Cancer - The Trophoblastic Theory

With Special Emphasis on Liver Cancer and Homoeopathy

By

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Dedication

To My Parents

Who Devised Us, Developed Us,
Devoted Themselves And Enabled Us,
To Be And To Cause Turmoil In This Cosmos,
An Anabolic Turmoil, To Rear The Social Mass,
For This Himalayan And Satisfactory End,
To Cheerfully Obligate And Congrate,
We Lovingly, Fervently, Cordially,
Gratefully And Ardently Dedicate.

Dr. Rajneesh Kumar Sharma

Preface

For last ten years, I have been working on cancer patients. I frequently met the fact that Homoeopathy works wonderfully in carcinomas. It really does miracles.

The theory of cancer simply says- any uncontrolled and unwanted over growth is caner. But why this growth occurs? What is the cause behind it? What are the differences between a cancer and normal cell? What makes it uncontrollable?

If we could know answer to any one of the above, we could ascertain the plan of treatment. Here, I am giving my views on morphological and physiological changes in a normal cell to become a cancer cell.

It has been frequently seen and repeatedly verified that a cancer cell tends to behave like a germ cell in its whole course. It starts growing just like a trophoblast cell. The normal trophoblasts grow up and divide in a fixed and strictly controlled fashion as guided by genetic information present in their nuclei while the cancerous cell does it in bizarre manner and totally uncontrolled fashion. This conversion of normal cell into cancer cell is almost proved to be due to a mutation, which converts normal cell into cancer cell. This mutation may be induced by some forms of special genes present in nuclei of somatic calls. These genes may be called as oncogenes.

Homoeopathy has a key role in preventing this mutation by suppressing these oncogenes if applied on basis of prodromal symptoms of a patient by its universal nature's law of cure.

I have given a special emphasis on liver cancer in my work with some king remedies for carcinoma liver.

I am cordially thankful to my parents, family, which supported to me a lot to complete my works, to my teachers and to the chance, which enabled me to toil hard and to achieve the goal.

Dr. Rajneesh Kumar Sharma

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What is Cancer

Definition

The terms cancer, neoplasia, and malignancy are usually used interchangeably in both the technical and popular literature.

Any unwanted and uncontrolled growth is cancer. The disease called cancer is best defined by four characteristics, which describe how cancer cells act differently from their normal parts.

1- **Clonality:** In most cases, cancer originates from a single stem, which proliferates to form a clone of malignant cells.
2- **Autonomy:** Growth is not properly regulated by the normal b chemical and physical influences in the environment.
3- **Anaplasia:** There is a lack of normal, coordinated cell differentiation.
4- **Metastasis:** Cancer cells develop the capacity for discontinuous growth and dissemination to other parts of the body.

Properties similar to each of these characteristics can be expressed by normal, nonmalignant cells at certain appropriate times, for example, during embryogenesis and wound repair, but in cancer cells the characteristic is inappropriate or excessive. The process, which a normal cell is converted into one, which exhibits the characteristic traits is termed malignant transformation.

TUMOR CELL BIOLOGY AND BIOCHEMISTRY

Since all cells in an organism originate from a single fertilized egg (zygote), all carry the identical genetic information. The proliferation and differentiation of this cell into an embryo, and eventually into a mature organism, involve selective and coordinated expression of the genomic repertoire. Control of gene expression is accomplished through incompletely understood molecular interactions, which can be modulated, in part, by chemical influences in the environment. The genomic repertoire includes information which permits cells to expand clonally, to function with varying degrees of autonomy, to differentiate and dedifferentiate, and to move from one part of the organism to another in a coordinated way. In the adult, the process of wound healing activates expression of these cellular characteristics in a more "embryo-like" fashion, but under well-coordinated control. In the us case of malignancy, the normal control process is subverted or have bypassed due to the anomalous activities of a selected group of genes i.e. (oncogenes) which have central importance to the regulation of the cellular activities.

CLINICAL FEATURES

Malignant diseases manifest themselves in a variety of ways. The presence of an abnormal accumulation of cells may, by virtue of its physical bulk alone, produce clinical symptoms and signs. Thus for example painless swellings in the breast or in muscle may indicate an underlying carcinoma or sarcoma respectively. Lymphomas usually present as painless enlargements of lymph nodes or spleen. Intracranial space-occupying lesions may cause focal manifestations, fits, headaches, vomiting and papilloedema. Tumors in the distal colon may partially obstruct the lumen of the bowel with a resulting change in bowel habit. Bronchogenic tumors may cause cough or shortness of breath resulting from partial or complete occlusion of an airway.

5- **Hemorrhage-** Malignant tumors not infrequently present as hemorrhage from an eroded epithelial surface. For example bronchogenic carcinomas may present with haemoptysis, gastric carcinomas with iron deficiency anaernia or occasionally, haernaternesis, colonic carcinoma with bleeding per rectum, and renal and bladder carcinomas with haernaturia.

6- **Pain**- is often thought to be an inevitable accompaniment of malignant disease but in fact it is not a common symptom especially at presentation of most cancers. When pain does occur, it is due either to nerve compression or to distension of an organ. The most common peripheral nerve compressions are due to involvement of the brachial plexus (carcinomas of the lung or breast), the sacral plexus (carcinomas of the rectum or cervix) or the paraspinal nerves (carcinoma of the pancreas). Metastatic tumors in the liver may cause pain as a result of distension and stretching of its capsule. Bone pain resulting from primary, or more commonly, secondary deposits usually occurs in the weight bearing bones, and results from compression secondary to weakening of the structural component of the bone. Pathological fractures may arise as a consequence. Patients may present with referred pain, most frequently in the shoulder, hip or knee, as when a nerve root is involved directly or by metastases.

7- **Cachexia-** is a clinical feature of many malignant diseases presenting at an advanced stage, especially carcinomas of the gastro-intestinal tract, lung, ovary and testis. It is, however, not a universal phenomenon and is rare in breast cancer and in tumors of the central nervous system, and uncommon in leukemia and lymphomas. Cachexia may arise as a direct result of malnutrition from a tumor in the gastrointestinal tract. Malabsorption may arise rarely as a consequence of tumor replacing the absorptive epithelia but more commonly from reduced exocrine function (from carcinomas of the pancreas), or loss of bile from carcinomas of the upper gastrointestinal tract that obstruct biliary outflow. Loss of taste and the malaise that accompanies many malignant diseases may contribute to poor food intake but all of these factors in promoting malnutrition do not of themselves fully explain the cachexia of malignancy. Although many patients will have a negative nitrogen balance, others who are in positive balance may show a caloric deficit. It has been shown that in the cachexia accompanying malignant disease, caloric expenditure remains high with an elevated basal metabolic rate despite reduced dietary intake (the reverse of the situation that follows starvation) which indicates that this phenomenon results from a profound systemic derangement of host metabolism, the pathogenesis of which remains unclear.

8- **Paraneoplastic features-** In addition to generalized clinical features that are commonly associated with the presentation of a malignant disease; there are a variety of syndromes for which the term 'paraneoplastic' has been used. These syndromes include many that arise as a result of the secretion into the blood of tumor products (usually polypeptide hormones), which produce clinical signs as a consequence of their action on target organs remote from the primary tumor. Although relatively rare, these syndromes are important since they may precede the clinical presentation of the primary tumor, facilitating early detection. In addition they may mimic metastatic disease and thus confuse management decisions. They may also serve as tumor markers to monitor therapy.

The ectopic production of ADH and ACTH are most commonly associated with an underlying small cell anaplastic carcinoma of the bronchus. Squamous cell lung cancers may produce parathyroid hormone manifesting as hypercalcaermia.

A number of neurological paraneoplastic syndromes have been described for which the tumor product remains unknown. These include peripheral neuropathies, a myasthenia like syndrome and sub acute cerebellar degeneration. Whilst all of these syndromes may improve with successful treatment of the primary tumor, complete resolution is rare.

Dermatomyositis and polymyositis present as gradually progressive muscle weakness predominantly affecting the proximal 'musculature, coming on over a period of months. Whilst these disorders are not universally associated with malignancy, patients surfing from them have a greatly increased risk of an underlying neoplasm compared with general public, and malignancies of the breast, lung, and gastrointestinal and genitourinary tract should be considered.

Acanthosis nigricans is a rare condition characterized by the appearance of black velvety verrucose lesions in the flexures around the neck, axillae and groin. It is particularly seen in patients with carcinomas of the stomach.

Tumor Markers

Definition

Tumor markers are substances that can often be detected in higher-than-normal amounts in the blood, urine, or body tissues of some patients with certain types of cancer.

Pathophysiology

Tumor markers are produced either by the tumor itself or by the body in response to the presence of cancer or certain benign (noncancerous) conditions.

