Special Article

Chorionic Gonadotropin in Obesity

Further Clinical Observations

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Sciences are judged by their fruits and in medical practice the outcome of a treatment is no less a test of the doctor's use of his conceptual scheme than is the outcome of a laboratory experiment a test of the theory of the experiment.

Lord Bacon (1)

It is universally acknowledged that to be overweight is a serious handicap. The literature abounds with insurance statistics which show that the death rate is higher among the obese of every age group. No informed person would deny that obesity is a cause for concern or that it is a legitimate—even essential—subject for much further scientific and clinical investigation.

The truth is that science has not yet produced an explanation for the disease, and obesity remains one of the most puzzling subjects in the practice of medicine. At a time when medicine can boast of successfully transplanting a human heart, it is only natural that our ego is pricked when we cannot answer the seemingly simple question of why some people get fat. The result is that a subject that is, in fact, still enshrouded in mystery calls forth many dogmatic and doctrinaire pronouncements from people otherwise famous for professional caution.

It is a little embarrassing to look back over my 40 years of medical practice and remember some of the far-fetched approaches I have been willing to try in the search for a breakthrough in the treatment of obesity (2), and I know that I am not alone. Suffice it to say that until the past decade, no technique—no matter how imaginative—has brought any significant success.

Although research in the past 20 years has developed much evidence to refute the traditional concepts of the cause of obesity, most physicians have clung to the view that obesity is caused by overeating, pure and simple, i.e., the intake of calories as food is greater than the expenditure of calories as energy.

Naturally, the treatment offered by these physicians consists of a reduced calorie diet, a lecture on self-discipline, and perhaps some medication. Otherwise, weight control has been relegated to a "do-it-yourself" project. Some have treated it as a moral problem rather than a medical problem, verbally punishing the patient for alleged deviation from the diet and thus adding more guilt to the already guilt-laden obese patient.

This treatment is doomed to failure in most cases, and the inevitable frustration it produces has caused many physicians to give up treating obesity altogether. Occasionally there is a tendency even to disparage—albeit subtly—other physicians who persist. The result has been a flourish-

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ing of fad diets and parascientific theories of metabolism.

I am one of the diehards who continue to treat the condition seriously. I believe that obesity is more than a simple disturbance of the caloric balance sheet and that there is a more intricate process at work. During the past 10 years I have been treating obesity with a method developed by Dr. A. T. W. Simeons (3) that uses human chorionic gonadotropin (HCG). I have treated well over 2,500 patients of both sexes, aged 15 to 75. Since all were private patients no double-blind tests or other experimental studies were undertaken.

It is with consternation that I must admit I cannot yet fully explain why Dr. Simeons' method works. And, it should be noted that not everyone shares my finding that it does work.

My own early skepticism of the method quickly dissipated after I had an opportunity to observe Dr. Simeons' work at his clinic in Rome. Since that time, experience has shown his method to be not only the most scientific approach to the problem but also the safest and most productive.

According to the dictates of the scientific method, a new theoretical concept cannot be incorporated into the body of accepted knowledge except on the basis of empirical research. In order to test the new idea, replication research must, of course, adhere meticulously to the author's original techniques. However, while a new theory is being tested, the practicing clinician's main concern is whether the new technique works—as long as it is safe. In the meantime, as far as the clinician is concerned, the new theory should give an intellectually satisfying interpretation of the processes underlying observable phenomena, should not violate known clinical facts, and should afford a precise, replicable technique, the results of which are easily assessed. In my judgment, Dr. Simeons' method satisfies all of these requirements.

To understand Dr. Simeons' method one must appreciate the theoretical framework out of which he developed the technique.

Basic theoretical considerations:
1) Definition
2) Fat-regulating center
3) Existence of different types of fat cells
4) Obesity during pregnancy
5) Nature of HCG
6) Safety of HCG in the treatment of obesity

Dr. Simeons' new concept of obesity is that it is a definite metabolic disorder, much as is diabetes, caused by a breakdown of a regulating mechanism located in the diencephalon, or hypothalamus. He calls this the fat-regulating center (3).

