

Comprehensive Cancer Care: Integrating Complementary & Alternative Therapies
Trophoblastic Hormones and Cancer: A Breakthrough in Treatment?

Moderator: Leonard Wisneski, MD

Presenters: Hernan Acevedo, MD; Nicholas Gonzalez, MD; Ralph Moss, PhD

Commentator: William Regelson, MD

Session 205: June 13, 1998

Dr. Wisneski: Welcome to the panel on trophoblastic hormones and cancer. My name is Len Wisneski. I'll be the moderator. I'm medical director of the Bethesda Center of a new adventure into integrative medicine called American WholeHealth. I enjoy a clinical practice of internal medicine, endocrinology and acupuncture.

On the panel with me is commentator Dr. William Regelson. Bill is professor of Medicine at the Medical College of Virginia, Virginia Commonwealth University, in Richmond. He's a specialist in medical oncology with joint appointments both in microbiology and biomedical engineering. He has been a leading researcher in the field of aging for over 20 years. He was formerly the scientific director for the Fund of Integrative Biomedical Research, dedicated to research on the biology of aging. In addition to extensive research and numerous scientific publications, he co-authored two popular books, *The Melatonin Miracle* and *The Superhormone Promise*, which has gotten much interest throughout the country.

The first speaker today will be Dr. Ralph Moss. Dr. Moss is internationally acclaimed as a science writer who has spent more than 20 years investigating and writing about cancer issues. Formerly Assistant Director of Public Affairs at the Memorial Sloan-Kettering Cancer Center, Dr. Moss is the author of such interesting books as *Cancer Therapy*, *Questioning Chemotherapy* and *The Cancer Industry*, as well as a PBS documentary called *The Cancer War*, which was quite popular.

He also wrote the 1994 Yearbook article on alternative medicine for *The Encyclopedia Britannica*, and he was founding advisor for the National Institutes of Health Office of Alternative Medicine. Dr. Moss is presently scientific advisor to the Rosenthal Center of Columbia University and the University of Texas School of Public Health. He is also a member of the advisory board of the medical journal *Alternative Therapies in Health and Medicine*. He will be addressing the history of trophoblasts in cancer. I'd like to call Dr. Moss to the lectern.

Dr. Moss: Thank you very much. I was the person who suggested to Jim Gordon that we have this panel. I did that because I have been aware for a long time of the work of Hernan Acevedo. I had never met Dr. Acevedo in person before this meeting. When I wrote *The Cancer Industry* (the book was written in 1979 and first published in 1980), there were two pages of the book devoted to his work. I don't even know if he knows this. I pointed out the extreme importance of a research group headed by Dr. Hernan Acevedo of the William H. Singer Memorial Research Institute confirming the fact that an organism called progenitor cryptocides produced the human growth hormone.

Dr. Acevedo said at that time that the impact of these findings in the fields of oncology, bacteriology, epidemiology, genetics and molecular biology is so great that a detailed description will be beyond the scope of this communication. It is apparent that this phenomenon exposes the need for a new approach to the analysis as well as to our current concepts of cancer.

Since that time, Dr. Acevedo has gone on to do some amazing work concerning the very basic biology of cancer. He'll be describing that to you. Essentially what he has found (and I hope I don't misrepresent this) is that the human chorionic gonadotropin, which is the so-called hormone of pregnancy, can be found on the surface of all cancer cells, or that's to say the beta

subunit of that or a portion or fragment of that. To the average person this would just be another esoteric finding in science. I also asked Dr. Regelson to come join us on this panel and am extremely happy and proud that he accepted. When this finding was published in *The Journal of Cancer*, Dr. Regelson, who has a history of tremendous courage in this field, published an accompanying editorial in which he hailed the importance of this discovery.

What Dr. Acevedo is saying is that, in effect, there is a universal marker for cancer. Therefore this points in some way to a unitarian theory of cancer, some commonality that's shared by the 100 or so different diseases, or 200 different diseases that we call cancer. This question of the multiplicity of cancer versus the unity of cancer is something that goes back to the very beginnings of cancer science. Why this is important for a meeting on complementary or integrative oncology is that the question of trophoblasts in cancer is absolutely central to the alternative view of cancer.

The first awareness that I ever got about the existence of an alternative movement was by going to a health food store and reading up on laetrile. In my keynote speech I talked about my own experiences at Memorial Sloan-Kettering in regard to laetrile. I realized that I was involved in some very strange events at Memorial around laetrile testing. Positive results were being denied in the face of what was believed by the leaders themselves and acknowledged in private conversations. So I went to the health food store to find out more about this. I picked up a book called *World Without Cancer*. It was a book published by people very close to the John Birch Society, and had a very weird take on the entire question of cancer.

The central thesis of this book and apparently of the entire laetrile movement was that cancer was trophoblastic in origin. In other words, cancer was a natural phenomenon that was actually pregnancy in the wrong time and the wrong place. The proof of this supposedly was

that you could find hCG, the predominant hormone of pregnancy, in every sample of cancer. If you looked in the classic standard textbooks, and still if you look in most of them, you will see 1) an acknowledgment that hCG is in fact the standard marker for testicular cancer, 2) that it's also present in many cases of ovarian cancer and so-called trophoblastic diseases, of which there are a number, but 3) that it's presence is extremely variable or limited in most other cancers.

There was a nice report in the fourth edition of Dr. DeVita's textbook from a well-known biochemist at Memorial Sloan-Kettering giving the figures for percentages for different kinds of cancer. You would conclude based on that report that there was no special correlation between hCG and cancer as a whole.

Dr. Acevedo has published in probably the preeminent journal of clinical cancer in the world, namely *Cancer: A Journal of the American Cancer Society*, stating that in fact there appears to be some justification for this earlier belief. What intrigues me as a historian is that this theory is one of the oldest theories in cancer, if not the oldest theory. It's very closely related to what was called the theory of embryonal rest that was put forward by Cohnheim in the mid-19th century. In fact it was the predominant theory of cancer until well into the 20th century.

In 1902, in *The Lancet*, a man by the name of John Beard published an article on the trophoblastic origins of cancer. In 1911 he published a book called *The Enzyme Treatment of Cancer and Its Scientific Basis*. It may not be immediately apparent to you or to anyone why trophoblasts would lead to the enzyme theory, but that's why I've also asked that Dr. Nicholas Gonzalez join us. Dr. Gonzalez is among other things the foremost practitioner in the country using pancreatic enzymes, in particular in the treatment of cancer.

I have with me a copy of John Beard's book from 1911. It's a photocopy. I've never been able to find an actual copy, and I've asked all over the world for booksellers. I know where

one copy was, and it disappeared with the death of its owner. If you read this book, and I've been reviewing it for this session, it is truly one of the weirdest books ever written. It's filled with all kinds of scientific facts and wonderful experiments, and also incredible invectives and argumentativeness towards the medical profession and towards surgeons in particular.

You have to understand that John Beard was a professor of embryology, a PhD professor of embryology at Edinburgh University, where he trained doctors. Edinburgh was at the time and for maybe 150 years the preeminent medical school in the English-speaking world. So he had a very high position, like a PhD professor at Harvard Medical School. Obviously he resented his students and he resented his medical colleagues, because the book undermines its own message by this hatred that's directed against doctors.

Essentially, Beard thought that he had figured out the entire cancer problem. It had to do with the alternation of generations between sexual and asexual generations. He had started out working in the Adirondacks as a researcher, working on a certain kind of fish. This fish had a peculiar life cycle where you could see the sexual phase and an asexual phase. Then he extended those studies to mammals, and to humans in particular. He concluded that cancer was asexual generation, or irresponsible trophoblast. In these words for the first time in human history the nature of cancer was laid bare. Owing to their extraembryonic origin, aberrant germ cells are quite common and they may be met with anywhere in the embryonic body.

It's interesting that this theory isn't entirely dead. There are certain forms of cancer in which we still talk about embryonal rests – certain kinds of kidney cancer and so forth. You'll find this in the standard DeVita and the other textbooks as well, but it's limited to a few instances. I'm not here to pass judgment on the truth or falsity of the theory. It's just very intriguing that this theory of trophoblast, or cancer as being pregnancy in the wrong time and

place, has woven itself through medicine and sometimes pops up as orthodox theory and sometimes pops up as nonconventional theory.