Application

Measurements of tumor marker levels can be useful when used along with x-rays or other tests in the detection and diagnosis of some types of cancer. In addition to their role in cancer diagnosis, some tumor marker levels are measured before treatment to help in planning appropriate therapy. In some types of cancer, tumor marker levels reflect the extent (stage) of the disease and can be useful in predicting how well the disease will respond to treatment. Tumor marker levels may also be measured during treatment to monitor a patient's response to treatment. A decrease or return to normal in the level of a tumor marker may indicate that the cancer has responded favorably to therapy. If the tumor marker level rises, it may indicate that the cancer is growing.

Finally, measurements of tumor marker levels may be used after treatment has ended as a part of follow up care to check for recurrence.

Limitations

Measurements of tumor marker levels alone are not sufficient to diagnose cancer for the following reasons:

1. Tumor marker levels can be elevated in people with benign conditions.
2. Tumor marker levels are not elevated in every person with cancer—especially in the early stages of the disease.
3. Many tumor markers are not specific to a particular type of cancer; the level of a tumor marker can be raised by more than one type of cancer.

Currently, the main use of tumor markers is to assess a cancer's response to treatment and to check for recurrence. Some of the most commonly measured tumor markers are described below.

I- Prostate-Specific Antigen

Prostate-specific antigen (PSA) is present in low concentrations in the blood of all adult males. Both normal and abnormal prostate cells produce it.

Elevated PSA levels may be found in the blood of men with benign prostate conditions, such as

1- Prostatitis (inflammation of the prostate)
2- Benign prostatic hyperplasia (BPH)
3- Malignant (cancerous) growth in the prostate.

While PSA does not allow to distinguish between benign prostate conditions (which are very common in older men) and cancer, an elevated PSA level may indicate that other tests are necessary to determine whether cancer is present.

A PSA level have been shown to be useful in monitoring the effectiveness of prostate cancer treatment, and in checking for recurrence after treatment has ended. In checking for recurrence, a single test may show a mildly elevated PSA level, which may not be a significant change.

II- Prostatic Acid Phosphatase

Prostatic acid phosphatase (PAP) is normally present only in small amounts in the blood, but may be found at higher levels in some patients with prostate cancer, especially if the cancer has spread beyond the prostate. However, blood levels may also be elevated in patients who have certain benign prostate conditions or early stage cancer.

Although PAP was originally found to be produced by the prostate, elevated PAP levels have since been associated with testicular cancer, leukemia, and non-Hodgkin's lymphoma, as well as noncancerous conditions such as Gaucher's disease, Paget's disease, osteoporosis, cirrhosis of the liver, pulmonary embolism, and hyperparathyroidism.

III- CA 125

CA 125 is produced by a variety of cells, but particularly by ovarian cancer cells.

Many women with ovarian cancer have elevated CA 125 levels. CA 125 is used primarily in the management of treatment for ovarian cancer. In women with ovarian cancer being treated with chemotherapy, a falling CA 125 level generally indicates that the cancer is responding to treatment.

Increasing CA 125 levels during or after treatment may suggest that the cancer is not responding to therapy or that some cancer cells remain in the body. CA 125 levels help to monitor patients for recurrence of ovarian cancer.

Not all women with elevated CA 125 levels have ovarian cancer. Cancers of the uterus, cervix, pancreas, liver, colon, breast, lung, and digestive tract may also elevate CA 125 levels. Noncancerous conditions that can cause elevated CA 125 levels include endometriosis, pelvic inflammatory disease, peritonitis, pancreatitis, liver disease, and any condition that inflames the pleura (the tissue that surrounds the lungs and lines the chest cavity). Menstruation and pregnancy can also cause an increase in CA 125.

IV- Carcinoembryonic Antigen

Carcinoembryonic antigen (CEA) is normally found in small amounts in the blood of most healthy people, but may become elevated in people who have cancer or some benign conditions. The primary use of CEA is in monitoring colorectal cancer, especially when the disease has spread (metastasized). CEA is also used after treatment to check for recurrence of colorectal cancer. However, a wide variety of other cancers can produce elevated levels of this tumor marker, including melanoma; lymphoma; and cancers of the breast, lung, pancreas, stomach, cervix, bladder, kidney, thyroid, liver, and ovary.

Elevated CEA levels can also occur in patients with noncancerous conditions, including inflammatory bowel disease, pancreatitis, and liver disease. Tobacco use can also contribute to higher-than-normal levels of CEA.

V- Alpha-Fetoprotein

Alpha-fetoprotein (AFP) is normally produced by a developing fetus. AFP levels begin to decrease soon after birth and are usually undetectable in the blood of healthy adults (except during pregnancy).

An elevated level of AFP strongly suggests the presence of either primary liver cancer or germ cell cancer (cancer that begins in the cells that give rise to eggs or sperm) of the ovary or testicle. Only rarely do patients with other types of cancer (such as stomach cancer) have elevated levels of AFP. Noncancerous conditions that can cause elevated AFP levels include benign liver conditions, such as cirrhosis or hepatitis; ataxia telangiectasia; Wiscott-Aldrich syndrome; and pregnancy.

VI- Human Chorionic Gonadotrophin

The placenta during pregnancy normally produces human chorionic gonadotrophin (HCG). In fact, HCG is sometimes used as a pregnancy test because it increases early within the first trimester. It is also used to screen for choriocarcinoma (a rare cancer of the uterus) in women who are at high risk for the disease, and to monitor the treatment of trophoblastic disease (a rare cancer that develops from an abnormally fertilized egg). Elevated HCG levels may also indicate the presence of cancers of the testis, ovary, liver, stomach, pancreas, and lung. Pregnancy and marijuana use can also cause elevated HCG levels.

VII- CA 19–9

Initially found in colorectal cancer patients, CA 19–9 have also been identified in patients with pancreatic, stomach, and bile duct cancer. Researchers have discovered that, in those who have pancreatic cancer, higher levels of CA 19–9 tend to be associated with more advanced disease. Noncancerous conditions that may elevate CA 19–9 levels include gallstones, pancreatitis, cirrhosis of the liver, and cholecystitis.

VIII- CA 15–3

CA 15–3 levels are most useful in following the course of treatment in women diagnosed with breast cancer especially advanced breast cancer. CA 15–3 levels are rarely elevated in women with early stage breast cancer.

Cancers of the ovary, lung, and prostate may also raise CA 15–3 levels. Elevated levels of CA 15–3 may be associated with noncancerous conditions, such as benign breast or ovarian disease, endometriosis, pelvic inflammatory disease, and hepatitis. Pregnancy and lactation can also cause CA 15–3 levels to rise.

IX- CA 27–29

Similar to the CA 15–3 antigens, CA 27–29 is found in the blood of most breast cancer patients. CA 27–29 levels may be used in conjunction with other procedures (such as mammograms and measurements of other tumor marker levels) to check for recurrence in women previously treated for stage II and stage III breast cancer.

X- Lactate Dehydrogenase

Cancers of the colon, stomach, kidney, lung, ovary, pancreas, uterus, and liver can also elevate CA-27–29 levels. First trimester pregnancy, endometriosis, ovarian cysts, benign breast disease, kidney disease, and liver disease are noncancerous conditions that can also elevate CA 27–29 levels.

Lactate dehydrogenase is a protein found throughout the body. Nearly every type of cancer, as well as many other diseases, can cause LDH levels to be elevated. Therefore, this marker cannot be used to diagnose a particular type of cancer.

LDH levels can be used to monitor treatment of some cancers, including testicular cancer, Ewing's sarcoma, non-Hodgkin's lymphoma, and some types of leukemia. Elevated LDH levels can be caused by a number of noncancerous conditions, including heart failure, hypothyroidism, anemia, and lung or liver disease.

XI- Neuron-Specific Enolase

Neuron-specific enolase (NSE) has been detected in patients with neuroblastoma; small cell lung cancer; Wilms' tumor; melanoma; and cancers of the thyroid, kidney, testicle, and pancreas. However, studies of NSE as a tumor marker have concentrated primarily on patients with neuroblastoma and small cell lung cancer. Measurement of NSE level in patients with these two diseases can provide information about the extent of the disease and the patient's prognosis, as well as about the patient's response to treatment.

Cancer .: The Trophoblastic Theory

The Criteria of Uniformity

1- Lactic acid and sugar content of the various exhibitions of cancer to be highly uniform.
2- A pronounced degree of uniformity is found in the concentration of eight B vitamins in a great variety of animal and human tumors, regardless of the tissue of origin or the manner of their induction.
3- Similar observations are seen for vitamin C
4- The addition of various substrates to malignant tumors of various types yields highly uniform respiratory responses.
5- An almost complete uniformity in cytochrome oxidase content in a number of mouse tumors is seen.
6- The presence of any exhibition of cancer uniformly results in a depression of the liver catalase.
7- Substantial evidence for an immunological uniformity among malignant tumors is seen.
8- An impressive degree of uniformity in enzyme concentration among malignant tissues is reported, regardless of their means of induction, tissue of origin or species of origin.
9- A uniformly low content of such aerobic catalytic systems as cytochrome, succinic, and d-amino acid oxidases, cytochrome-c, catalase and flavin is also described.
10- Further phenomena of uniformity are observed in the elevated water and cholesterol content of malignant tumors as well as other primitive tissues.
11- The induction by a single steroid carcinogen, such as methylcholanthrene, of malignant exhibitions as diverse as leukemia and malignant melanoma, attests to a uniform etiology.
12- The uniformity of various exhibitions of cancer is correlative to an uniformity of malignant tumors in the ability to metastasize as in-

I. Respiratory properties
II. Lactic acid production
III. Vitamin content
IV. Enzyme content
V. Action on a given substrate
VI. Effect on liver catalase
VII. Cytochrome oxidase content
VIII. Immunological properties
IX. Several characteristics in their amenability to heterotransplantability
X. Autonomy
XI. Invasiveness
XII. Erosiveness.