Although Simeons was among the first to suggest the role of the hypothalamus in obesity, the literature abounds with evidence of some regulating mechanism in the hypothalamus that governs the intake of food and its utilization (4–8). Others in the field have expressed belief in the presence of a similar regulating mechanism. Sir Vincent B. Wigglesworth (9), the noted British biologist, in his work with insects emphasizes the importance of the nervous system as a source of secretions that regulate metabolism and insists that evidence points to similar action in mammals.

The genetic factor in obesity fits into this concept, since offspring can inherit various types of regulating mechanisms from their antecedents in the same way that they inherit various other attributes (10, 11).

Different Types of Fat Tissue

Dr. Lester B. Salans and his co-workers (12) at Rockefeller University found that
Gusman

adipose cells in the obese differ from normal fat cells. These obese cells are not only more numerous, but the individual cell is larger and seems overstuffed. Furthermore, these overstuffed cells metabolize glucose less efficiently than the normal adipose cells. This cytological evidence would indicate that normal fat tissue differs from the abnormal fat deposits of the obese.

Normal fat tissue is essential to good health and serves two functions, as structural material and as reserve storage for fuel.

As structural material, it serves to protect such organs as the kidneys and the coronary arteries and it provides a pad in the sole of the foot, without which we could not walk. It also provides the padding underneath the skin which keeps it firm and smooth.

Since fat is the highest possible concentration of fuel for energy, a certain amount is distributed all over the body and serves as a reserve storage of fuel. This is converted into energy when starvation is forced on the individual or during a protracted illness. Even if the body stocks this normal fat to capacity this is not considered to be obesity.

Abnormal fat tissue is that accumulation, in certain parts of the body, from which the obese patient suffers. This type of fat is also a potential reserve for fuel, but is not immediately available in nutritional emergencies. Only after the normal fat reserves are exhausted will the body yield its abnormal fat to be utilized for the emergency.

When an obese patient severely reduces his diet he first utilizes his normal fat reserves to make up the nutritional deficit. By the time the normal reserves are exhausted and the abnormal fat tissues begin to make up the nutritional deficit, the patient is already complaining of weakness and hunger while the ugly fat deposits—of which he originally wished to rid himself—have hardly been reduced. At this point, the patient often becomes depressed and frustrated, and the diet is abandoned. The increased food intake that follows soon replenishes the normal fat stores, the patient feels much better, and the overweight is perpetuated or even increased. This is probably the best explanation for the many failures to reduce weight.

Pregnancy and Obesity

There does exist one special kind of nutritional emergency when all types of fat cells are immediately utilizable. During pregnancy every ounce of the normal reserve fat as well as the abnormal fixed deposits are placed at the disposal of the growing fetus. Simeons has suggested that it is the presence of large quantities of HCG during pregnancy that brings about this change through the hypothalamic center. If true, this would account for two interesting phenomena of pregnancy:

a) A woman may gain weight during pregnancy but she never becomes obese in the true sense of the word. The excess fat is more evenly distributed all over the body.

b) Secondly, if an obese woman does become pregnant, it is the best time, and the easiest, to reduce her excess weight without harm to herself or the fetus.

The presence of HCG in the body as such has no reducing action. A loss of weight can only be brought about by a concomitant nutritional deficit. During pregnancy the needs of the embryo act in this direction but in treating the obese with HCG this deficit must be obtained by a very low (500 kcal) diet.

The Nature of HCG

Found only during pregnancy, HCG has a protective influence on the health and nutrition of mother and baby. In fact, it has long been called “the protective hormone of pregnancy.” It could well be one of the most important hormones in pregnancy and, therefore, in the propagation
of our race. Yet, it has not received much attention in research.

Human chorionic gonadotropin was first utilized by the two German scientists, Aschheim and Zondek, who discovered it in the urine of pregnant women. When several cubic centimeters were injected subcutaneously into immature mice, hemorrhagic follicles were produced in their ovaries and this became the basis for the first biological test for pregnancy, known as the Aschheim-Zondek test (13).