The thing that preserved the work of Beard but also discredited it in the eyes of the medical profession was this. When it was completely forgotten, really dead and gone in the 1930's, when Beard himself had passed away and nobody knew about this, a fellow by the name of Ernst Krebs came along. There was a father and son team. The son was a very strange guy who was a graduate student at UC Berkeley. He never finished his work, and he was a very cantankerous and difficult individual, but with very brilliant and weird ideas. He glommed onto this book and established The John Beard Memorial Foundation, John Beard being the author that we're talking about.

The purpose of this foundation was to establish the truth of the trophoblastic theory. As fate would have it, Ernst Krebs senior, who was a physician, and Ernst Krebs junior also were the inventors of laetrile. They were convinced that, as Krebs himself often said, this was not just the trophoblastic theory of cancer, this was the trophoblastic fact of cancer. He would not talk to anyone who didn't accept the factual nature.

According to the theory (this is not part of Dr. Acevedo's work, and I'm not sure how much if any of this he would agree with), the intrinsic treatment for cancer is pancreatic enzyme, because pancreatic enzymes start to be produced by the embryo at 56 days and at that point the trophoblast stops growing. So if you want to slow the growth of a trophoblastic thing you would give the person pancreatic enzymes. According to Dr. Beard they have a dual role in the body. Their first role is to digest protein in the intestines. The second role is to digest aberrant protein wherever it occurs in the body, and particularly cancer.

Laetrile came in because for whatever reason they didn't feel that the intrinsic antitrophoblastic factor was sufficient. They wanted to bring in an external or extrinsic anticancer factor. That was what laetrile was supposed to be. It certainly was not, but that was the theory behind it. It was Krebs' advocacy of Beard, ironically enough, that led to both its preservation and its being ostracized, because he was a very combative, dogmatic individual. It lived on, but it lived on in a kind of limbo.

Dr. Acevedo (who has no connection to the laetrile movement or any other movement as far as I know) is a meticulous scientist who was not afraid to go into areas that have minefields in them if he feels there's something valuable to be learned. His work is entirely mainstream science. He also has taken on the task of looking at the work that Virginia Livingston and John Beard did. He credits John Beard in his papers, which is extraordinary, so I wanted you to hear some of what the background of this is, and how important this. This really could be something of earthshaking importance. Thank you very much.

Dr. Wisneski: Thank you, Ralph. I'll accept a few questions from the floor at this point. Go to the microphone, please.

Participant: Dr. Moss, is there a relationship between Ernst Krebs and the Krebs cycle?

Dr. Moss: None whatsoever, but the name Krebs means cancer in German, so that's another kind of synchronistic thing.

Participant: In the book, *A World Without Cancer* it mentions the Asheim-Zondek pregnancy test of the urine. I believe it said it was 97 or 98% accurate. Is there any medical reason not to use that as a screening test for all forms of cancer?

Dr. Moss: Yes, the Asheim-Zondek test and also the other tests. Another ironic synchronistic thing was that H. H. Beard (no relation to John Beard), who was a pretty well known biochemist, became one of the main advocates of the Beard thesis and also of laetrile. He was a pretty good scientist. He had a test of his own, a urine test based again on detection of hCG. In the Philippines there is a fellow named Nararro, who to my knowledge still, if you send him a sample of the urine, will process it, look for hCG and tell you whether or not you have cancer.

What's so weird about this is that this has never been reproducible by standard laboratories. I don't want to get paranoid about this, but I don't understand how it is that nonconventional labs claim to be able to detect hCG 100% of the time or 99% of the time, and good biochemists in America could never do so. Maybe Hernan can explain this.

Dr. Acevedo: I am going to take you, in my presentation, by the hand. I'm going to tell history. I'm going to take all of you by the hand, because from my point of view and others who have heard me give this lecture, it's one of the most incredible things in respect to how hCG and its attachment to cancer evolved.

I'm telling you in advance that what we have is more than a theory. It's a fact. The vaccine against hCG was developed for fertility control by the World Health Organization and an American biotechnology company has the patents for its application in cancer. The WHO,

because of the way things are arranged in Europe, cannot deal with cancer matters, only with population control. I'm going to tell you the history of the whole thing step by step. We are going to talk and you are going to learn, because most of you are not specialists in the different stages of human development.

The anticancer effects of the anti-hCG vaccine are a fact. We have all the proof by strict science using the most modern immunological and molecular biology methods. What we are going to present here is experimental data that nobody can negate, unless they negate all the work and everything we know about DNA, about translatable levels of messenger RNA, etc. Please be a little bit patient. When I am making the presentation, which is going to be a slide presentation, if I'm not clear, please interrupt me or put up your hand and ask a question, so I can clarify immediately.

Dr. Wisneski: With that, I'm very tantalized. I can't wait to introduce you and have you begin the lecture. Dr. Hernan Acevedo is here to present the role of hCG, human chorionic gonadotropin, in cancer. This is the result of phenomenal work on his part, and he will go through it in a stepwise sequential matter. Dr. Acevedo received his PhD in Chemistry from Catholic University of Chile. He has a fellowship in endocrinology from Duke University School of Medicine, and he is currently professor of pathology and laboratory medicine at Allegheny General Hospital.

Dr. Acevedo also has a professorial appointment at the Allegheny-Singer Research Institute, Hahnemann School of Medicine, and Allegheny University of the Health Sciences in Pittsburgh. He is a former British Research Council Fellow at St. Bartholomew's Medical College in Britain, and also he was a fellow at the University of Sao Paulo in Brazil. He's the

author of over 162 publications, and is the foremost American researcher on the role of human chorionic gonadotropin in the genesis of cancer. It's an honor to present you, Dr. Acevedo.

Dr. Acevedo: Thank you. One thing I want to make clear from the very beginning is that hCG, human chorionic gonadotropin *does not cause cancer*. It has nothing to do with the etiology, which is the cause, of the disease. Cancer is produced by a hundred different things – what you eat, the multitude of chemical compounds around you, excess population, poverty, cosmic radiation, the tar of our streets, etc., whatever you want to call it. All these factors start a process that we call the process of malignant transformation, a step by step process that has been pretty well described.

My friend Dr. Regelson knows perfectly well about the step-by-step process of malignant transformation. Fortunately for us, from the point of view of energy work, it is a process that is, in general, very slow. It is an extensive process that, unfortunately, we have been unable to control, and it finishes in the disease we call cancer today. hCG comes out as a product of the process for malignant transformation.

To start, I'm going to show the first slide. Glycoproteins are proteins that have sugars, and some membrane proteins are glycoproteins which covalently bond carbohydrate side chains. As with glycolipids, the carbohydrates of the glycoproteins are located almost exclusively on the external surface of the plasma membranes, that is the cell membranes. Cell surface carbohydrate has an important function. Every living cell in nature, including plant cells, has a negative charge. The negative surface charge of cell is ascribable to the negatively charged sialic acid, also known by N-acetyl neuraminic acid, of glycolipids and glycoproteins. Therefore, we have a negative charge that is a normal charge in the cell membrane of every cell.

When malignant transformation occurs, the genes of hCG are activated. So what is hCG, biochemically? There you have hCG. You have two subunits, the alpha subunit and the beta subunit. They can exist separate from each other or together to make the whole hormone. You see the amount of carbohydrates (sugars) marked as CHO that this molecule has. You also see in this slide that this is a very small protein, having a molecular weight of about 17 kilodaltons. To make comparisons, I am going to talk now about antibodies. Do you know what antibodies are? Antibodies are also proteins! The molecular weight of an antibody, like a monoclonal antibody, is about 150 kilodaltons! Look at the size. Your immune system works with antibodies, and those antibodies have a size much bigger than the size of the hCG molecule.

Now I will show the characteristics of the hCG molecule. The next slide shows what we call a bead model of the molecule. The carbohydrates (sugar chains) are in blue. The part shown in red we call the carboxy-terminal peptide composed by 37 amino acids. By the way, hCG was the first hormone discovered in nature by Drs. Asheim and Zondek, who produced the first pregnancy test. But I can tell you that Asheim and Zondek were not the first ones. It was first discovered by Japanese investigators about three years before. The problem is that they published in Japanese, and the scientific literature of that time, at least in Japanese, was not available in the West.