Indeed, there is no known basic property unique to any single display of cancer-the only variation being a morphological one, which is partially reprogrammed by admixed benign or somatic components.

The degree in the uniformity of the factors above described increases with the increasing malignancy with which the tumor is exhibited.

i.e. the degree of the uniformity of factors $\propto$ malignancy of the tumor

or the more the malignancy of the tumor, the more is the similarity or uniformity of the tumor.

Thus with an increasing degree of malignancy, all malignant exhibitions converge toward a common tissue type. For this reason the cells of the most malignant cancer types should summarize the properties of the malignant component in all other exhibitions of cancer.

Now the data can be glanced briefly that is at commonplace to cancer research. However the logical consequences of these data have seldom been examined.

Since the phenomenon of cancer is truly a Unitarian one, then, of logical necessity, the variations in the biological malignancy of different exhibitions of cancer must be a function of the *concentration of a cell of an intrinsically uniform malignancy.*

Position Of the Cancer Cell

We have two alternatives to understand origin and nature of malignant cells with common features. The definitively malignant cell either has–

1- Normal counterpart in the life cycle or
2- The malignant cell is without a normal cellular counterpart.

Therefore, it arises as a spontaneous generation.

Since spontaneous generation is an illogical conjecture, the only alternative is that the malignant cell has its counterpart in the life cycle. Now the question arises whether this counterpart is–

1- A relatively developed cell or
2- The most primitive cell in the life cycle.

Since the primitivity of the cancer cell is a general, in looking for its cellular counterpart in the life cycle we turn to the most primitive cell in this cycle. This is the trophoblast cell. Then as a logical inference of the Unitarian thesis, we should find the trophoblast as the constant malignant component in all exhibitions of cancer: The malignancy of the cancer varies directly with its concentration of trophoblast cells and inversely with its concentration of somatic cells.

i.e. Malignancy of the cancer $\propto$ concentration of trophoblast cells in tumor.
Malignancy of the cancer $1/\propto$ concentration of somatic cells in tumor.

If the Unitarian thesis is valid, then the most malignant exhibition of cancer possible should be comprised almost completely of frank trophoblast cells. Hence being so comprised, they should summarize the cellular and other phenomena shared by exhibitions of a lesser malignancy. The most highly malignant exhibitions of cancer known are the chorionic epitheliomas. They are comprised of frank trophoblast cells, which are–

1- Cytologically similar
2- Endocrinologically similar
3- Otherwise indistinguishable from normal pregnancy trophoblast cells.

If cancer is an Unitarian phenomenon and whose malignancy is a function of the concentration of trophoblast cells within a given tissue, then the greater the concentration of such cells within a tissue the higher the malignancy of the tissue and the more profound its cytological deviation from the cytology normal to the tissue.

If the Unitarian thesis were valid, then the single exception to this generalization would comprise the most malignant of all exhibitions of cancer, chorionepithelioma of pregnancy trophoblast. It is most significant that when

pregnancy trophoblast is malignantly exhibited as primary uterine chorionepithelioma there is no ascertainable cytological, endocrinological or other intrinsic change whatever from the normal trophoblast cells. As Boyd has phrased it, "microscopically the chorionepithelioma is an exaggeration of the condition normally found in pregnancy. All other tumors represent an attenuation of the condition of their normal tissue of origin.

Properties of the Trophoblast Cell

If cancer is trophoblastic, as a Unitarian phenomenon, we should expect to find, occasionally in the male- where trophoblast never normally exists. This must be in at least some cases, in which the failure in somatic resistance to the definitive malignant cell (trophoblast cell) is so complete that the trophoblast is frankly exhibited as such in the fiercely malignant testicular or primary extra-genital chorionepitheliomas. The chorionepitheliomas are unquestionably the most malignant tumors in either sex, and the degree of their malignancy is routinely determined by measuring the gonadotrophin excreted by their trophoblast cells.

If the trophoblast cell, presented outside the normal canalization or checks of pregnancy, is truly the cancer cell, then it must be impossible for the trophoblast cell or its hormone-"chorionic gonadotrophin"-ever to be found in the male or, aside from the canalization of normal pregnancy, in the female except in a malignant fashion.

Neither the trophoblast cell nor its hormone has ever been so found except as cancer. And whenever the trophoblast cell or its hormone has been found in the male or the non-pregnant female, the associated malignancy is observed to vary directly with the urinary excretion of trophoblast cell-produced gonadotrophin.

Even a superficial examination of the trophoblast cell indicates that it possesses such properties of the cancer cell as–

1- Invasiveness
2- Erosiveness
3- Autonomy
4- And ability to metastasize throughout the organs of the host.

Indeed, though normally canalized to physiological ends, the pregnancy trophoblast in carrying the conceptus from anatomically outside of the maternal host to implantation within the uterine wall must behave in a profoundly malignant fashion. No malignant cell invades any tissue any more rapidly and completely than the pregnancy trophoblast does the human uterus in the first few weeks of gestation.

If the trophoblast cell, then, is intrinsically malignant, this malignancy should become especially apparent when the trophoblast is removed from the normal extrinsic checks and controls surrounding it in its normal canalization of pregnancy. Maximov is among those who have observed normal pregnancy trophoblast in tissue culture pari passu non-trophoblast. He describes as follows a tissue culture preparation of a normal rabbit embryo plus the contiguous trophoblast:

"From the very first moment of their formation in vitro, the trophoblastic elements, whose function under normal conditions is to destroy, resorb, and penetrate into the uterine mucosa, attack the growing embryonic tissues. They

glide between cells through the intercellular spaces, along blood vessels, gnaw large holes in epithelial sheets.... Wherever they appear they dissolve, destroy and resorb everything surrounding them. The picture sometimes bears a striking resemblance to chorionepithelioma malignum. As in vitro there is no maternal tissue, the destructive tendencies of the trophoblast are directed toward the net and only available---the embryonic tissue itself. This is rapidly destroyed and totally used up for the nutrition and growth of the trophoblast."

We have been unable to find a single point of dissimilarity between the cancer cell and the trophoblast cell. The points of identity, of course, are those shared exclusively by the cancer cell and the trophoblast cell and not shared by any somatic cell.

The Cell of Origin and The Means of 'tis Differentiation

If cancer is a Unitarian phenomenon, then its cellular origin as well as its cellular nature is exemplified in the origin and nature of the most malignant exhibition of cancer- primary uterine chorionepithelioma.

Pregnancy trophoblast arises through the differentiation by meiosis of a diploid totipotent cell in response to organizer stimuli, which are afforded through the sex steroids. The meiosis of the diploid totipotent cell results in a haploid gametocyte whose only alternative to death is division, which may be sexually or parthenogenetically induced with the consequent production of trophoblast. The only cell from which the most primitive cell in the life cycle, the trophoblast cell, can arise is the most undifferentiated or most potent cell in the life cycle: the diploid totipotent cell. It is this cell alone that is competent for meiosis. In fact, aside from the explanation of spontaneous generation, only two alternatives exist for the origin of the malignant cell. Like all other growth phenomena, it may arise as the result of the differentiation of an undifferentiated cell in response to organizer stimuli. Alternatively, it may be ascribed to the ontogenetic "reversion" of normal cells to a primitive state. Even though the very opinion of such reversion is a thermodynamic fantasy inadmissible by modern biology, if a normal cell could revert, the most primitive cell in the life cycle toward which such reversion could occur is still the trophoblast cell. Hence, aside from the errors of spontaneous generation or cellular reversion, only the phenomena of cellular differentiation are justifiable in accounting for the origin of the cancer cell- though the stimulus to such differentiation may, of course, be diversely mediated.

It is thus a simple embryological fact, that the malignant component of the most malignant of all exhibitions of cancer, viz. primary uterine chorionepithelioma, represents the unchecked growth of normal trophoblast that has arisen through the differentiation of a diploid totipotent cell, by reduction division, and the division of the consequent haploid gametogenous cell to produce the trophoblast.

This has been seen the proof of this in the extremely malignant behavior of rabbit trophoblast removed from the checking influences of the maternal host and placed in tissue culture. This trophoblast, of course, came into being through processes normal to the production of all trophoblast in normal gestation. This is true also of the trophoblast of primary uterine chorionepithelioma.