Because the immature ovaries were stimulated, the material in the urine was thought to be gonadotropic, and it was misnamed human chorionic gonadotropin (HCG). It has since been established that the observed changes can be brought about only in immature animals with intact anterior pituitary glands (14). The conclusion, therefore, is that HCG is not gonadotropic and not a sex hormone at all. Its action is probably produced by stimulation of the hypothalamus, which in turn influences the anterior pituitary gland. It should not be confused with the true gonadotropic hormones of the anterior pituitary, namely, follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

Only quite recently have some of the properties of HCG been actively researched. In 1967, an article in the Journal of Endocrinology referred to HCG as "a hormone complex" with probable metabolic capabilities (15).

Is HCG Safe?

Consider the following facts about HCG:

a) Its universal existence exclusively, and in large amounts, during a most important stage of human development.

b) Its presence in large quantities in the blood stream of both mother and fetus during the entire pregnancy, without any untoward effect on any organ system of either the mother or a fetus of either sex.

c) The excretion of surplus HCG through the kidneys for 9 months during pregnancy, reaching as much as a million units daily, as compared with a dosage of only 125 units daily for a course of treatment lasting 40 days.

Many physicians needlessly hesitate to use small doses of HCG for a limited time, although they prescribe daily doses of such powerful hormones as thyroid, insulin, cortisone, estrogen, and many others. In the many thousands of cases where HCG has been employed, not a single substantiated case of adverse reaction has been reported. Clearly, Dr. Simeons' HCG treatment can be acceptable to the clinician as a safe procedure.

What About Its Effectiveness?

Much has been written about Simeons' method, both in this country and abroad. Reports have been controversial, but most of the adverse criticism has come from men who have disregarded some of the basic rules of the procedure.

I have carefully examined all the adverse criticism in an attempt to reconcile it with my own clinical observations. In each case I have found basic methodological flaws or interpretive errors, and my confidence in the procedure remains unshaken.

Let us examine the opposition. In all, there have been six negative articles from which all adverse criticism has been quoted (Table 1).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Number of cases</th>
<th>Double-blind tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sohar (16)</td>
<td>1959</td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td>Carne (17)</td>
<td>1961</td>
<td>196</td>
<td>12</td>
</tr>
<tr>
<td>Kalina (18)</td>
<td>1961</td>
<td>42</td>
<td>none</td>
</tr>
<tr>
<td>Craig et al. (19)</td>
<td>1963</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>Frank (20)</td>
<td>1964</td>
<td>48</td>
<td>24</td>
</tr>
<tr>
<td>McGanity (21)</td>
<td>1962</td>
<td>none</td>
<td>none</td>
</tr>
</tbody>
</table>

Numbers in parentheses are reference numbers.
kcal (in food amounts instead of calories), and a nurse visited their homes daily to administer the HCG. Patients were not observed by a physician except at the beginning and end of the experiment. Average loss of weight in all 44 patients was 20 lb. in 40 days. His series proved that patients can lead a normal life and perform their usual daily tasks on the prescribed diet.

Conclusion: Simeons' method is effective, but HCG is only a placebo.

Carne. He used Simeons' method in about 200 patients (only 12 were placebo tests) and his patients lost an average of over 20 lb. in a 6-week period. He approved of the 500 kcal and the time limit of 6 weeks. He admitted "the treatment has some value," but found that those patients receiving saline injections in place of HCG lost in weight almost as much as those that received HCG. In other words, he approved of the method, but questioned the effectiveness of HCG.

Kalina. He used Simeons' method in 42 patients over a period of 2 years. His report was in the form of a letter to the editor of The Lancet, in which he claimed that he did not get the good results reported by the others, but concluded, "In spite of the shortcomings and the unknown mechanisms involved, I continue to find this procedure a useful tool in some obese patients." He further agrees with Sohar about the doubtful value of HCG.

