when an operation is performed risk of infection is present. However, this risk does not appear to be much greater in intramedullary fixation than any other type of operation, especially when done under closed reduction. Some investigators consider compound fractures contra indicated for this treatment; however, with the use of penicillin and careful management, infection can be controlled. Secondary infection has occurred in cases of intramedullary nailing, but there are no cases of severe osteitis or extensive wound infection reported in the English Literature. Another factor to decrease the possibility of infection is the incision being made at a relatively safe distance from the fracture site.

5. *Disturbance of Primary Callus*: Always considered to be an important cause of delayed union or non-union. I have not come upon any articles which discuss this factor. One must admit that callus formation is very outstanding in certain cases treated with the Kuntscher Nail; however, when investigators such as Boeler and some Swedish surgeons mention poor callus formation and non-union in their papers, the possibility of disturbance of the primary callus must be considered as a definite cause. Perhaps it is not too unreasonable to say that the Kuntscher Nail should be introduced either early before the formation of the primary callus (within the first day or two at the most) or should be left until the method of treatment chosen has proven unsatisfactory and delayed or non-union is evident by X-ray.

6. *Breaking and Bending of Pin*: As one would imagine, serious problems have arisen from breaking or bending of pin. Angulation, rotation

and delayed or non-union can occur under these circumstances. Removal of the pin is very difficult under these circumstances. In the future improvement as to the type of pin used will probably alleviate these types of problems.

7. *Exposure of Operator to Radiation*: Always to be considered in treatment of fractures under fluoroscope or X-ray and must be avoided if possible by the operator.

8. *Technique Limited to Larger Centres*: Special tables and instruments, and X-ray equipment as well as teamwork required for the technique, makes it a method applicable only in centres dealing with a large number of fractures.

Merits Discussed

1. *Callus formation*: Most reports indicate that early and copious callus formation at the site of fracture is associated with the healing of a fracture treated with a Kuntscher Nail. Other reports state that callus formation is retarded. Experiments have been carried out in an effort to find why early and large callus formation is formed. Many theories have been postulated, e.g. central pressure on the cortex, presence of a foreign body defence reaction have been considered, but the answer appears to be in the exactness of reduction and possibly axial impaction, extremely firm fixation and early mobilization of the limb. All these combine to give bone healing. The callus is eventually replaced with normally constructed bone trabeculae. The normal pull of muscles produces close apposition and is probably more physiological than certain types of traction applied in treatment of fractures.

2. *Reduction, Fixation, Immobilization and Restoration of Function*: Practically anatomical reduction is obtained in this type of treatment. This is, of course, necessary before the pin can be introduced. Fixation is extremely good. However, some cases such as fractures of the lower humerus and tibia require assistance from plaster of paris cast to prevent rotation of the distal fragments. Any force placed on the pin is spread throughout the whole length of the pin. Immobilization is complete. Partial use of the limb within one to two days after treatment is carried out. Within two to three weeks the patient is walking with the aid of crutches and shortly after this obtains practically full use of the limb involved.

3. *Simplified After Treatment*: Since there is very little atrophy of muscles, extensive physiotherapy and a great deal of nursing is not required. Joint movement which can be carried out within a day of the operation decreases the possibility of joint stiffness.

4. *Reduced Pain and Other Subjective Symptoms*: Marked pain associated with varying degrees of shock is a prominent feature of fresh fractures which are suitable to early treatment with the Kuntscher Nail. Pain is also marked in old fractures complicated by pseudoarthrosis as well as in pathological fractures. Introduction of the Kuntscher Nail relieves a

great deal if not all of the pain, improves the general condition of the patient and decreases the accompanying shock.

5. *Very Little Shock to the Patient*: The procedure is more detailed than difficult. If open reduction is required in order to achieve accurate reduction of the fragments, little shock and minimum disturbance is produced where soft tissues do not need to be cleared back with stripping of the periosteum as in plate and screw fixation. The technique is less complicated and produces less effect to the patient if open reduction is not required.