You can see one important thing. In the carboxy-terminal peptide of that model you have four groups of carbohydrates. Inside the molecule you have two groups of carbohydrates. We call that the core of the molecule. Those carbohydrates that are over there in the red part of the carboxy-terminal peptide are what we call oxygen-linked (O-linked) carbohydrates because they are attached with an amino acid called serine. The other carbohydrates in the core are N-linked,

nitrogen linked, because they are attached to a different type of amino acid that has nitrogen. These are very important in the biochemical and biophysical characteristic of the hormone.

If we look at the map of the carbohydrates, in the upper part we see that the N-linked carbohydrates finish in two sialic acid residues, while in the O-linked carbohydrate you can count six sialic acids. Therefore, there is a large amount of negative charges in this small molecule. Taking the alpha and the beta subunits, the core and the carboxy-terminal peptide, we can see that the number of sialic acids (negative charges) is incredible. As I told you, in nature, every cell has a negative charge. In contrast, the normal cell, which does not have hCG, has a negative charge because of the glycoproteins which are called mucopolysaccharides. For each molecule you only have one or two sialic acids.

In the cell membrane, if the mucopolysaccharides are replaced by hCG in any of its forms, you can imagine what is going to happen in that cell membrane. It's going to increase the negative charge in a fantastic way. This has been scientifically proved. There are several papers which show that those cells that have hCG in the cell membrane, as happens in cancer cells, are the ones that have the normal mucopolysaccharides replaced by the HCG.

As we will see, these changes in the surface of the cancer cells are very important. Let's go to our immune system. This is important for pregnancy as well as for cancer. The first line of defense in our immune system are what we call natural killer cells (NK cells) and macrophages. If you get hit, or you get a cut, it turns red. Immediately you have inflammation, one characteristic that your immune system is working. So you have NK cells coming there and you have macrophages to eliminate the garbage.

If something very bad happens and the macrophages and NK cells are not enough, the macrophages take an imprint of the enemy and give the imprint to a cell called B-cell, and these

cells produce antibodies that will kill the invaders. This is the normal immune response. Then we will have what we call cell mediated cytotoxicity. That is the way in which your immune system works. Do not forget that all the cells of the immune system have a normal negative charge.

Cells, like embryonic cells or cancer cells, that have the hCG molecule in the cell membrane, do not permit our immune system to work. Remember, NK cells and macrophages have also a negative charge, but the amount of the negative charge is a “normal” one. The cancer cell or the embryonic cell has a much higher negative charge. Therefore, here comes the macrophage, tries to approach and cannot, tries to touch it and cannot. You can have the best immune system in the world, and you will get cancer. Why? For the same reason that you get pregnant. These cells (cancer and embryonic) become immunologically inert. Your immune mechanism does not work. That is why you have cancer.

There are two normal cells that produce hCG. Here you have a very well known cell, an old friend of all of us. A spermatozoon. Of course, the spermatozoon after ejaculation has to go a long way to be able to get in touch with the ovum and start a new life. So it has to have defenses, because the immune system of the woman is going to attack immediately. That is the reason why you don't need more than one to start a new life. As my colleagues in San Antonio, Texas said in the study of problems of fertility in males, it's not the amount of spermatozoa that the male produces, it's the quality.

The next slide shows what happens during embryonic development. We go to the early process of development; the morula stage. This is the immunofluorescence analysis using antibody against hCG beta. We have only about eight cells in this stage. They all show hCG. The next slide illustrates something that is incredible. It shows how the early embryonic cell

(cytotrophoblast) penetrates the uterine tissue, exactly as cancer cells do. They go inside the tissue and get into the blood vessels. Not only that, they have the capability to expand the blood vessels so they will receive enough blood necessary for the new being.

Cytotrophoblasts produce three hCG subunits. The whole hormone, the alpha and beta, is not produced in very early pregnancy. Placenta has not evolved yet. Placenta produces a particular type of cells, the syncytiotrophoblasts. They produce whole hCG, the hormone, as well as free subunits. This is one of the most beautiful things from Mother Nature. The way in which it is done gives an illustration of what occurs in cancer.

Here is another thing with respect to hCG. hCG is formed from two parts, the alpha and the beta subunit. The alpha subunit is only one gene. Remember, genes make proteins and nothing else. One gene, one protein. We learn now that for practically every gene we have a protein. We need about 120,000 proteins in our life. So you can imagine the amount of genes we need. One gene, one protein. There are a few exceptions. Calcitonin, a hormone, has two genes. Hemoglobin has also two genes. For hCG we have a cluster composed of four genes, one pseudogene, and a last gene that codes for hLH beta (human luteinizing hormone).

Give me the next slide, please. Remember when I told you the amount of carbohydrates that the molecules of hCG beta and hCG alpha have to be perfect to make the whole hormone? There is one phenomenon that we call hyperglycosylation, and this occurs very early in pregnancy. At this stage, the free subunits have the capability to increase the number of carbohydrates. This is incredible. And it does not permit the molecule to be the complete hormone (whole hCG).

Every one of these proteins has a stage that we call a tertiary structure. The alpha and beta have to be perfect to be able to attach noncovalently. Any change in the tertiary structure

avoids the formation of what we call the quaternary structure of the whole hormone, that is the one that is going to act as a hormone. Hormone means that it's going to stimulate, to produce. It has nothing to do with the other types of biological activity. That does not mean that those separated parts of the molecule are not active. They have other types of activity that we have already talked about.

The alpha subunit is common to four hormones that are fundamental for life. One is human chorionic gonadotropin. The others are follicular stimulating hormone, thyroid stimulating hormone and human luteinizing hormone. Those hormones are produced in the pituitary gland, which is located in the brain, in a part of the gland called the adenohypophysis (anterior lobe). The posterior lobe is called the neurohypophysis. These pituitary hormones are fundamental for life. The alpha subunit is one gene only. The alpha subunit is common to the four hormones. The alpha subunit conforms to the body of the beta subunit to make the whole hormone. In respect to genes, hCG beta is different, and don't ask me why. We have a cluster of genes composed of four genes, one pseudogene and a last gene that corresponds to the luteinizing hormone beta (hLH beta). While the single gene of the alpha subunit is located in chromosome 6, the hCG beta genes are located in chromosome 19.

If anything activates those genes to manufacture a product (in this case, of course, it manufactures hCG beta), there is always going to be a little bit of LH beta. We found LH beta also in cancer cells for that reason. Genes have to be activated. The way genes are activated, especially in cancer, is by translocations of the genes, amplification and formation of special genes (abnormal). That is the phenomena of gene activation. In the case of hCG, we did DNA analysis using different reagents to be absolutely sure of what we did. We used as a control our normal genes from the trophoblasts from placenta, that is the normal gene for hCG. The DNA

analysis of the hCG gene shows – you see the amount of cancers *in vivo* and *in vitro*. We see that in all cases the DNA is absolutely perfect. There is no amplification, there is nothing. The hCG DNA in all cancers is perfectly correct, no changes. Next slide, please.

Here you have it with another enzyme, the same thing. We have every type of cancer – lymphomas, leukemias, everything that you can imagine in the book. The genes (the DNA) of the hCG beta are absolutely normal. Next slide. That proves that the activation of the genes for hCG beta is not done in the usual way. I want to tell you immediately, because the unusual way in which it is activated is the basis of every one of you and me being here. We call the process of gene activation that occurs in the case of the hCG, patterns of methylation. During the embryonic process and the fetal life, during your whole development to be a human being, and this occurs in all animals also, those genes are activated and deactivated by patterns of methylation.

What do we call patterns of methylation? Patterns of methylation are one of the most beautiful ways that Mother Nature has for the maintenance of the species. Genes are composed of four bases. One of them is cytosine. Cytosine is methylated. It can be methylated and demethylated, so you have methyl cytosine or cytosine without the methyl. How does it work? Let me give you an example. You are in your car. You are running your car. You hit a red light. You apply brakes. If your car is in good condition, your wheels stop, but the motor continues working. Then you push the accelerator again and the car takes off, if everything is okay.

In methylation it is just like that. You take out or you put in the methyl group. What you do is you stimulate the complementary DNA (cDNA). To have DNA and activate DNA you have to have complementary DNA, that is cDNA. To have gene activation you have to produce

complementary DNA, cDNA. By putting in and taking out the methyl group in the cytosine, you produce, you stimulate cDNA synthesis. From cDNA you go to messenger RNA and then you go on. We measure translatable levels of messenger RNA that tells us that the product (hCG beta) is there. This is the way in which the genes are activated and deactivated during all the embryonic development. The way this process works is absolutely incredible. In reality, its mechanism is very simple.