Craig et al. This report covers 20 women patients, 11 of whom received HCG by double-blind technique. The diet consisted of 550 kcal, including many foods not found in the recommended 500 kcal of Simeons' diet. They were all treated by a clinic nurse and weighed once weekly. The average weight loss in a 6-week period was about 6.5 lb., considerably less than the expected 20 lb. or more as reported by Sohar and Carne. Thus, the technique received another negative vote, despite the small number of cases in the study and the admittedly poor cooperation of the subjects in the matter of proper diet.

One significant feature of this report bears emphasis. A considerable number of laboratory tests was performed on all patients treated, including BMR, fasting blood sugars, PBI, serum cholesterol, and serum lipid concentrations. All of these were done at the beginning and end of treatments with no appreciable change in values. This indicates that HCG does not produce any untoward effect on any of the organ systems.

Frank. This author treated 24 obese subjects with HCG, but because "it was thought to be impractical from both the standpoint of office traffic and convenience of the patient" he altered the diet and the technique to such a degree that it was unrecognizable from the original. To list a few of the author's important discrepancies: a) He prescribed a daily diet of 1,030 kcal (instead of 500); b) Each patient received three weekly injections of 200 units of HCG (instead of daily injections of 125 units); c) Each injection was given by an Army corpsman subcutaneously (instead of deep intramuscularly). The author states that he examined and interviewed each participant at the beginning of the study, but he does not mention whether he ever saw them again after that. Naturally, this study failed to prove or disprove anything.

McGanity. His criticisms were published in the Journal of the American Medical Association in answer to a query on HCG. Since he does not claim to have tried HCG in treating obesity, it is reasonable to assume that he was asked by the editors of the journal to answer the query because he is a member of the Obstetrics–Gynecology Department of the University of Texas Medical Branch and is undoubtedly familiar with the physiology of the human hormone of pregnancy known as HCG.

He takes Dr. Simeons to task for choosing a commercial lay magazine to disseminate his information instead of a medical journal. This is entirely untrue as the first publications appeared in The Lancet and The Journal of the American Geriatric
Society years before anything appeared in the lay press. His remarks are rather caustic and decidedly unjust, considering that he does not claim to have tried the method.

Furthermore, he neglected to investigate the background of the individual whom he was attacking. He carelessly links him with the author of Calories Don’t Count—a book which the Pure Food and Drug Department finally made possible to be transferred to the Fiction List of “best-sellers.” This link is about as pertinent as linking the author of Calories Don’t Count with Dr. McGanity because both are obstetricians and gynecologists.

McGanity prefers his method of choice for weight reduction, namely, the old unreliable reduction of calorie intake while maintaining the usual level of activity or the increase of energy demands by increasing activity while maintaining the same level of calorie intake. This recommendation is about as realistic as recommending the reduction of sugar intake for the sole treatment of diabetes mellitus. While it is true that all weight-reducing regimens must include a calorie deficit during the treatment, and it is also true that normal exercise will help all programs, we can no longer claim that overweight is simply a disturbance of the caloric balance sheet. If it were, the problem would have been solved long ago.

It is interesting to note that of all the above authors, only McGanity has not tried the method clinically in obese patients—yet only McGanity contends that adherence to the daily 500 kcal for 40 days is “potentially more hazardous to the patient’s health than continued obesity.” All the others found no untoward effects and some actually praised the diet of 500 kcal.

In an overview of these critical articles, several points emerge:

a) The number of cases studied by each author is too small to draw any conclusions. I well recall that after using the technique in about the first 200 patients, I too was skeptical about the results that Dr. Simeons claimed. Only after my visit to his clinic in Rome and after adjusting exactly to his technique did my results improve.

b) Although Sohar was the only author to admit that he assumed from the start that the procedure would not work, it appears that the others also had misgivings at the outset of their studies. This is unfortunate, for it is hardly conducive to unbiased research.

c) Where individual adherence to a rigid diet is the key factor of a clinical experiment, the double-blind method is of very little value unless the daily intake of food is carefully prepared for all participants in the same diet kitchen and the exact number of calories for each of them carefully calculated. Unless this is observed, the individual variance of diet by each participant invalidates the double-blind aspect of the experiment. This is important since the obese patient is notorious for his inability to evaluate the caloric values of his food or to keep to a rigid diet.