Indications For the Use of the Kuntscher Nail

1. *Fractures of the Femur*: The transverse simple fracture of the mid-shaft of the femur is the ideal case for the treatment by the Kuntscher Nail. The technique is not too difficult and excellent results are obtained. Compound, grossly comminuted fractures of the lower part of the femur diaphysis are best treated by other recommended techniques. Poor results from the above types of fractures may then come under the category of treatment with the Kuntscher Nail.

2. *Fractures of the Tibia*: Fractures of the mid-shaft and the upper one-third of the tibia are successfully treated by intramedullary nailing. Most investigators advise the use of plaster paris cast from toes to mid-thigh to aid in preventing rotation. In ten days the first cast is removed and a new one is applied with a walking caliper. The patient is then allowed to return home. Very satisfactory results have been obtained with this method of treatment. Fractures treated by other methods resulting in non-union or pseudoarthrosis may satisfactorily be treated by this technique.

3. *Fractures of the Humerus*: Here treatment by intramedullary nailing is indicated in comminuted and difficult spiral fractures, as well as in anyone who might have difficulty handling a hanging cast, e.g. an older, senile patient. This, of course, is for fractures of the upper and middle third of the humerus. Here again the Kuntscher Nail is contra indicated in compound fractures.

4. *Factures of Radius and Ulna*: Fractures of the radius and ulna requiring internal fixation are best treated by intramedullary nailing.

5. *Age*:

a. *Younger age group*: Intramedullary nailing is contra indicated in fractures involving a young person in whom the bones are still growing. Damage to the epiphyseal plate may retard or interrupt the normal growth of bone, producing shortening in the involved limb. Fractures in young people are more prone to heal than in the older person, and therefore a more simple procedure is, as a rule, quite adequate.

2. *Older age group*: Intramedullary nailing in time may replace hypostatic pneumonia as "the old man's friend". This refers to patients who come into the category for treatment by intramedullary

nailing, as indicated earlier in this paper. The early ambulation of the patient is the major factor here.

6. *Pseudoarthrosis*: Very good results have been obtained in treatment of pseudoarthosis by intramedullary nailing, e.g. Anders Westerban, a European surgeon, treated a woman 70 years old who had a pseudoarthrosis of the mid-shaft of the femur. The woman was on crutches within three weeks, osseous healing occurring three months later. Bone graft can be combined with intramedullary nailing. The sclerosed bone ends in pseudoarthrosis may give a great deal of difficulty, due to extension of the sclerosed tissue into the medullary cavity, making it practically impossible to introduce the Kuntscher Nail. The sclerosed tissue must be cleared away until normal bone is present at the end of the fragments before introduction of the nail.

7. *Pathological Fractures*: Treatment of pathological fractures with intramedullary nailing has proven very satisfactory. Although the treatment is more or less palliative, relief from pain, early return to the family, and a minimum of nursing care is afforded the patient. The average period of hospitalization is approximately two weeks. There is no evidence of the treatment producing dissemination of the tumor, or of the terminal cancer being hastened. This method has been used in Paget's disease, carcinomatosis and multiple myeloma with good palliative results.

8. *Arthrodesis of the Knee Joint with Intramedullary Nailing*: Excluding inflammatory lesions of the knee joint the Intramedullary Nail is indicated for any disability requiring arthrodesis, such as, total paralysis of the limb after poliomyelitis, fibrous ankylosis after shell injury or other forms of traumatic injury, rheumatoid arthritis and arthrosis with cancellous bone graft. By varying the position of introduction of the pin the joint may be placed in the degree of flexion desired.

The advantages of this method are:

a. It does away with the use of plaster cast.
b. Shortens the period of convalescence.
c. More stability is afforded the joint due to the greater area fixed.
d. As well as the merits of the method introduced earlier in the paper.

Surgical Aspects of the Technique

Type of Anesthesia Recommended:

a. *For the leg*: Most investigators use spinal anesthesia in treatment of the lower limb. Another type used is epidural block.

b. *For the arm*: Brachial plexus block is probably the method of choice. By using these types of anesthesia, the patient remains conscious and is able to cooperate in reduction of the limb if necessary.