We use the methyl group in our organism in a tremendous amount of reactions by different glands, like adrenal glands, etc. Everything is methylation and transmethylation. Basic reactions, intermediate reactions and all that, all our endocrine system. We even produce methoxysteroids, we get a methyl group there. The enzyme used is called methyltransferase. Beautiful. If you control the methyltransferase you control everything. Wonderful.

The problem is that methyltransferase is a family of enzymes and there are more than 80 different methyltransferases. Which one of those families are the ones that are acting in this process? And every one of those methyltransferases needs a tremendous amount of other compounds to be able to be active. We call those cofactors. We know about 200 to 300 different cofactors, including methyl ions, zinc, selenium, vitamins, etc. We have found it interesting that you have to have metals like zinc and selenium for the reactions to occur.

There is no computer or model in the world, not even the Pentagon has it, that can put all this together. If we know in which way this is done, we have practically the secret of life, and Mother Nature doesn't like that. Can you imagine a knowledge like that if you want to change populations in this world, in the hands of a Hitler, or to purify races, or things like that? You can control life completely. Fortunately, there is no way that we see. Perhaps in 100 years more we will be able to do something about it, but there's nothing we can do about it now, thank heavens.

Now we have analyzed the molecule completely. And we have created antibodies to each part of the molecule (epitopes). The scientific name of the point to which the antibody will attach in a molecule is antigenic determinant. We have a great amount of different monoclonal antibodies directed to different epitopes of the hCG molecule. Monoclonal antibodies means that these are unique, totally purified reagents. They are absolutely pure, perfectly well defined, immunoglobulins.

In our work, the first analyses were done by flow cytometry, that is analytical flow cytometry. We created the method. We published the method. It's absolutely quantitative and you work only with live cells. Every dead cell is thrown out. You see that we have the carboxy-terminal peptide. I show it in the model, in the upper part of the molecule. We have two antibodies to that part. You see for the beta subunit we have all those different antibodies. When the alpha and the beta subunits are separated, we have antibodies to demonstrate, that measure, only the free beta subunit. Not only that, we also have what we call a conformational antibody, in which the place of attachment exists only when the two subunits are together. So we have practically antibodies to every part of the molecule, and I have shown very few in reality. We have I will say about 120 different antibodies. So we have mapped the molecule completely.

Next slide, please. Here you have a typical flow cytometric analysis of three cancers. You can see for each one of the antibodies, quantitatively, how many of those cells are presenting that particular type of antibody. This we prepared to be published in *Cancer*, I think it was in 1992, all the methodology also.

Next one, please. These are all living cancer cells. This is *in vivo*, not *in vitro*, taking cancer cells from tissue.

Next one, please. Here we've got a series. Here you have another patient – same thing, analyzing every part of the cell membrane, living cells.

Next one, please. Here is a control. Here we have a nonmalignant (benign) tumor that is very common, leiomyoma of the uterus. It can kill if you don't take it out. You see that it is absolutely negative for every one of the antibodies, again the different parts of the molecule that we used. Absolutely negative.

Next one, please. Here I have a list of all the types of cancer that you can imagine, just to give you an idea. Every one shows exactly the same thing.

Next one, please. We can detect the cancer cells by immunocytochemistry using the same type of antibodies. Here we have tumor cells detected with one of the antibodies. This was again the free beta subunit. The way in which this tissue is fixed for cytochemistry is different. We don't fix in formalin. To have a result in immunocytochemistry, when you're dealing with hCG, aldehydes kill glycolipids and carbohydrates, so we have to use a picric acid type of fixative, Bouin's fixative. The next section of the same tumor was treated with an antibody against the whole beta subunit. You see the interesting thing – the number of cells that react with the antibody against the whole hCG is less. It is typical that in cancer you have more free subunits than the complete hormones..

The next slide is the control. You eliminate the first antibody and use only the second antibody – totally negative. You repeat this control with every antibody that you use.

Next one, please. Do you see those cells? Those cells are very nasty. For every pathology I want to see those cells there.

Next one please. Here we have a frozen section. A frozen section is beautiful. You can detect the hCG in this cancer. This was the carcinoma of the adrenal gland, but it was the liver

metastasis. This is the analysis done in the biopsy of the liver metastasis. We froze it, we read the reactions right away and there was the hCG.

Next one. Here you have the whole tissue of the same cancer and you see the amount of hCG beta.

Next one please. Here again is the control.

Next one, please. Is there anyone here that can read and can see pathology slides? Any pathologist will tell you this is characteristic of cancer cells, the nucleus is totally abnormal. When we do electromicrography, microphotography, when we look in the microscope and make the analysis of cancer, we look at the nucleus. How many nuclei are there? Is there a normal nucleus? Is it a strange form of nucleus? We look at all those things.

There's a ratio of nucleus to total amount. You can have more than one nucleus – binucleated, trinucleated. In the electron microscope it is beautiful because you can see the extraneous forms, the ratio of the nucleus to the cell. Not only that, look at the amount of things like filaments coming from the cell. We call them pseudopodia.

The next slide. You see the nucleus. It's a beautiful cancer cell. Well, let me tell you that is not a cancer cell. That is a cell from the lung of a female fetus 14 weeks old. That cell from the lung of a female fetus 14 weeks old looks exactly like a cancer cell.

Next one, please. To explain this slide, you have to remember that when I started my presentation, I mentioned that hCG was the first protein hormone that was discovered. Now I have to say that it was the last one that was totally purified and crystallized. This work was published in the June 9, 1994 issue of *Nature*. This achievement was accomplished by the team effort of scientists of the Department of Chemistry, University of Glasgow, UK, the Department of Medicine, Columbia University, NY, USA, The St. Vincent Institute of Medical Research,

Melbourne, Victoria, Australia, and the Department of Biochemistry, Latrobe University, Melbourne, Victoria, Australia.

The three dimensional structure of hCG showed that each of its two different subunits has a similar topology, with three disulphide bonds forming what is called a cystine knot. This same structure is found in three growth factors, the platelet derived growth factor-beta (PDGF-beta), the nerve growth factor (NGF), and the transforming growth factor-beta (TGF). In this slide, the hCGbeta spatial tertiary structure is the one that is on the right side; the other three structures present the same thing in the middle, the cystine knot. The three showing very similar structure and exactly same knot are the three growth factors – the platelet derived growth factor, the nerve growth factor and the transforming growth factor- β . So here we have a hormone that is not only a hormone, the hormone of development and differentiation, but it is a growth factor by itself. Therefore, cancer cells can stimulate their own growth without the presence of anything else. These growth effects have been proven and published by us and other investigators. Adding hCG to cancer cells causes the cancer cells to proliferate faster.

Next one, please. Here we go now to the molecular biology experiments. The following slides show the results of the analysis of hCG beta translatable levels of messenger RNA in different types of cancer cells. We use normal placenta as control. The results demonstrated that the different genes are activated and produce hCG, because we proved the presence of translatable levels of messenger RNA. There you have a bunch of different cancers.

Next one. Another group. We put controlled normal tissue in the medium and so on.

Next one, please. That's the whole list.

Next one. There you have more.

Next one, please. More. The others were controls in which you aren't supposed to have it. We didn't, of course.

Next one. More cancers.

Next one. More cancers, with control over there. More cancers.

Here we go now to the vaccine. These are the first results of the vaccine. This is how we are vaccinating the animal. At that time we used the Population Council vaccine. We eliminated the formation of metastasis in the lung. The left one is the that is vaccinated.

Next one. Here is the result of the first experiment in women for fertility control in Australia. This was very important because it was demonstrated by my friends in Edinburgh, Scotland, taking the serum of the women that presented the higher antibody titer, the antibodies worked in the same way.

Next one, please. We have demonstrated in our last publication, and here are the tables of that last publication, that there are very special antibodies against hCG, very rare, that are exceptional. They have the capability to kill, to destroy the cancer cell in the total absence of the immune system. In other words, they are cytolytic and cytotoxic. We already patented the activity because that is permissible. Only one of the three antibodies produced by the vaccine against hCG that is in clinical trial has that type of activity. So we have demonstrated the mechanism of action of the vaccine. That is the reason it works. The paper will be published in the August 15, 1998 issue of *Cancer*. Thank you very much.