It is necessary that we emphasize here the fact that our description of the origin of any trophoblast cells is merely a recapitulation of general, universally accepted embryological data. Let us add that it has been experimentally

established that in mammals the haploid gametogenous cell in either the male or the female may be non-sexually activated into division with the consequent and inevitable production of trophoblast.

Because the trophoblast cell of primary testicular chorionepithelioma is indistinguishable from that of the normal pregnancy trophoblast cell or a trophoblast cell of primary uterine chorionepithelioma, the general agreement in pathology that chorionepitheliomas arise from the division of a gametogenous cell (non-sexually activated), derived through the normal meiosis of a diploid totipotent cell, is biologically and logically sound. It is likewise generally recognized that primary extra-genital chorionepitheliomas occurring in both sexes represent trophoblast that shares a common cellular origin with all other trophoblast; an origin from an haploid gametogenous cell (through fertilization or non-sexually) that has arisen through the meiosis of a diploid totipotent cell. This principle is congruent with the axiom that cells, which are alike, arise from pre-existing cells that are alike.

Index Of Malignancy

If cancer is supposed to be an Unitarian phenomenon in which all morphological exhibitions share, in varying degrees, the known malignant component of the chorionepitheliomas, then it follows that the malignancy of a growth will vary directly with its concentration of trophoblast cells and inversely with its concentration of body or somatic cells.

i.e. Malignancy of a growth $\propto$ its concentration of trophoblast cells
And Malignancy of a growth $1/\propto$ its concentration of body or somatic cells

The trophoblast cells comprising a malignant lesion must possess the capacity for being morphologically masked or obscured by the tissue in which they primarily occur or to which they metastasize. Testicular chorionepitheliomas afford an interesting bonus point for the examination of these possibilities.

Not only the trophoblast, when frankly exhibited as such in the primary site, metastasize to be morphologically masked in the secondary site, but the primary trophoblast itself may be morphologically masked by the soma and be frankly exhibited only when metastases occur into tissues of relatively lower reactivity in which the trophoblast is not morphologically masked but is frankly exhibited as such. The masking of the trophoblast by the reactivity of the somatic cells is a measure of the resistance of the host: the degree to which such somatic resistance against the ectopic trophoblast fails determines the malignancy with which the trophoblast is exhibited. Thus, the greater the incidence of a chorionepitheliomatous exhibition (trophoblast) in the metastases, the greater the degree of malignancy.

i.e. Incidence of a chorionepitheliomatous exhibition (trophoblast) in the metastases $\propto$ degree of malignancy

Competent Cell and Organizer

The origin of every new cell is the result of the apposition of a competent cell and an organizer stimulus. All new cells arise as the result of cellular differentiation, which is a process by which a new cell type of a higher degree of individualization and a lower degree of developmental competence is produced. There are no exceptions to this generalization, not even the cancer cell. While a differentiated cell may become plastically deformed or necrobiotic, it can never

form a new cell type through any means except the forward-moving course of cellular differentiation. Cellular reversion is a thermodynamic impossibility; it has never occurred and can never occur. Water does not run uphill, not even in cancer. The cancerous cell is neither a deformed nor a necrobiotic one. Its lethality resides in the fact that intrinsically; it is a normal cell, though its planetary and temporal relationship to the organism-as-a-whole is an abnormal one. The trophoblastic or Unitarian thesis simply recognizes that:

1- The cancer cell is contained within the life cycle and
2- That it is the most primitive cell in that life cycle.

Though the diploid totipotent cells, which give origin to trophoblast, are known to be very abundant in the gonads, the question next arises as to their occurrence extra-genitally. Most modern pathologists recognize the existence of so-called ectopic germ cells (diploid totipotent cells). Embryologically, these cells are nothing more than totally undifferentiated cells that have not participated in bodybuilding but have reserved their total potency or competency since the initial cleavage of the zygote. Cells of various degrees of undifferentiation exist within the body as a reservoir from which tissue repair and regeneration occur. Only the totally undifferentiated cells of the body are competent for meiosis; these cells are the diploid totipotent cells. Of course, all cells in the soma are diploid, but only those that are totally undifferentiated are totally potent or totipotent, hence competent for meiosis. That such cells exist as well as function in the body is further proved by the occasional occurrence of primary extra-genital chorionepithelioma in the male in such regions of low tissue reactivity as the pineal gland and the anterior mediastinum. The frankly exhibited trophoblast cells are correctly attributed to the only ancestor of trophoblast, a diploid totipotent cell that has undergone reduction division or meiosis to form a haploid gametogenous cell that has trophoblast formation as the only alternative to death.

Carcinogenesis is thus seen to be a phenomenon involving a spatially anomalous differentiation in response to organizer stimuli. The differentiation involves the phenomenon of meiosis with the consequent production of trophoblast, which, presented ectopically, is inevitably exhibited as cancer, the malignancy of which depends upon the extent to which such ectopic trophoblast is resisted. Thus in the Unitarian thesis we see the malignant component in all exhibitions of cancer deriving from precisely the same cell type from which the chorionepitheliomas arise. We see all producing the same cell type-trophoblast.

We see this cell doing ectopically precisely what it does in its normal canalization:

1- Eroding
2- Infiltrating, and
3- Metastasizing.

One of the most important problems in cancer research is concerned with the question of why primary tumors metastasize.

If cancer is trophoblastic, the problem of metastases is resolved: the normal pregnancy trophoblast is the only cell in the life cycle that regularly metastasizes, doing so throughout the maternal host in the early months of pregnancy.

The stimuli to malignant differentiation are exemplified in the sex steroids, which induce the meiosis of diploid totipotent cells in their normal canalization. In

view of the relatively specific organizer action of steroids, it is significant that practically all of the carcinogens either are steroids or, like diethylstilbestrol, possess the physiological properties of steroids. Though carcinogenesis may be mediated by highly diverse means, the ultimate common pathway involves the apposition of competent cell and organizer stimuli. The competent cell is always a totally undifferentiated cell (diploid totipotent cell) and the organizer stimulus ultimately involved appears to be a steroidal compound.

Agents producing a chronic inflammation can also prove indirectly carcinogenic because chronic inflammatory sites have a marked capacity for localizing or concentrating steroidal sex hormones as well as other substances. Certain chemicals may also prove indirectly carcinogenic through impairing the somatic detoxification mechanism for steroids. Under special and very limited circumstances, viruses may also contribute to the common pathway by which malignant differentiation is accomplished in birds and rodents.

Estrogens

The meiosis of normally canalized diploid totipotent cells is accomplished in both sexes through the organizer action of steroidal sex hormones. The normal estrogens bear as crucially a basic relationship to the origin of malignant cells, under ordinary circumstances, as chorionepithelioma bears to their cellular identity.

The phylogenic homologue of the trophoblast (extra-embryonic blastoderm) in birds is known to exhibit, under certain conditions, malignant properties.

Viruses and Somatic Mutation

Since the virus theory is subsumed under the Unitarian thesis as a specialized contributory means of eliciting the malignant differentiation, the chief remaining theory is the somatic mutation hypothesis. This hypothesis explains nothing and is in fact, little more than a circular definition: cancer is due to a change; a change is a mutation. This change occurs in the body or soma; therefore, cancer is due to a somatic mutation. On the other hand, the trophoblastic or unitarian thesis does embrace a very definite genetic "mutation." This "mutation" is expressed as meiosis. With the division of the consequent gametogenous cell, the ectopic trophoblast (cancer) cell presented to the soma is, through the necessity of meiosis, of a genetic composition unique from the soma and therefore, in the most literal genetic sense a neoplasm.

Even were one uncritically to accept the somatic mutation hypothesis or the virus theory of cancer, it would be necessary either to seek their resolution in the unitarian or trophoblastic thesis or to turn to a non-unitarian explanation. In which case it would be necessary, then, to postulate an indefinitely large variety of unknown cancer viruses or a similar variety of unknown somatic mutations to account for the origin of the cancer cell. But not even these would suffice since neither hypothesis could account for the fiercely malignant behavior of normal trophoblast in vitro, nor for the fact that this cell has never been found in a non-pregnant organism except as cancer.

Meiosis

We have observed that the extra-genital dispersion of diploid totipotent cells is a commonplace fact. We have specifically ascribed the origin of all

morphological exhibitions of cancer to the meiosis of one or more such diploid totipotent cells with the consequent production of a gametogenous cell whose only alternative to death is division with the resulting production of trophoblast.

In the normal reproductive canalization the only way in which trophoblast can arise is through the meiosis of a diploid totipotent cell and the consequent division (non-sexually or by fertilization) of the resulting gametogenous cell to produce trophoblast. Therefore, one question alone remains here: can the same diploid totipotent cell in an extragenital site undergo meiosis to eventuate in trophoblast production?