1) The exact diet of 500 kcal (of the prescribed foods) in the exact division of two meals, including daily minimum intake of 2 quarts of liquids.

2) The daily dose of 125 units of HCG given deep intraglutally, 6 days weekly for 40 treatments.

3) Daily interviews with patient to scrutinize and discuss daily progress.

4) Encouragement to stay with the program until approximate normal weight is reached and attempt to direct reeducation toward good eating habits and normal amount of exercise at the conclusion of the program.
d) Of the above six studies, five substantially altered the original technique of Dr. Simeons, so that they cannot claim they tested his method.

e) Most of the above authors stressed the same criticism “no significant difference in weight loss between patients given HCG or a placebo.” It is my impression that Dr. Simeons concurs with this conclusion. Neither Simeons nor anyone else ever claimed that the injection of HCG alone could accomplish the loss of weight.

Even without any medication at all, there has always existed the strong-willed overweight patient who successfully reduced his weight in spite of all the difficulties. Unfortunately, the vast majority of obese patients do not fall into this category. To most of them, dieting is a most unhappy time of their lives. They are constantly hungry, weak, complaining, and generally out of sorts. This is not so with patients under the HCG and 500 kcal technique. The most hardened “professional dieters” will often volunteer their reactions that somehow this time they feel different. Most of them are neither hungry nor tired, and they experience a sense of well-being, something they never had on previous diets.

The above six reports constitute the entire literature from which criticism is quoted against Simeons’ method. They are put forth as scientific evidence from controlled experiments that the use of HCG is not effective. After careful scrutiny, I do not feel the criticism holds up.

Clinical Findings

I have chosen to study the records of my last 500 patients only in order to present a current picture of about the last 3 years. The patients were divided into two groups, those of 3 weeks treatment and those of 6 weeks. If they did not conclude at least 20 days they were not included. For those patients who did not conclude 6 weeks, the weight recorded at the end of 3 weeks was used and their category changed to 3 weeks.

Of the last 500 patients who consulted me, 450 completed 3- or 6-week courses. This in itself indicates an advantage over previous methods in that 90% of those attempting treatment for their obesity were able to stay with the program long enough to receive some benefit of treatment.

Table II is a record of 450 patients who

<table>
<thead>
<tr>
<th>Number</th>
<th>%</th>
<th>Age, years</th>
<th>Average age</th>
<th>Number at 3 weeks</th>
<th>Average loss, lb., at 3 weeks</th>
<th>Number at 6 weeks</th>
<th>Average loss, lb., at 6 weeks</th>
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</thead>
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<tr>
<td>Males</td>
<td>81</td>
<td>18</td>
<td>15-75</td>
<td>41</td>
<td>67</td>
<td>15</td>
<td>90</td>
</tr>
<tr>
<td>Females</td>
<td>369</td>
<td>82</td>
<td>15-72</td>
<td>39</td>
<td>327</td>
<td>12</td>
<td>320</td>
</tr>
<tr>
<td>Total</td>
<td>450</td>
<td>100</td>
<td>40</td>
<td>394</td>
<td>13.5</td>
<td>410</td>
<td>25.5</td>
</tr>
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received a total of 804 courses of treatment of either 3 or 6 weeks duration. (Some patients received more than one course of treatment; the outcome of each course is charted separately.)

A follow-up of all these 450 patients in order to establish the present status of their overweight proved impossible; however, several pertinent conclusions can be drawn from the study as a whole:

1) Ninety percent of the patients attempting to reduce their obesity were able to receive some degree of benefit of treatment.

2) About 60–70% were able to reach its desired normal weight or approximately so.

3) A majority of the patients, when asked to compare this regimen with previous forms of treatment, proclaimed this to be the easiest and most successful.

4) Many of the patients who had regained some or all of their weight claimed that they were able to keep their weight down for longer periods than previously and did not mind returning for further treatment. Some even went as far as confessing that they did not try very hard to keep their weight down because they knew that they could return and repeat their loss of weight.