Dr. Wisneski: Thank you. That's quite amazing work. Before I take any questions I'm going to ask Dr. Regelson to give a commentary to Dr. Acevedo's lecture.

Dr. Regelson: It's very important to point out what may be a universal biomarker for malignancy, from the point of view of diagnostics, with these monoclonal antibodies that have been developed. What we have here is a universal biomarker for malignancy. We have now the demonstration of a final common pathway that defines cancer as a syndrome that is unified.

Everybody says each cancer is different from the other. To kill a cancer you have to be able to separate your left ear from your right ear. What we now have is a parallelism between what is involved in pregnancy and what is involved in malignant transformation. So going back to Cohnheim and Beard and all these other people who focused on this phenomena, we now have the realization that this may be true.

What is even more important, apart from passive vaccination, which has been developed as a population control vaccine to prevent pregnancy, this also has antitumor potential. The idea is that postoperatively, once you have a diagnosis, or once you have a cytologic diagnosis, you can develop a resistance to tumor development, which would be the same thing as trying to develop a resistance to pregnancy. We've shown that we can do this for pregnancy. Why can't we do this for cancer?

Even more importantly, what Hernan Acevedo has developed is a cytotoxic monoclonal antibody that can kill tumor cells. Most monoclonals are diagnostic, and he showed you the diagnostic capability of what he had. What he has now are several monoclonal antibodies that could not only attach to the tumor and diagnose it and recognize it, but kill it. So we now have a therapeutic entity.

What is most disturbing to me (particularly in view of the publicity that we've seen in regard to Antremed and Folkman, who've done good work in regard to blocking angiogenesis), is that we have here an alternative observation which is absolutely fundamental and

revolutionary to our thinking. We have this presented at an alternative medicine meeting, when you would think, relevant to its publication and to the visibility that it has had, that nobody has picked up on this. Why Hernan Acevedo is not seen as a hero and somebody else is seen as a hero, relevant to public relations and visibility within the framework of American medicine, I haven't got the faintest idea. All I can say is it's very important that there be alternative platforms for people who are presenting original ideas, with solid information, that I feel is of Nobel quality from the point of view of what it means.

What we have to do is test it. It isn't a major effort. These monoclonal antibodies can be readily made. The next step is to try them out, and then we have to start getting into clinical trials. It's not going to take, based on what I've seen from the data, major trials involving 1,000 patients to determine validity. I go back to the days when vincristine first become available to treat acute lymphoblastic leukemia. I had seven children dying of acute lymphoblastic leukemia. Vincristine came along and they all went into complete remission. Dr. Acevedo has introduced a monoclonal that will prove itself very quickly. It's an honor to be on the same platform with him.

Dr. Wisneski: I'd like to take license as the moderator and a clinical endocrinologist to give a more artistic viewpoint from my vantage point. Human chorionic gonadotropin is the hormone that supports the growth of a new life. We know hCG supports the growth of the embryo and fetus, as was shown so elegantly. Are we seeing that hCG is elaborated to support the growth of another new life, ergo cancer?

It creates thermogenesis. It stimulates the thyroid gland. It helps promote angiogenesis or new vessel formation. Therefore, if we really think about this, if this is what's happening at a

very fundamental level, and if we can develop monoclonal antibodies against this very growth factor that is occurring perhaps at the wrong time, we may have a universal hopeful solution to many forms of cancer. I totally concur that Dr. Acevedo needs to have further platforms, as I'm sure he will. Thank you.

We can entertain questions at this time. Please go to a microphone.

Participant: I found this very interesting and stimulating. A lot of times with these things that are in research, people are waiting and trying to push it through, saying when the research is done and we get our drug treatment then we can finally apply it. I'm wondering if there's not some natural way to apply this. In other words, can you modify your own body chemistry through diet, massage, acupuncture or whatever you want that could possibly implicate on this? I know a lot of other therapies in the conference are doing some treatment.

Dr. Acevedo: The vaccine is already in clinical trials. Clinical trials have been done in five different places in the country, all FDA approved. Of course, I cannot take part in them. I can tell you that as things are going with the new company – it's a very big company. Clinical trials are going to cost us about between 70 and 80 million dollars in the way the clinical trials are done in this country. We calculate that the vaccine will be for public use about three years from now. I'm telling you this in advance, because it's going to happen.

We are having results, especially in advanced cancer, that I did not expect, especially in colon cancer. You have to have a minimum tumoral mass, because if I give you a vaccine.... Let's say I vaccinate you against tetanus toxoid, and I vaccinate myself, and then I measure the amount of circulating antibody that I do and the amount of circulating antibodies that you do. It

varies. It varies from individual to individual. It's incredible that, in spite of that, it looks that even patients with advanced disease are able to produce an effective response.

We would like to have passive immunization, that is, to use the same monoclonal antibodies that the vaccine produced. We already proved that one of the three monoclonal antibodies is directly cytolytic. We cannot produce this antibody by the usual ways, and believe me we tried. We spent more than one million dollars in trying. The hybridoma technique, for which the Nobel Prize was given, requires the use of a cancer cell (the fusion partner) to create the hybridoma and immortalize the cell. So what happens? Here you have the antibody that is a killer antibody and the cancer cell that is the companion, that is producing hCG. So this hybridoma does not survive; it committed suicide. This is the reason we cannot produce in this way a material that could be used in humans.

We can do it in animals, of course, with no problem, but I cannot give you a mouse antibody because your human immune system recognizes the foreign (animal protein) material. There is a possible way to do it. This is by producing the specific monoclonal antibody using molecular biology techniques. These are the things that modern biotechnology can produce.

Dr. Wisneski: In the interest of time, I'm going to introduce Dr. Gonzalez, and at the end we will have more time for questions. Dr. Gonzalez has clinical input for us which will round out the picture.

Dr. Nicholas Gonzalez will present a discussion of trophoblasts and pancreatic enzymes. He completed his undergraduate education at Brown University and received his medical degree from Cornell in 1983. Dr. Gonzalez subsequently pursued clinical training in internal medicine and immunology. While an immunology fellow, he evaluated the effects of an aggressive

nutritional approach on advanced cancer. Since 1987 Dr. Gonzalez has been in private practice in New York City where he continues to study the effectiveness of nutritional support in the treatment of cancer patients. He's also interested and very much engaged in some very exciting research. Dr. Gonzalez.

Dr. Gonzalez: First, I see Dr. Burzynski. I hope all of you will attend his lecture, because he certainly is one of the heroes of both orthodox and unorthodox medical research. It's very good to see you. He really deserves a round of applause.

Ralph touched on our friend John Beard, and I'm going to talk a little bit about John Beard. He was a very interesting fellow. He was a very eminent professor of embryology at the University of Edinburgh, as Ralph said. When I first became interested in the trophoblastic approach to cancer, I had a friend of mine actually go to Scotland and go through the old archives to see if they could find anything about Beard. He kind of disappeared after his death, I think it was in 1923. It's as if he left no heirs. No one followed up his work except sporadically.

My friend was able to find only one thing, a diary written by an English medical student. It was one of these Tom Brown goes to Edinburgh turn of the century things. He wrote a lengthy section in his diary about Beard. He was attending one of his lectures. He said he was conceivably the dullest man who ever lived and his lectures were conceivably the dullest lectures that had ever been given in the dullest English or Scottish university. Apparently he left no children. No one seems to know whether he was married or not, and I suspect his interest in pregnancy and embryology was strictly theoretical. No one even knows what happened to his library, which apparently was very extensive.

Beard was a very brilliant embryologist, and indeed some of his discoveries are still quoted in the embryological literature. I've run across them. Even during my own training you would find his name mentioned. He had many interests, and one of them was the placenta. As most of you know, and the placenta has been discussed today in bits and pieces, the placenta is produced after the fertilization of the egg in the fallopian tubes.

The egg basically initially lives like any other egg, be it duck or human. It lives off its own substance, but the mammalian egg doesn't have a lot of substance to live off. It faces one immediate problem: how to get nutrition. It passes into the uterus and it faces a second problem. In the mammalian system, the growing embryo develops *in utero* inside the mother. It's not like a duck egg that's just out there and grows independently. It has to anchor to the uterus. It also has to get nutrition from the mother. It has to have a conduit to get rid of its own wastes and carbon dioxide, metabolic waste. It has to have a place to pick up oxygen.