As early as 1879 Arnold observed gametoid (meiotic) mitosis in malignant tissue. About twenty years later Farmer, Moore and Walker reported the occurrence of meiosis (heterotypic mitosis) at the border of malignant tumors. In 1929 Evans and Swezy described in inflamed somatic tissue changes "strikingly similar to those of meiotic mitosis. In 1936, Hearne observed meiotic changes in tissues cultured with methylcholanthrene and Molendorff made similar observations in 1939 with estrone.

Diploid totipotent cells are dispersed throughout the soma. Meiosis occurs within the soma. Frank trophoblast cells occur within the soma, though inevitably in a malignant exhibition. They can arise only through the division of a gametogenous cell produced by the meiosis of a diploid totipotent cell. Frank trophoblast cells have never been found in the soma except as the most malignant exhibition of cancer with the exception of pregnancy.

Indeed, the difficulty is no longer one of accounting for the origin of the definitive malignant cell through the phenomena discussed, but rather one of seeking any explanation of how the meiosis of ectopic diploid totipotent cells, exposed to adequate organizer stimuli, could invariably be averted so as to prevent their normal differentiation to trophoblast, whose ectopic exhibition has never been known except in a malignant fashion. Frankly exhibited, such trophoblast comprises the most malignant exhibition of cancer possible, though when morphologically masked by the somatic response of the hostal cells the malignancy of such trophoblast is moderated.

Unitarian V/S Non Unitarian Thesis

The trunk of experimentally established facts comprising modern oncology is formidable. It is not possible for any definitely defined thesis to stand unless it is similar with, or at least not contradictory to, such facts. Only the unitarian thesis finds such congruence. The thesis opposite or alternative to the unitarian one is that each morphological exhibition of cancer represents a biologically distinctive phenomenon, each with a malignant component different from all others. This would mean literally hundreds of different types of cancer cells, each type being normally unrepresented in the life cycle; therefore, each being spontaneously created. Not only would it become necessary to postulate the existence of hundreds of distinct species of cancer cells, but also a postulate of an almost infinite number of subspecies of each type of cancer cell would be required to account for the varying degrees of malignancy exhibited by a given malignant lesion in the course of its evolution. A single chemical carcinogen can evoke practically any malignant exhibition. Now it would become necessary, according to any non-unitarian concept, to conclude that causes that are alike produce effects that are unlike. On the same basis, the occurrence of the frankly exhibited trophoblast cells of extra-genital chorionepithelioma in the male

(identical with those of the primary uterine form) would require the unbiological conclusion that cells which are alike arise from cells that are unlike. The logical contradiction of any non-unitarian hypothesis is further apparent in the experimentally defined uniformity of cancer cells in every one of over twenty factors.

In contrast to the alternative non-unitarian hypothesis, the unitarian thesis holds that the malignant component in all exhibitions of cancer is the same. And this component is not spontaneously created but represents the most primitive cell in the life-cycle; that this cell arises not through "reversion" but through differentiation; that the varying morphological exhibitions are simply conditioned by the nature and resistance of the tissue in which the ectopic trophoblast finds itself; and that the malignancy of the exhibition is, roughly, expressed in the degree of deformation of the somatic tissue by the ectopic trophoblast, and that this is reflected in the morphology from which histological diagnoses derive.

The unitarian thesis and the trophoblastic thesis are of logical necessity synonymous: the most malignant exhibition of cancer (chorionepithelioma) comprises cells intrinsically identical with pregnancy trophoblast cells. Then, if cancer is an unitarian phenomenon, the malignant component of the varying morphological types must be trophoblastic.

Finally, were we to set aside all else, evidential of the unitarian or trophoblastic nature of cancer, and scrutinize but a single datum, we should find that neither experimental fact nor scientific reasoning can offer any alternative to the trophoblastic nature of cancer in explanation. This one datum is the fact that many authors over the past half-century have described frank trophoblast (chorionepithelioma) metastasizing from a primary site to appear at the secondary site in an adenocarcinomatous or other exhibition. In addition, the contrary has frequently been seen. Moreover, frankly exhibited trophoblast (chorionepithelioma) often has been described as merging by imperceptible degrees into an adenocarcinomatous or sarcomatous exhibition.

Trophoblast and the Pancreas

The cancer or trophoblast cell protects itself against pancreatic enzymes through the production of specific antitryptic substances. The occurrence of tryptic inhibitors in cancer sera has been frequently proven.

'The malignant exhibition of the trophoblast of the placenta is the expression of a lack of extrinsic growth' restraints against the trophoblast; this fact was demonstrated in the tissue culture of normal rabbit trophoblast.

A quantitative relationship between the concentration of cancer cells and the titer of specific chymotrypsin inhibitor has been seen. This titer was observed to fall after the surgical removal of the malignant tumor and to rise linearly with its recurrence. Thus the data on the antitryptic properties of cancer sera are not only proof of the antithesis between the cancer cell and the pancreatic enzymes, but are further evidential of the unitarian--and thereby trophoblastic--nature of cancer.

Since the malignant cell is not spontaneously created but has its normal counterpart in the most primitive cell of the life cycle, each organism in the span of its own gestation destroys the cellular counterpart of cancer. This destruction is accomplished through the pancreatic enzymes, notably chymotrypsin and amylase.

When the mammalian organism totally fails in this, the pregnancy trophoblast overgrows as chorionepithelioma. A partial failure is reflected as a toxemic pregnancy, and/or a hydatidiform mole accompanied by an abnormally high excretion of chorionic (trophoblastic) gonadotrophin. For this reason hydatidiform, moles are most frequently associated with toxemic pregnancies, while the risk of sequent chorionepithelioma is 2,000 to 4,000 times greater after hydatidiform mole than after normal pregnancy. The reason for "the much higher curability rate of choriocarcinoma preceded by hydatidiform mole," is that the precedent hydatidiform mole represented at least a partially successful antithesis on the part of the maternal host to the trophoblast.

The reason why primary uterine chorionepithelioma can within a few weeks arise and kill the patient is that this most malignant tumor simply represents a hyperplasia of normal trophoblast cells freed from their extrinsic restraint, just as the in vitro culture of the rabbit trophoblast freed from the maternal environment yields a fiercely malignant exhibition.

It is well established-

1- That the pregnant diabetics exhibit a greatly increased incidence of the pregnancy toxemias.
2- That the severity of such toxemias varies directly with the overgrowth of cellular trophoblast as reflected in the abnormally elevated excretion of chorionic gonadotrophin.
3- That the phenomenon involves a non-insulin deficiency of the pancreas gland.
4- That the predisposition to pregnancy toxemias is noted as early as five years before the clinical onset of diabetes.
5- That the administration of steroidal sex hormones in such pregnancy toxemias frequently ameliorates the condition
6- And that this amelioration is reflected in a proportionate depression in the urinary excretion of chorionic gonadotrophin.

Since such steroidal sex hormones (as estrogen) depress the proliferation of the cellular trophoblast both in normal and toxemic pregnancies, as reflected in a depression in the urinary excretion of chorionic (cytotropho-blastic) gonadotrophin, it is significant that in primary uterine chorionepithelioma the administration of stilbestrol resulted in a clinical improvement that paralleled the decline in the urinary excretion of chorionic gonadotrophin.

It is a commonplace observation that the administration of estrogen or testosterone during pregnancy will often depress the production of chorionic gonadotrophin sufficiently to cause the Ascheim-Zondek test or its Friedman modification to become negative.

Above all is the impudent independence called autonomy. Certainly, no other property is more characteristic of the cancer cell than autonomy; yet in the most malignant exhibition of cancer possible we find the trophoblast cells showing the same susceptibility to the checking influence of sex steroids as is found for the normal pregnancy trophoblast.

If cancer is trophoblastic, and as such a Unitarian phenomenon, it would seem that, the steroidal sex hormones should suppress the growth not only of pregnancy trophoblast and chorionepithelioma but all other exhibitions of cancer as well. That this would be the case were sufficient localization of the steroidal sex hormones possible at all malignant sites is shown in the fact that these

hormones do act to suppress the growth of mammary cancer, prostatic cancer, and their metastases involving the skeletal system. Morphologically, the difference between a primary mammary cancer and a prostatic one is much less pronounced than the difference between either and a primary chorionepithelioma.

The placenta, the prostate, and the mammary gland are notably capable of the selective localization of steroids; hence, trophoblast in any of these areas will show a like response to the injection of steroidal sex hormones. In the case of prostatic and mammary growths, the use of the physiologically antagonistic steroid is rational, since such causes the somatic elements in the growth to atrophy. That the palliative effect is dependent upon the ability of the somatic elements in the tumor to localize the steroids is shown in the fact that the skeletal metastases from the prostate as well as from the mammary gland are responsive specifically to estrogen and testosterone, respectively. Yet this amenability is lost as, with increasing malignancy, the original somatic elements in the skeletal metastases are lost. That such a loss is not directly due to the increasing malignancy but indirectly to the loss of the specific somatic cells responsible for the localization of the steroids is indicated by the fact that in the placenta, while the localizing somatic elements remain, the growth of the vastly more malignant chorionepitheliomatous exhibition is checked.