Area for Introducton of the Pin:

a. *Femur*: A small incision is made over the greater trochanter. The soft tissues are displaced and a hole is made at the junction of the greater

trochanter and the neck of the femur. This is the place at which the medullary cavity is reached.

2. *Tibia*: An incision is made over the anterior part of the tuberosity of the tibia. A hole is trephined at the lower insertion of the patellar tendon.

c. *Humerus*: An incision is made over the head of the humerus, and the pin is introduced through the head towards the elbow.

d. *Radius and Ulna*: In the ulna the pin is introduced through the olecranon process towards the wrist. In the radius the pin is introduced through the distal end towards the elbow.

Note: In fractures of the femur and humerus the metal guide is introduced across the fracture site, the pin being introduced over the guide. A plaster of paris cast is recommended in fractures of the tibia, radius and ulna and all fractures involving the lower one-third of the bone involved. The plaster of paris must immobilize the joint above and below the fracture site.

Removal of the Pin:

A special instrument is required for this procedure and an attempt to remove the pin is not recommended without this instrument available. As a rule a great deal of force is required. Generally it can be said the pin should be removed in four to six months; this of course varies with radiological evidence of osseus healing.

Summary and Conclusions

A critical discussion of Intramedullary Nailing has been presented. The merits of the procedure and the objections of same have been discussed. The indications for this treatment as yet are still under question, however the treatment is certainly desirable in simple transverse fractures of the femur, fractures of the middle and upper third of the tibia, fractures of the humerus which would be difficult to treat by more simple procedure, and fractures of the radius and ulna which require internal fixation. In pseudoarthrosis and pathological fractures intramedullary nailing is to be recommended. The technique at the present time is contraindicated in compound fractures, although some investigators are getting satisfactory results using the method in this type of fracture.

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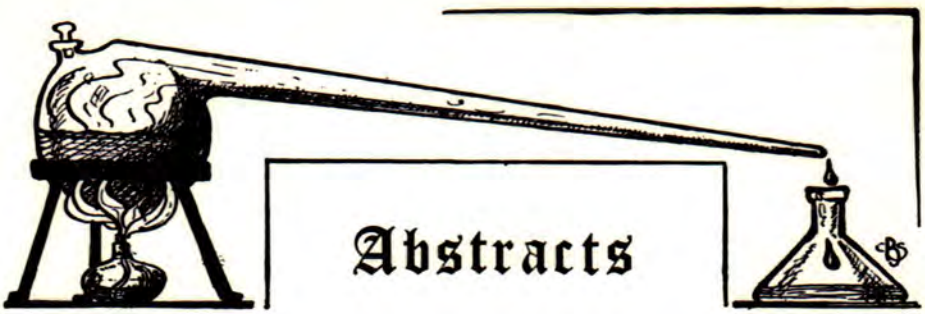

DIAGNOSIS AND TREATMENT OF VIRAL PNEUMONIA

GORDON MEIKLEJOHN

Am. Pract.: 4:210-213, 1949.

Viral pneumonias are a group of diseases which have various etiologies. Primary atypical pneumonia, psittacosis, and influenza have viruses as their etiological factors; the other member of this group, Q fever, has as its causative agent, a member of the rickettsia.

The treatment and diagnosis of the above diseases has been clearly presented in this review. The efficacy of such chemotherapeutics as the sulfonamides, penicillin, streptomycin and chloramphenicol (chloromycetin) in treatment has been discussed. These drugs promise to alter radically the whole outlook as regards viral pneumonia.

At least three of the etiological entities classified as viral pneumonias are amenable to certain of the above-mentioned chemotherapeutic agents as listed below. The efficacy of the different drugs varies with the various members of the viral pneumonia group.

1. Sulfonamides have little use in the treatment of viral pneumonias.
2. Penicillin is limited to treatment of psittacosis.
3. Streptomycin is of limited value and is used only in Q fever.
4. Aureomycin and chloramphenicol have the most value in the treatment of the viral pneumonia group as a whole, with the exception of influenza, which is still resistant to all the therapeutic agents mentioned in this abstract.