It starts producing, as has been discussed, a layer of tissue called the trophoblast, which very aggressively invades into the uterus. This invasive tissue functions in two ways. First, it is the simple physical anchor for the growing embryo. Secondly, as it develops it becomes the point of contact between the blood supply of the fetus, the developing embryo, and the mother. These blood vessels intermingle. The fetal waste products will be released into the mother's blood supply, carbon dioxide, metabolic waste, and the fetus will absorb nutrients and oxygen from the mother.

Beard was fascinated by the placenta, and he studied it in a number of animal models. He came across one bit of information that really perplexed him. It shows you the way a genius works. I would never in a thousand years think about doing this kind of research because it requires such meticulous science. I would probably just lose track. He found that in every

mammalian species he observed, be it mouse or horse, the trophoblast will grow, invade the uterus, develop into the placenta, and at a certain point in time the placenta stops growing. This happens at a specific time in every species he identified. There's been some debate, and Ralph and I have talked about this in the past, as to whether his times are exactly correct, but certainly the idea is valid. He found, for example, that in the mouse I think the placenta stops growing at 10 days. In the horse, it's maybe 30 days.

In the human, he said almost invariably at day 56 the placenta stops growing. This was an extraordinary observation to make. In view of the level of sophistication of science at the turn of the century it was doubly extraordinary, because it really required meticulous observations. He found and he confirmed that at day 56 the human placenta stops growing. This raised a question, and this is the difference between genius and the rest of us. The fact that he discovered this would be enough. He could produce a paper, which he did. But he said this is a very interesting phenomenon. Why should this happen?

He knew the placenta, or the trophoblast, the precursor to the placenta itself, was a very aggressive tumor. Although at that time he didn't know the details, we now know it produces a number of hormones and enzymes, like collagenase elastase, hyaluronidase, that allow it to invade the tissue of the uterus. It obviously produces a number of hormones that allow for angiogenesis to allow the placenta to develop blood vessels that will intermingle with the blood vessels of the mother. Although he didn't know the sophisticated biochemistry at the time, Beard said, "Why is it that a certain day the placenta will stop growing?" This was kind of the question that perplexed and obsessed him for a number of years.

There are two possibilities. There's some factor from the mother that causes the placenta to stop growing, or there's some factor from the fetus that stops the placenta from growing. He

first ruled out any factor from the mother. Then he systematically began to go through the developmental stages of the different organ systems of the fetus to see whether he could correlate the activation, or some change in a specific organ system or specific organ, with this day 56 cessation of placental growth in the human.

He went through the nervous system and the way the nervous system develops. He went through the endocrine system and the way the endocrine system develops. He was unable to find any correlation until he got to the digestive system. The digestive system is a complex system. It has the intestinal tract, the pancreas and the liver, which all embryologically develop from the same tissue, the endoderm.

He found that the day the placenta stops growing, in every mammalian species that he observed and studied, was the very day that the embryonic pancreas became active, a simple fact. You say, “Well, what a big deal.” It’s interesting when you think about it that the pancreas would become active at all during embryonic development. We all know that the embryo in a human develops in a fluid environment – the amniotic sac surrounded by amniotic fluid.

It doesn’t breathe, to talk about the lungs for a second. It doesn’t need to breathe. It gets all the oxygen it needs from the mother through the placenta. It gets rid of all its carbon dioxide, its respiratory waste, into the mother’s blood supply, and it doesn’t use its lungs. They sit there inactive until the day of birth. We all know from movies that when the baby is born, the doctor picks it up by its feet and slaps it on the back. The purpose of that is to stimulate the first breath. It isn’t until the moment of birth that the lungs need to become activated. We have no need for lung function during embryonic development. Although they develop, they’re not active. They’re quite inactive. They just sit there.

The same is true for the pancreas. The pancreas is part of the digestive system. The fetus really doesn't need to have a very active digestive system because it gets all the nutrients it needs in a perfectly predigested form handed to it on a silver platter from the mother's blood supply. It doesn't really need the pancreas. The pancreas produces insulin to control sugar metabolism. The mother's blood supply provides adequate insulin to maintain normal blood sugar levels. It doesn't really need a lot of insulin. It needs some.

In addition to the endocrine production of insulin, the pancreas also produces pancreatic enzymes. There are three general classes of pancreatic enzymes. The first is the proteolytic enzymes, which include things like trypsin and chymotrypsin that very specifically break down proteins. Trypsin for example breaks down proteins where there's an arginine amino acid. Chymotrypsin tends to break down proteins where there's an amino acid such as phenylalanine. These proteolytic enzymes are very specific in the way they break down proteins.

The amylases are the carbohydrate digesting pancreatic enzymes. They break down starches into simple sugars. The lipases break down fats. There are these three basic categories of enzymes that serve a very important digestive function in adults, but in a fetus they're really not necessary. The fetus gets all its food in a perfectly predigested form handed to it from the mother. It doesn't need digestive enzymes.

Yet Beard learned that long before birth the pancreas is quite active and producing copious amounts of pancreatic enzymes. Interestingly enough, and coincidentally enough, the day it starts producing pancreatic enzymes is the day the placenta stops growing. He studied this for years and became very convinced that the single factor in the developing fetus that controlled placental growth was the pancreas.

Because Beard was a genius unlike the rest of us, he made another step. He was an excellent histologist. He was a man of many talents. He not only was a brilliant embryologist, but he was a very good histologist. Although we think of science of 90 years ago as very primitive, histology at that time was actually quite well developed. I've looked at textbooks of histology from that time. Histology is the microscopic study of tissues. They really were very elegant. They had a very good idea of the microscopic structure of the nervous system, the different organ systems, the intestinal tract, the endocrine system. They may not have known what all these tissues and organs did, but they certainly knew what they looked like.

Beard had a hobby, which was cancer research. Cancer research wasn't very sophisticated at that time, but physicians knew what cancer basically was. Most tissues and organs tend to be very sophisticated in what's called the histological morphology, in terms of the way the cells and the tissues look. You can show a second year medical student a slide of a liver and he'll identify it as a liver. You can show him a slide of a nervous system brain section and he'll know that this is nervous system. You can show him a slide of the intestinal tract and he'll know what that is. Tissues in the adult mature organ have a very specific look, a very specific structure. You can stain them in certain ways and different tissues will stain differently under the microscope. A liver cell looks like a liver cell. A small intestine cell looks like a small intestine cell. A kidney cell looks distinctively like a kidney cell.

Beard and scientists at his time knew that cancer differed from these mature, sophisticated, very elegant cells from mature tissues, and that it was a very undifferentiated type of cell. It tended to look like an amoeba. It didn't tend to have the differentiation in terms of structure that you'll see in a liver cell or kidney cell. Cancer cells in their more aggressive cells from a kidney or a liver will actually tend to look alike. They lose a lot of their secondary

characteristics. They lose a lot of their distinctive microscopic anatomy. They tend to be very primitive. They don't have the kind of structure that you'll see in an adult cell. Beard knew this.

He spent a considerable amount of time correlating the way placenta cells looked under the microscope and the way cancer cells looked. He determined that placental cells tended to be very undifferentiated cells. They didn't have a lot of secondary and sophisticated structure. They didn't have the kind of elegant morphological structure that you see in an intestinal tract cell or a nervous system cell, which are very distinctive. They tended to be blobs of protoplasm. He began to correlate the fact that the placental cells tended to look, histologically under the microscope, like a cancer cell.

He made an extraordinary leap of faith. He knew that the placenta normally stops growing 99.9% of the time. There are cases, of course, when the placenta doesn't stop growing. At that time, in fact until recently, the uncontrolled placental growth could lead to a very deadly cancer called choriocarcinoma which was for a long time one of the most aggressive cancers. Basically that was trophoblastic or placental cells growing uncontrollably. Usually mothers could be dead within six weeks to six months.

This is one of the few cancers that currently can be easily controlled with chemotherapy. Methotrexate will produce remissions and cures in 80 to 90% of the women who suffer this cancer. It is a rare cancer. It was rare then and it's rare today. Beard was aware of the existence of this cancer, as rare as it was, and that it was a placenta that grew uncontrollably, that didn't seem to operate under the controls and balances that would prevent this uncontrolled growth.

He thought maybe it's because in this situation where we develop choriocarcinoma, the embryonic pancreas isn't producing enough pancreatic enzymes to control placental growth.