Thus, we find the unitarian principle of cancer implicit in the sex hormone therapy of cancer, as in all other useful forms of cancer therapy. Moreover, in the unitarian principle the use of steroidal sex hormones in cancer finds its first rationale. Since a non-insulin pancreatic deficiency has been identified with the overgrowth of pregnancy trophoblast, which overgrowth has been shown amenable to steroidal sex hormones, two questions arise:

1- What is the nature of the deficient pancreatic factor, and
2- Is the deficiency of this factor associated with the overgrowth of all trophoblast?

There is a concomitance between the commencing function of the fetal pancreas, as indicated by the appearance of zymogen granules in the gland, and the precipitate degeneration of the trophoblast or its phylogenetic homologue. In the span of normal gestation, the pancreatic enzymes are responsible for checking the growth and ultimately destroying the gestational trophoblast or its homologue. In the 56^{th} day in the span of human gestation, the cellular trophoblast undergoes a sudden degeneration. 'The trophoblast cell produces chorionic gonadotrophin' has been discovered.

If the urinary excretion of chorionic gonadotrophin persists at the original level after the 56^{th} to 70^{th} day in the span of human gestation, the process is inevitably exhibited as chorionepithelioma. In fact, if the abnormal elevation of chorionic gonadotrophin found in pancreatic dysfunction in pregnancy exceeds a certain level, again the process is exhibited as chorionepithelioma.

In view of the antithesis of the pancreatic proteases to the trophoblast cell, it is clear why both pregnancy and cancer are associated with high titers of trypsin and chymotrypsin inhibitors: antithesis is a two-way street, so to speak.

If the pancreatic enzymes are antithetic to the cancer cell, if they resist the cancer cell as the cancer cell is known to resist them (through the specific antitryptic inhibitors) why does cancer of the pancreas gland occur? Why is it that

cancer is not only primary in this gland but that this gland itself may be subject to secondary growths through metastases or direct invasion?

The pancreatic proteases exist in the pancreas in the form of their inactive zymogens. These are not converted into the corresponding active enzymes until they are acted upon by the kinases of the blood or, especially, by those of the small intestine. In view of this, one may ask why the small intestine, then, is not practically immune to cancer. "One of the most striking features about the pathology of malignant disease is the almost complete absence of carcinoma in the duodenum and its increasing frequency throughout the gastro-intestinal tract in direct proportion to the distance from this exempt segment."

It is noteworthy that the small intestine is not only practically immune to primary tumors but also to metastases. A fulminating malignant growth may exist in the pyloric end of the stomach a few millimeters from the immune small intestine, but, as William Boyd points out, "The duodenum is never invaded, the tumor stopping short at the pylorus. Spread to neighboring organs usually involves the liver or the pancreas." The incidence of malignancy is, of course, high immediately distal to the ileocecal valve.

The pancreatic enzymes not only normally occur in the active state in the blood stream, which possesses an optimum pH for their action but the clinical determination of serum amylase and trypsin are standard procedures, especially in pancreatic diseases.

The Pancreas and Carcinogenesis

The fact that pregnancy occurs in the presence of a normal concentration of pancreatic enzymes indicates that trophoblast can exist for a while under such conditions. It must be remembered, however, that such trophoblast is:

1- Held in check until the 56th day of gestation and almost completely destroyed shortly thereafter (with the commencing function of the fetal pancreas) and
2- That implantation occurs after the trophoblast has had about a four-day period of growth anatomically exterior to the host.

The trophoblast carries with it its own anti-tryptic enzymes against the pancreatic proteases. As we have seen, carcinogenesis involves ectopically precisely the same basic mechanisms involved in the production of canalized trophoblast. The prolonged exposure of a tissue to carcinogens results in a prolonged depression in its respiratory mechanisms. This may result in the appearance and persistence of ectopic trophoblast in the exposed tissue. The trophoblast or cancer cell is autonomous of the hostal respiratory system and is obligatively anaerobic, undergoing anaerobic glycolysis even in the presence of a free oxygen supply. The trophoblastic thesis explains the long- known identity of trophoblast cell metabolism with that of the cancer cell. An obligative anaerobic system is obviously a necessity in a primitive parasitic cell like the trophoblast (or cancer) cell.

When cancer is elicited experimentally from a normal laboratory animal, the lesion usually does not metastasize, but attains a large size and is almost completely somatic. Herein reside the scientific limitations of artificially induced or transplanted animal tumors in the scientific study of chemotherapeutic agents. Such tumors are practically benign in the biological sense. Because the

pregnancy trophoblast regularly and normally metastasizes in the early phase of gestation, we must expect metastases ultimately in any "full blown" cancer.

While a low-grade malignant growth (primarily somatic tumefaction) can be induced ultimately by sufficient carcinogenic stimuli in the presence of normal pancreatic function, a highly malignant exhibition is invariably accompanied by at least a relative pancreatic insufficiency implicit in the correspondingly high serum titer of antitryptic and antichymotryptic enzymes.

That the induction of the ectopic trophoblast is usually accomplished against great difficulty, regardless of pancreatic adequacy, is indicated in the fact that non-chorionepitheliomatous exhibitions in man usually have a latent period of years, while a chorionepithelioma in pregnancy may arise from the preexisting trophoblast and destroy the host within a few weeks.

The extent to which the soma resists malignant involution is reflected in the fact that only two cellular differentiations, meiosis of the diploid totipotent cell and subsequent division of the resultant gametogenous cell, divide the malignant cell from the benign one. This explains the all-or-none suddenness classic to the malignant change, and the absence of true transitional cells.

Cancer a Composite Tissue

The malignant lesion is a composite tissue comprising –

1- Trophoblast plus
2- Somatic elements.

The malignancy of a lesion varies directly with its concentration of trophoblast and inversely with its concentration of somatic elements as already described. The normal placenta, too, represents a composite tissue; for, here the trophoblast cell finds its normal canalization in the life cycle. Just as the malignancy of a placenta, in a chorionepitheliomatous exhibition, varies directly with the concentration of trophoblast cells, so in the ectopic presentation of trophoblast that comprises cancer the malignancy of the lesion varies with its concentration of trophoblast. The only fundamental difference is that in the latter the trophoblast cells are morphologically masked by the resisting soma, except in the most malignant of extra-genital tumors: chorionepithelioma.

A tissue can be malignant only by being a composite one. Malignancy is an inimical relationship between cells and finds being by virtue of a thetic benignancy. In its simplest terms, then, a malignant tumor comprises somatic tumefaction plus a malignant component. It is for this reason that the greatest tumefaction is usually associated with the least malignant exhibitions and the least tumefaction often with the most malignant exhibitions. Since trophoblast normally metastasizes, tumors of the highest malignancy and lowest tumefaction tend to be the most metastatic. Thus the increase or decrease in the malignancy of a given tumor is not the result of a continuing spontaneous generation of an infinite variety of cancer cells, but merely the expression of the increase or decrease in the concentration of ‘A CONSTANT MALIGNANT COMPONENT’. As the antithesis of this component determines the malignancy of the lesion so that the soma determines its benignancy.

Leukemia

In the leukemia, the constant malignant component (trophoblast) is present in the lymphopoietic or myelopoietic tissues. The reaction of such tissues

to the malignant component results in the proliferation of somatic white blood cells of varying degrees of maturity. This is the counterpart of tumefaction in the sessile tumor. Thus the Unitarian or trophoblastic thesis, different from the non-unitarian concept, finds no contradiction in the fact that often the most malignant phase of the leukemic process, the so-called aleukemic leukemia, actually involves a leukopenia. This phase is the most malignant because the somatic cells (leukopoietic tissue) have lost their ability to resist through virtue of the destruction of the leukopoietic tissue by ectopic trophoblast. For this reason, the aleukemic or leukopenic stage is often terminal to a preceding highly leukemic or leukocytic phase.

Trophoblastic Hormones

The routine utilization of the trophoblastic hormone, chorionic gonadotrophin, is, of course, a clinical commonplace as a means of diagnosis as an index to therapeutic response in the case of the most malignant exhibitions of cancer, the chorionepitheliomas and certain other exhibitions of cancer. The excretion of this hormone varies directly with the malignancy of the tumor, which, in turn, varies, directly with the concentration of trophoblast cells.

A similar gonadotrophin is reported in 100% cancer patients examined, and none in the blood or urine of the control series, with the exception of pregnancy.

Zondek reported the hormone in the urine of 82 per cent of females afflicted with cancers of the genital organs and in 36 per cent of female patients suffering from extra-genital tumors.

It is necessary to emphasize that the original work of Zondek as well as other workers was done on the erroneous assumption that the hormone was produced by the anterior pituitary gland. Even after tissue culture studies had proved the trophoblast-cell-origin of the hormone, its occasional identification in cancer urine, with the Ascheim-Zondek or Friedman tests, was usually dismissed as an inexplicable datum of an inexplicable disease. Only within the context of the unitarian or trophoblastic thesis was sufficient theoretical justification found to concentrate and selectively extract the urine of the less malignant exhibitions of cancer specifically for the same hormones (chorionic gonadotrophin and syncytial steroids) always found by ordinary techniques in the most malignant exhibitions.