—JOHN LUSK, '52

HEART MURMURS — PART I

WILLIAM EVANS

Br. Heart J., 9 Jan., 1947

This article is an account of various murmurs seen commonly in practice. The author has dealt with these in sections, laying stress on phono-cardiographic interpretation of murmurs and correlating his findings with those of the E. C. G., cardioscopy, and other clinical data. The article has many representative illustrations which bear out the statements of the author.

I. The Innocent Murmur

These murmurs are found in the mitral area and are often the cause of many patients being invalided or restricted needlessly. 330 cases with this type of murmur were studied and the findings are represented in an excellent chart which is well worth looking up.

II. The Murmurs of Mitral Valve Disease

A diagnosis of long standing mitral stenosis usually presents little difficulty because there are obvious clinical signs. It is when the lesion is early that its recognition may be difficult. Although radiology may be of help, there are many factors which tend to lead to confusion. The three murmurs associated with mitral disease are considered separately:

(a) The Presystolic Murmur: Phonocardiograms were made of 33 patients with mitral stenosis who showed this murmur. In 31 cases the murmurs started during the P-R interval; the other 2 showed it starting after. This murmur, in 31 cases, took place in auricular systole and therefore is more informatively designated as an "auricular systolic murmur".

(b) The Systolic Murmur: Phonocardiograms were taken in 41 cases of mitral stenosis with this murmur. In 33 patients, the murmur started during the P-R interval of the electrocardiogram. This is rather surprising, being the same as in the patients having a presystolic murmur. The remaining 8 showed a murmur which commenced after the S-line and in each, a mid-diastolic murmur was present. 13 cases showed a mid-diastolic which was prolonged and joined the auricular murmur; in the remaining 28, the mid-diastolic had almost spent itself prior to auricular systole.

(c) The Mid-Diastolic Murmur: With the phonocardiogram, the investigation showed the presence of a mid-diastolic in every one of the 74 cases On auscultation, 33 of these cases also had a presystolic murmur, and 41 had a systolic murmur. Clinical auscultation elicited the mid-diastolic murmur in 51 cases only, and in 21 of these cases, it was heard towards the axilla only after the patient was positioned and tachycardia was induced.

(d) Auricular Fibrillation in Mitral Disease: In a phonocardiographic study of 20 patients with mitral stenosis and auricular fibrillation, the systolic murmur started at the onset of ventricular contraction This finding assists the diagnosis of mitral stenosis as a cause of auricular fibrillation by the position of the murmur and it is confirmed by the presence, in every case, of a mid-diastolic murmur.

These studies by Dr. Evans would indicate that the phonocardiogram is yet another tool enabling cardiologists to reach a more lucid interpretation of the various heart murmurs.

Part II of this article will be abstracted in the next issue of this journal.

—P. G. POWER, '51

AEROBACTER AEROGENES INFECTION OF THE URINARY TRACT: EFFECTIVE TREATMENT WITH AUREOMYCIN

S. F. WILHELM, ET AL

J.A.M.A., 141:837-839, 1949

An increase in the pathogenicity of Aerobacter aerogenes in urinary tract infections has been observed in several clinics in the United States. In one New York hospital, studies on 100 consecutive admissions to the urological service indicated that A. aerogenes was present in the urine of 50 of these patients. Bacteremia caused by A. aerogenes was proved in 24 patients, 7 of whom died.

Various drugs were tried on A. aerogenes infections. These included sulfathiazole, sodium mandelate, methenamine mandelate, and aureomycin. Aureomycin proved most consistently effective. Out of 50 cases treated with aureomycin, 42 gave excellent clinical response. However, there were many recurrences, some even as late as two months after treatment. In most of the recurrent cases, however, additional aureomycin treatment sterilized the urine.

Aureomycin appears to have a bacteriostatic action, few toxic effects and in this particular study, no strains of A. aerogenes developed resistance to aureomycin.

—JOHN AGNOS, '52