Indeed, if that's true, then maybe the pancreatic enzymes represent the body's main defense against cancer. It was an extraordinary leap of faith, but he did a series of experiments that confirmed his belief. There actually were animal models for cancer at that time. There was a sarcoma model, that he had in his own laboratory. He injected, almost on a whim, trypsin, which was available at the time. He injected it into these animals and he got regression of the tumor.

He presented his work initially in 1902, in an article in *Lancet*, and subsequently presented his work at the Edinburgh Scientific Society where he was almost universally derided. I say almost because there was an army captain physician in the audience who was quite intrigued by Beard's work. After the meeting he got together with Beard. This man was a surgeon who had a series of cancer patients.

At that time there was very little that could be done for cancer other than surgery. Once surgery failed, there really wasn't any chemotherapy, and radiation was only at the beginning steps of being used. This physician was willing to try some of these injectable enzymes in his patients. Ralph knows the first case. It was a case of laryngeal cancer that was quite extensive. Beard got this enzyme preparation, and he injected the trypsin into this patient. I guess today it would make the front pages of *The New York Times*. The tumor basically dissolved within a matter of weeks.

This case report was presented in the medical journals. After that there was a flurry of interest in the use of pancreatic enzymes to treat cancer. There were dozens of case reports written between 1902 and about 1915. In 1911, as Ralph said, he published his book, *The Enzyme Therapy of Cancer*. There were actually what would be considered controlled trials, where a series of patients under academic supervision were given pancreatic enzymes.

The results were mixed. There were some very impressive regressions of cancer, and even cures. Some of these were discussed in the major medical journals, like *Lancet*, the British medical journal. There were several articles, even a discussion and a debate in *JAMA*, about 1915, discussing the use of proteolytic enzymes in the treatment of cancer. It was extremely controversial.

It started to get some recognition, and then Madame Curie presented the theory that radiation therapy was a simple, easy way to cure all cancers. Madame Curie was a very prominent scientist at the time. Her access to the press basically overrode any interest in Beard's work, and he died in total obscurity in 1923.

It's very interesting to think about Beard and the trophoblast, particularly in view of what we've already heard today, and think about where cancer actually comes from. When I was a medical student, we were taught that cancer actually develops from what are called stem cells. Every tissue, organ and gland has primitive, undifferentiated cells in it, that under proper stimulus can grow and develop and mature into the mature tissue cell.

For example, every several days the entire intestinal lining is sloughed off. This requires an enormous amount of replacement of the intestinal cells that line the intestinal tract. These cells are very distinctive. They tend to be columnar cells. They look like rectangles. They have a very microscopic, what's called a brush border, where there are all kinds of hills and valleys that increase absorption in the intestinal tract. These cells are eminently suited for absorption of nutrients and fluid and water.

There has been a lot of research that shows that indeed intestinal tract cells develop from a primitive type of undifferentiated stem cells. If you think of the large intestine, an analogy might be to think about your teeth, where there are flat areas and then valleys, and then flat areas

where the tooth is and valleys between the teeth. The colon kind of looks like that. It's got peaks and valleys and peaks and valleys. The peaks and valleys increase the surface area that increases the absorption of nutrients in the large intestine, particularly water and electrolytes.

The lining of the large intestine is sloughed off, as I said, every several days, so it requires a pretty extensive replacement process. We now know that the cells that evolve into these very specialized mature, differentiated colon columnar cells originate from a primitive, ameboid, undifferentiated cell in the bottom of the valleys. They're called crypts. These cells sit there, and under a certain signal they start migrating up the crypts, up the valleys towards the tops of the hills where they then sit and absorb the nutrients. As these cells migrate, they start developing the characteristics of the mature colon columnar cell. They get elongated. They develop this brush border, where there are very microscopic hills and valleys on the cellular surface itself.

There obviously are signals that allow the cell to differentiate and develop into the mature colon cell that will function as this absorptive cell. It's now known that two of the most important substances involved in this differentiation process are calcium and vitamin D. We all know about vitamin D. It's the sunshine vitamin. It helps bring strong bones. It's required for the absorption of calcium.

Vitamin D is really a hormone, rather than a vitamin. It's produced in its first step from the action of sunlight on 7-dehydrocholesterol, which is produced in the skin. That is converted into 25-hydroxy D in the liver and in the kidney ultimately to the active form of vitamin D. It circulates like a hormone. It has a similar structure to the steroid hormones, because vitamin D is ultimately made from cholesterol. Estrogen, progesterone, testosterone are also made from cholesterol. They have a similar steroid ring. Vitamin D and calcium act on this primitive

undifferentiated cell that sits in the crypt of the colon cell as it migrates up, and actually allow that cell to become a mature cell.

Vitamin D helps with the absorption of calcium. Now calcium is not only the structure of the bones. It's also a very powerful hormone. Once inside the cells it sets off what's called the second messenger process, where it activates things like cyclic AMP and cyclic GMP which functions in hormones within the cell itself. These hormone-like substances act on the nucleus and stimulate the DNA and the genes. This allows this primitive undifferentiated cell to migrate up and mature.

If the signals for differentiation and maturity of a colon cell go awry (and some people think a deficiency of vitamin D and or calcium can do this), the cell will not become a mature, sophisticated cell that any medical student can identify. Instead it tends to grow and remain undifferentiated and primitive. There are those who believe that it's this undifferentiated cell that actually becomes colon cancer.

Cancer can theoretically arise two ways. It could arise from a mature cell under proper stimulus, or improper stimulus, such as a genetic break. Think of a mature colon cell sitting there doing its job, and something goes awry in its DNA or its chromosomes. It mutates and becomes a primitive, undifferentiated cell. Over the last 90 years there have been waxing and waning theses on what cancer actually is and where cancer actually does develop from.

Some people believe indeed that it's the mature cell that goes awry and becomes aberrant. It goes berserk. During Beard's time this was the general thesis, that cancer developed from mature, histologically sophisticated cells that somehow go berserk. They lose any check and balance, lose the ability to stay within the architecture of the tissues, become invasive, grow uncontrollably and actually become immortal.

When a colon cell matures, it loses its immortality. It has a finite life span, and eventually it will die. When that cell stays in its immature, precursor stem cell, undifferentiated primitive cell form, it actually is immortal. If it doesn't go through the stepwise differentiation, it will become a very aggressive, invasive cell that doesn't respect boundaries, that doesn't communicate with other cells properly, that loses all sense of control and becomes basically a cancer.

Beard believed that cancer cells do not develop from mature cells. They don't develop from the mature, histologically sophisticated cells. They develop from primitive undifferentiated cells that he believed existed in every tissue and organ in the body. We now know that these stem cells, such as exist in the colon, do exist in every tissue and organ.

They exist in the bone marrow and serve as the precursor for the development of all the red and white cells. They exist in the liver. When the liver is damaged, the liver can regenerate. It's thought that stem cells may be largely responsible for this. If you cut out one kidney, the other kidney will double in size, and it's thought that stem cells allow for this growth and then that one kidney can basically function as two kidneys.

Beard believed it was these primitive cells, these primitive, undifferentiated cells that existed in every tissue and every organ of the body, that, if they lost the control of the pancreatic enzymes, would lose the ability to differentiate. They would stay undifferentiated and could, without adequate pancreatic enzyme in the environment, become very aggressive cancers.

Beard spent years going through histological specimens and claimed that he saw these primitive undifferentiated cells in every tissue and organ in every mammalian species he observed. This was thought to be impossible. It was only with recent histological advances that we began to realize that there were these primitive cells in every tissue and organ that could

develop into the mature cell, or if the differentiation signals go awry, could become cancerous tumors.

You said three to five minutes, so I guess that's about it. Beard's thesis is starting to stimulate a lot of research interest, particularly around my own work. We're in the process of clinical trials, which I'll talk about tomorrow. A lot of the histological observations that he made 90 years ago, which were laughed at, are turning out to be true. A lot of the observations he made about the trophoblast, as you heard today, are turning out to be true.

He believed all cancer results from trophoblastic cells, from placenta cells that go awry. He believed that every tissue, organ and gland contained these trophoblastic cells, that in its context of the deficiency of pancreatic enzymes, would lead to tumor growth. He believed, and I believe, that pancreatic proteolytic enzymes, particularly things like trypsin and chymotrypsin, represent the body's own natural way of controlling those trophoblastic cells. Having said that, I've run out of time, so I'll stop.