Thus to the already established uniformities for 20 or more known factors among the various exhibitions of cancer, we now find an hormone (not only evidential of the unitarian thesis but of the specific trophoblastic nature of cancer as well) in the trophoblast cell-produced hormones. Like all other uniformities found in the malignant lesion, that for the trophoblastic hormones becomes increasingly apparent with the malignancy of the growth, so that frank chorionepitheliomas are found excreting as many as one million International Units of chorionic gonadotrophin every 24 hours, while the much less malignant exhibitions with no frank trophoblast cells excrete 50 or fewer units of the trophoblastic hormone.

Diagnostic implications

There are only two fundamental kinds of cancer tests:

1- The indirect tests concerned with the detection of a substance produced by the soma as the result of the presence of cancer cells; and
2- The direct tests concerned with the detection of a substance produced by the cancer cell themselves.

Though the incidence of a specific somatic change may bear a high correlation with the presence of an uniform stimulus, the correlation can never be a truly specific one, since obviously no somatic reaction is so specifically reserved for the presence of cancer or trophoblast cells that it can not be falsely elicited by other stimuli.

The limitations of the indirect tests have been well demonstrated in practice. The only reliable and generally accepted serum or urine tests for cancer are the direct ones, such as the Ascheim-Zondek test and its numerous modifications. Just as hundreds of indirect tests have been tried and discarded for pregnancy diagnosis, so have hundreds of indirect tests for cancer been tried and then discarded. The only tests for either pregnancy or cancer that have survived are those direct tests depending upon the identification of a substance unique to cancer and pregnancy: the hormone of the trophoblast cell. Since cancer is trophoblastic, its most malignant exhibition, chorionepithelioma, is highly amenable to the direct test. In fact, the possibility of either an indirect or direct general diagnostic test for cancer depends upon cancer being a unitarian phenomenon.

The efficient clinical implementation of the trophoblastic or Unitarian thesis depends upon the development of a simple, reliable and highly accurate quantitative test for the specific products of the trophoblast cell.

While we have identified the presence of chorionic gonadotrophin in the urine of patients with all exhibitions of cancer, we have found the technological evolution of a quantitatively precise chorionic gonadotrophin test difficult for the less malignant exhibitions of cancer. When we consider that a chorionepitheliomatous exhibition of cancer in the male may yield over 1,000,000 I.U. of chorionic gonadotrophin while metastatic testicular cancers of a much lower malignancy, though biologically still more malignant than most extra-genital growths, may yield fewer than 50 I.U. for a like volume of urine, then the physical difficulties in the case of most of the extragenital tumors of still lower malignancy is obvious.

From the urine of patients with the common exhibitions of cancer, the authors have obtained highly active preparations of chorionic gonadotrophin, and are now engaged in the crystallization of chorionic gonadotrophin, by the method of Claeson, Hogberg and Westman (1948), from pooled urine of various exhibitions of cancer. It is recognized that the specific steroidal hormones of the syncytial trophoblast also comprise a most important avenue to the development of a satisfactory diagnostic technique. However, these steroidal hormones have not been studied as intensely as chorionic gonadotrophin, which is now characterized as a glucoprotein containing 18% acetylglucosaminedigalactose polysaccharide.

Several cancer tests relying on the detection of trophoblastic hormones are now under study for achieving a sufficiently practical quantitative test for general use.

Clinical implications

As a composite tissue, cancer in its somatic component represents many diseases; in its constant malignant component, one disease; and, in its totality, a local manifestation of a general disease.

Both clinician and experimentalist are generally agreed that the somatic or anatomical changes produced by the malignant process are largely irreversible. Surgical extirpation or the primarily non-selective cautery of radiant energy may destroy the composite tissue of a primary tumor. However, the vague hope for an agent that will cause the "reversion" of an organized malignant tumor to normal tissue is scientifically indefensible. Aside from the physical destruction of the tumor itself, one primary factor can contribute to the amelioration of the effect of the tumor on the host. This is the growth inhibition or destruction of the constant malignant component of the tumor. Selective ablation of the malignant component will not alter the already existing somatic dysplasia nor histologically change the architectonics of the tumor, except in highly malignant anaplastic exhibitions. Here the histological as well as the gross changes take an expected course: a histological increase in connective tissue elements with a palpable increase in fibrosity.

In the advanced and well-organized lesion, the possible changes are not, as a rule, dramatic. Were the malignant component ablated, the somatic component would tend to persist largely unchanged or even show a slight increase in benign tumefaction. Since none of the cells in a malignant tumor is per se a "diseased" or pathological cell, but rather a cell normal to the life cycle, cancer does not itself produce any "toxic effects." Its lethality is eminently a physical matter involving the normal behavior of normal trophoblast in a spatially abnormal relationship.

Above all, cancer is a natural phenomenon ultimately involving the soma in irreversible changes. To question the results expected from the selective ablation of the constant malignant component in a malignant lesion would be to suggest that, aside from actual tumor destruction, no malignant tumor has ever spontaneously regressed, that no highly anaplastic cancer has even spontaneously gone into a less malignant scirrhous exhibition, or that no patient has ever survived for five years or more after exhibiting an inoperable and highly malignant lesion. It is not necessary to review here an impressive literature on spontaneous regression. Much more important to a sound comprehension of the clinical implications of the trophoblastic or unitarian thesis are the thousands of cases of cancer in which the host is able to resist and to live with the cancer cells for years.

What are the factors-

1- Cells, tissues, organs, and their secretions, contributing to such resistance?
2- What causes trophoblast in the pregnant diabetic to overgrow, despite a normal insulin supplement?
3- Why do the specific inhibitors to pancreatic chymotrypsin and trypsin rise with the increasing malignancy of a growth and decline following its amelioration?
4- Why is the small intestine practically immune not only to primary tumors, but to direct invasion and metastases as well?

5- Why does the growth of the invasive, erosive and metastatic trophoblast of normal gestation cease and degeneration commence concomitant with the commencing function of the fetal pancreas gland?
6- Why does the urinary excretion of chorionic gonadotrophin fall concomitantly with the degeneration of the trophoblast?
7- After more than 99 per cent of the trophoblast has been removed from the placenta, why does its size remain unaffected though its invasive and erosive properties are entirely lost?
8- Why are pregnancy trophoblast cells often indistinguishable histologically from the somatic cells in the uterine wall of the pregnant host?
9- Why is it that the removal of normal pregnancy trophoblast to tissue culture will result in a fiercely malignant exhibition of such trophoblast toward all nontrophoblast cells?
10- Any attempt to implement clinically the trophoblastic or Unitarian thesis should be made in the light of the answers to these questions.

Radiation

Were malignant cells actually selectively susceptible to radiation, the most malignant exhibitions of cancer would be the most amenable to therapy, since they then, would, contain the highest concentration of radiosensitive cells.

1- Chorionepithelioma and malignant melanoma represent two of the most malignant exhibitions of cancer, yet they are radio-resistant.
2- Glioblastoma multiforme and neurogenic sarcoma are also examples of highly malignant exhibitions of cancer that are radio-resistant.

The answers to these questions reflect the cogency of Oberling's prediction: "Some day, perhaps, it will turn out to be one of the ironies of nature that cancer, responsible for so many deaths, should be so indissolubly connected with life."

We may generalize that the malignant component of a tumor is slightly less radio-resistant than the somatic connective tissue stroma but considerably more radio-resistant than the somatic parenchyma.

i.e. the order of increasing radiosensitivity is:

Somatic Connective Tissue Stroma < Somatic Parenchyma < Malignant Component of the Tumor

This is why radiation often results in an increase in tumor fibrosity, which would be an excellent sign were this achieved at the cost of the radio-resistant malignant component (trophoblast) rather than at the cost of the somatic parenchyma. The so-called radio-sensitivity of a tumor is determined primarily by the radio-sensitivity of the somatic cells in which the constant malignant component happens to reside, not by the uniformly radio-resistant constant malignant component: the ectopic trophoblast.

Radioactive Elements

The most commonly used radioactive element is that of iodine in the therapy of thyroid. The limitations of this therapy are as follows:

"The more cancer malignant and destructive forms tend to pick up (radio-active iodine) to a lesser and lesser degree as the invasiveness increases."

With an increase in the malignancy of the exhibition, there is necessarily an increase in the concentration of the definitively malignant cells (trophoblast) and a consequent decrease in somatic thyroid cells, which are the only cells, involved in the selective uptake of radioactive iodine. The decrease in tumefaction as a result of the uptake of radioactive iodine is an expression of the loss of functional somatic cells.

Surgery

The lower the concentration of trophoblast cells in a malignant lesion, the more amenable the lesion is to successful surgery. For this reason highly malignant growths like chorionepithelioma are generally inoperable.