5) An almost universal finding in nearly all of the patients is the "euphoria" that patients experience. This occurs in spite of the marked low intake of food. I have worked with many obese patients on diets twice the 500 kcal used here and do not recall many who were happy about their situation of dieting. We do not yet have an exact explanation for the "euphoria" and the high rate of "patient acceptance" so often encountered with our method, but I cannot believe that it is due to a placebo effect or a psychological reaction between patient and physician. It is far too regular.

6) As in all the other methods of treatment of obesity the markedly obese show the most striking and the most satisfying results. With regulated rest periods between 6-week courses of treatment, many of these obese successfully reduced 100 lb. or more. Of special gratification are the results we obtain with those markedly obese who have accompanying diabetes mellitus of the maturity onset or stable type. Most of these patients show a marked improvement in their diabetic state as well as in their obesity. While this is true with all forms of successful weight reduction, the improvement is more marked with HCG.

SUMMARY

After 40 years of trying every new approach to the treatment of obesity with little or no success, I believe a new method that works has been made available to us. It works with about 60–70% of obese patients of both sexes aged 15 and up, provided the method is followed meticulously as the author has developed it.

No one can yet say for certain how or why it works, and a great deal of research will be needed. I hope that this report of my own clinical findings together with some possible tentative explanations will act as a stimulus for this research.

While it is true that obesity is due to excessive calorie intake, this tells us nothing of the basic causes. What needs further explanation and discovery are the mechanisms that regulate calorie intake and output as well as the reason for the failure of these regulating mechanisms in some individuals that results in obesity.

Recently, Dr. Margaret Albrink (34) has made a very interesting observation that while man has elaborate and efficient mechanisms for surviving starvation, his techniques for handling a surplus of food—a frequent necessity in modern societies of abundance—are limited and easily saturated. As a result, she suggests, the metabolic abnormalities leading to...
atherosclerosis may be a result of over-burdening the mechanisms for storage of fuel, i.e., overstuffing the adipose cell. It is intriguing to speculate on a parallel explanation for the metabolic abnormality that leads to obesity.

Further weight to this possible explanation is brought to bear by the fact that the adipose cell in the obese has been found to be larger than the normal fat cell. It follows, therefore, that at least two types of fat cells exist, the normal cell storing the reserve fuel that is necessary for good health and the abnormally large cell that becomes overstuffed and forms the excess fat tissue of the obese.

This approach to obesity also lends further credence to the belief that the manner in which food is utilized and stored in the body is a more complicated mechanism than previously believed and that there is a controlling center in the brain.

Medicine must not neglect nor abandon the problem of obesity for many reasons, not the least of which is its relationship to cancer and the process of aging.

A. Tanenbaum and H. Silverstone (35) suggest that nutrition plays a role in the formation of cancer in man. "When living cells are subjected to carcinogenic influences they may undergo changes that finally result in growing neoplasm. The energy and substance for the development of the first cancer cells are derived principally from the animal; the new cell type increases in number by assimilating nutrients from the host. It may be expected then that the diet and the nutritional state of the host influence the formation and the growth of tumors."

The process of aging as defined by Howard J. Curtis of the Brookhaven National Laboratory "may be considered as an increasing probability of developing a degenerative disease." Furthermore, M. H. Ross (36) in his experimental studies with rodents has shown that a calorie-restricted diet delays the onset of development of all the degenerative diseases in rodents (and presumably in man) and obesity speeds their development.

Medicine must neither accept nor abandon Dr. Simeons' method until it has been properly tested through research or until a completely different and a better method is discovered. Dr. Simeons himself has begun such testing and research in his clinic. He has often told me in person and has more than once said publicly that critics and researchers in this field are welcome at his Clinic to study his results and observations. Let us hope some of them will accept his offer soon.

A clinician must contribute to science from the great wealth of material as chance presents it. He must weigh, observe and analyze at every opportunity. Often, he can neither plan nor control his experiments, yet critical evaluation of his successes as well as his failures can add immeasurably to the sum total of our knowledge and clinical judgment (T. Messerman, personal communication).

REFERENCES
1. HENDERSON, L. J. Science 94: 1, 1941.