Dr. Wisneski: Thank you very much. I'd like to ask the first question as an endocrinologist. We know that hCG promotes growth of the placenta. We also know that within this time period we start getting the production of human placenta lactogen or HPL, which alters the growth characteristics. What are your thoughts about the potential role of HPL in this process? Any comments? HPL might be the counter regulatory hormone in so far as growth of the placenta. I'm just asking for any potential comments on that.

Dr. Gonzalez: That's possible.

Dr. Acevedo: There is work done in early pregnancy. This was done before. Our government and all the governments in Europe say we cannot work with human fetal embryonic tissue, even tissues obtained at abortion clinics and all that. It is absolutely against the law. It has to be fresh, because it decomposes very fast. We cannot work with fetal or embryonic tissue. There was a short time in which it was permitted in Europe, and friends of mine dedicated to early pregnancy were asking the same question.

There is a factor, and this has been published already. They have presented their findings. Let me put it this way. If you take the development of an embryonic fetus, in 45 weeks it comes to birth, goes out, and that individual starts to grow in the normal way a human being will grow. Some scientists I think at Carnegie Mellon and others at MIT did a calculation. What will happen if a human being continues growing at the same speed as the embryonic fetus grows after the moment of birth? They put it in their computer and the calculation came out that one human being will occupy a space like this. From here to planet Mars. This was perfectly well calculated.

What stops it? The principle that stops this growth is a low molecular weight substance. They were able to obtain a small amount, but it was very difficult. They were completely unable to crystallize it. We know that it has a low molecular weight, and there is no way that we can work and learn more about this substance. There was enough to be able to do some experiments and these were published. In those experiments you put a little bit of this in cancer cells in tissue culture. The cancer cells completely separate each from other, and in a short time they die, even if you add nutrients. So there is something in respect to that, and we absolutely cannot do any experiments because the laws don't permit it. We throw out tissue, good tissue that could be used to help in organ and tissue transplant. Our country and the rest of Europe say no.

Dr. Wisneski: This is the time for the audience. Please use the microphone sir. Ma'am you've been waiting a long time for your question. Why don't you go ahead and pose it?

Participant: I was prescribed to take hCG. I'd like opinions from each of the doctors as to what is the risk in taking this? I was given it for weight loss, and I don't have a diagnosed health problem. Although I do have a health problem, I don't know what causes it. If taking hCG can exacerbate an issue that you don't even know you have, am I at risk in taking it?

Dr. Acevedo: No. There is no risk to taking hCG. It will be very expensive for you to take hCG in the way we take it, because the commercial hCG (Profasi) from Serono, a pharmaceutical company, 5,000 units costs about \$40. If you inject hCG intramuscularly, the life of the hCG in your body will be less than one hour and a half. So you have to use tons of hCG to try something like that. In Europe several clinics were using hCG thinking that it's possible that you can use weight. In reality, when experiments were done, serious trials, the thing was so variable that it could be the psychological factor was as important as the hCG. There are clinics (with my wife we have been in one of those in Switzerland) where they did use hCG as part of their method to correct excess overweight. They did also a tremendous amount of surgery and all that.

In respect to the vaccine the company that has the license or the patent – you can find it in your computer. It is called

Dr. Moss: Someone asked if I had heard about the work of Dr. Valentin Gavallo in Moscow. At my web site, www.ralphmoss.com, you'll find both a couple of articles that I've written about that and also the interview that Harris Coulter did with Dr. Gavallo.

Dr. Wisneski: I personally as a clinical endocrinologist would suggest a reevaluation of the use of hCG for the purposes that you mention. Next?

Participant: Because of risks?

Dr. Wisneski: Potential. Who knows? Next?

Participant: I'm Dr. Hankins. I've found both of these things very stimulating. It's been a long time since I've read the trophoblast literature and so forth. I too am an endocrinologist and I'm going to go back and think a lot about this. I appreciate both talks and I've been very stimulated. I thank you for that.

Second, I'd like to ask a question. Number one, do the antibodies that you're using work on cells in culture? Number two, there are a number of other ways that many of us are using to knock out hormones or to knock out receptors that are not antibody ways, such as soluble receptors and things like that. Have you tried those kinds of approaches?

Third, I'd like to make a general challenge. One of the organizations that I volunteer for is the International Cancer Alliance. We're trying to find ways to stimulate new clinical trials and help them to get off the ground. One of the things that we talked about is the possibility of having a patient-funded venture capital group. There are enough patients who are interested in

alternative medicine, more and more these days, that it's possible that you might be able to stimulate some money. That's probably a better approach than trying to get the rest of the world to wake up very quickly.

Dr. Wisneski: Thank you, sir. Is there a specific question you'd like answered? Okay, next.

Participant: I'd like to direct two short questions to Dr. Gonzalez. First of all, what is known about the effects of the proteases specifically? What do you think it is that they're doing? Then secondly, would you say a little something about what you think happens when protease inhibitors are used as anticancer agents and how in any way might this play into what you're talking about?

Dr. Gonzalez: There are some animal studies which investigated the use of pancreatic proteolytic enzymes (although it's minimal numbers) in tumor models in mice, where they got very good results. There was a study published in 1965 (which goes back over 30 years) where they hypothesized the mechanism was increased immune surveillance and increased immune stimulation. There was a study out of the University of Texas in 1994 where they also got very good results in an animal model. They proposed possibly immune stimulation or a direct antineoplastic effect where they somehow dissolved the cell membranes. No one really knows. The Germans who use proteolytic enzymes as an adjunct for cancer therapy think it's through immune modulation and immune stimulation. They have some studies that document that.

As for the second question, soy is being promoted as a very powerful anticancer element. One of its mechanisms of action is that it has protease inhibitors. It has probably the most powerful trypsin inhibitor of any food on earth. On my program, soy is a total disaster. It knocks out the trypsin, which we think is the main anticancer enzyme, faster than any substance we know of. If patients eat a lot of soy on my program, it's a step to disaster. You have to be very careful with soy. If you're trying to use enzymes to treat cancer and you add enzyme inhibitors, it's not going to work, or it has the potential not to work.

Participant: What about plant based enzymes? Do they have the same effect?

Dr. Gonzalez: No. Although that's often claimed, I've never seen bromelain and papain have a direct antineoplastic effect. They seem to help in blocking inflammation, but I've never seen that they have an anticancer effect.

Participant: I was recommended instead of taking wobe enzymes to take enzymes which have a plant base.

Dr. Gonzalez: In my experience, which goes back 17 years, I've never seen plant-based enzymes to be effective against cancer. I know that it's being done. I know there's a group in Texas doing that. I've just never seen any documentation that's true. They seem to have a very nice anti-inflammatory effect. Bromelain and papain and other plant enzymes do work with animal-based proteolytic enzymes in terms of attacking cancer, but by themselves I don't think they do.

Participant: The book I read on enzymes said they are to be used together because of the different workings as far as the pH.

Dr. Gonzalez: That's correct. Bromelain has a much wider pH optimum, from about pH 2 to about pH 9, whereas pancreatic enzymes, proteolytic enzymes are operative only in a very narrow pH range. It's slightly alkaline, like about pH 7 to pH 9. It's true that plant enzymes have a greater variability, but they're not effective as a primary anticancer agent in my experience.

Dr. Acevedo: In respect to the vaccine, the company that has the license or the patent – you can find in your computer. It is called AVI BioPharma. This new company came about by the merger of Immunotherapy Corporation, a private company, with Antiviral, a public one. They have a capital of 100 million dollars. Remember, the clinical trials cost a lot of money. You can see in the computer the price of the shares. The last time I saw it in the NASDAQ index was about three to four dollars per share.

Dr. Wisneski: Thank you, Dr. Acevedo. One more question and then we will adjourn. Could you please use the microphone? I'll try to repeat your question.

Dr. Gonzalez: We've just finished one which we're trying to publish now and we're about to start one other. We're about to start a randomized controlled trial (barring unforeseen

obstacles, of which there are always many) at Columbia University under Dr. Antman. That should hopefully start within the next couple of months. It's going to be with pancreatic cancer.

Dr. Wisneski: You have a clinical presentation tomorrow?

Dr. Gonzalez: Yes.

Dr. Wisneski: You might want to go to that. I'd like to adjourn the panel at this time.

Thank you.