Pancreatic Enzyme Therapy

The palliative use of the crystalline pancreatic enzymes in advanced human cancer rests entirely upon the validity of the unitarian or trophoblastic thesis of cancer.

Conclusion

Our own studies, too, appear to confirm the unitarian or trophoblastic thesis of cancer. The independently proved uniformities, which increase in degree of uniformity with the malignancy of the growth, of malignant lesions in the:

1- Concentration of eight water-soluble vitamins
2- In vitamin C content
3- In water content
4- In cytochrome-c
5- In effect on liver catalase of the host
6- In Warburg's criteria of glycolysis
7- In lactic acid formation
8- In sugar content
9- In the respiratory response to added substrates
10- In a common means of induction
11- In antichymotryptic factors
12- In autonomy, invasiveness and erosiveness
13- In ability to metastasize
14- In amenability to universal therapeutic measures
15- In the general anticarcinogenic effect of caloric restriction on the incidence of mammary tumors and leukemia alike in experimental animals
16- In heterotransplantability
17- In loss of specialized function as malignancy increases (in all tumors except chorionepithelioma)
18- In departure from the histology of the site of origin (except in primary uterine chorionepitheliomas)
19- In numerous enzymes

All these uniformities, indeed, exclude any but a unitarian nature of cancer. Then as we examine the most malignant exhibition of cancer possible, chorionepithelioma, to find it comprised of trophoblast cells indistinguishable cytologically, endocrinologically or otherwise from those of normal pregnancy trophoblast, the fact becomes impelling that if cancer is, indeed, an unitarian phenomenon all of its properties must be exemplified in these most primitive of

all cells in the life-cycle, the trophoblast cells. These cells in their normal canalization of pregnancy (as well as in vitro) exhibit every known property of malignant cells, though normally directed in pregnancy toward the physiological exploitation of the truly malignant process implicit in the embedding of the tissue of the conceptus into that of the mother.

Then, were all else evidential of the unitarian or trophoblastic nature of cancer set aside, and were there left for scrutiny but the single fact that primary exhibitions of trophoblast (chorionepithelioma) are not infrequently seen that metastasize to an adenocarcinomatous or sarcomatous exhibition, and vice versa, then reason would admit of only one explanation: the trophoblastic or unitarian fact of cancer.

Were the cellular counterpart of cancer not an inextricable component of the life-cycle, represented in the most primitive cell of that cycle, the processes of natural selection themselves would have precluded the survival of the spontaneously generated cells that any alternative to the trophoblastic fact of cancer necessitates.

The unitarian thesis is not a belief inflexibly held by its proponents; it is merely the only explanation that finds total similarity with all established facts on cancer. While the unitarian or trophoblastic thesis seemingly admits of no alternative, it warrants the most corrosive scrutiny. For cancer either is or is not a unitarian phenomenon, and thereby it is either trophoblastic or not trophoblastic in nature. The definitive cancer cell is either the most primitive cell in the life cycle or it is not the most primitive. It is either the result of the differentiation or meiosis, however spatially or temporally irregular, of a cell or it is not the result of cellular differentiation.

These are, indeed, instances in which the exception proves the rule; for, were cancer not trophoblastic, its most malignant exhibition, chorionepithelioma, would then show the greatest loss of function and the greatest deviation from the histology of the site of origin, instead of actually showing an accentuation in the normal function of trophoblast, as it does. Yet were one to attempt to ascribe to the malignant exhibition of trophoblast some intrinsic but subtle change from that of the non-malignantly exhibited trophoblast, such an attempt would be rendered nugatory by the fact that the most malignant exhibition of cancer possible in the male, chorionepithelioma, comprises trophoblast cells indistinguishable from those of pregnancy or chorionepithelioma in the female; yet, in the male chorionepithelioma represents the widest possible deviation in histology and function from the site of origin. The latter fact corroborates the proof of a rule previously proved by its exception.

The life cycle, and thus is the result of cellular differentiation; or it has no cellular counterpart in the life cycle, does not arise through cellular differentiation, and, therefore, is spontaneously created. The diploid totipotent cells within the soma, like their normally canalized daughter cells, can either undergo meiosis and subsequent trophoblast production, in response to sufficient organizer stimuli, or they cannot. The occurrence of frank trophoblast cells within the soma (invariably as the most malignant exhibition of cancer) is either the result of the meiosis of a diploid totipotent cell or it is not; and, therefore, is the result of a spontaneous generation. The trophoblast or the cancer cell either produces specific inhibitors to pancreatic chymotrypsin and trypsin, or it does not (and the twenty or so independent workers how have so reported are all in error). A malignant tumor is either a composite tissue or it is not a composite tissue. The

malignancy of a tumor is either determined by the concentration of a constant malignant component; or it is not so determined and depends, therefore, upon the successive spontaneous generation of a series of specific cells to account for the increasing malignant evolution of the tumor.

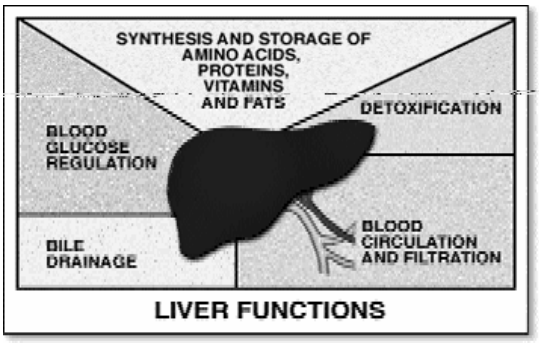
The trophoblastic or unitarian thesis holds the affirmative of all these propositions. The unitarian thesis recognizes the need for an orderly defined common ground of theory upon which all workers in cancer may at least meet, if not agree. It holds as reasonable the thesis that the more tenable of two distinctly opposed hypotheses should be given the greater credence in determining the direction of future research. It holds that in the intensive study of the peculiar metabolism of trophoblast both in pure cultures and in vivo, with the goal of the selective lysis of the trophoblast cell or the occlusion of its metabolism, the cancer problem may find practical resolution. It holds that the cancer problem need not offer amnesty to unbridled empiricism and negation to the most basic tenets of the rational process.

Above all else, the trophoblastic or unitarian thesis urges that the alternative non-trophoblastic or non-unitarian thesis, which is at present overwhelmingly the dominant hypothesis, be scrutinized in the light of whatever experimental evidence might exist in its support. Indeed, the evaluation of any alternative to the trophoblastic or unitarian thesis, within the context of experimental facts and scientific logic, by those who find the trophoblastic or unitarian thesis untenable or tenuous should prove most instructive. For in cancer, as in all else, facts do not speak for themselves but must be spoken for.

The Liver

The liver is the largest gland in the body weighing approximately 1500 grams and is located in the right hypochondrium i.e. right upper quadrant of the abdomen. It is glossy in appearance and dark red in color due to the rich supply of blood flowing through it. Approximately a quarter of the cardiac output flows to the liver. It performs diverse substantial functions:

1. The uptake, storage, and disposal of nutrients i.e. protein, carbohydrates and fat, drugs and toxins.
2. The production of synthetic proteins (critical for blood clotting).



3. Metabolism of substances produced by the body.

Digestive Function of the Liver

Sometimes referred to as the great chemical factory of the body, the liver creates regulates, and stores a variety of substances used by the gastrointestinal system and it serves a number of important digestive functions.

The main digestive chemical synthesized by the liver is bile. During a meal, liver cells secret the bile, which travels through the hepatic duct system into the small intestine where it is used to break down fat molecules.

Between meals, bile is stored in the gall bladder. Bile further serves as a waste disposal system for toxins removed from the blood by the liver.

The liver also plays a major role in the regulation of blood glucose. The liver synthesizes, dissolves, and stores amino acids, protein, and fat. It stores several important vitamins like B12 and Vitamin A. The liver also disposes of cellular waste and breaks down harmful substances, like alcohol.

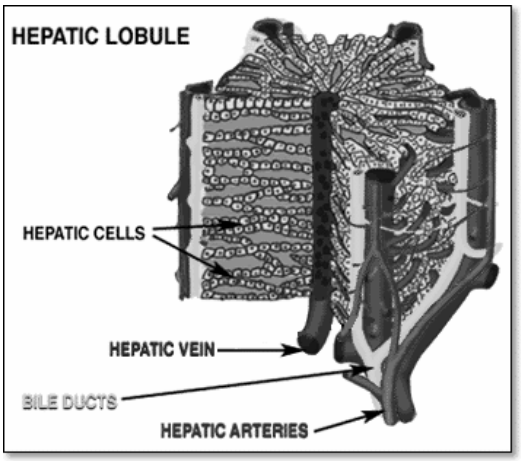
Circulatory Function of the Liver

Though the liver is technically a part of the gastrointestinal system, it also plays an important role in blood circulation too. The liver has been called the antechamber of the heart because it collects and processes all of the gastrointestinal blood through the portal vein and delivers it to the right side of the heart. The liver receives blood through two vascular systems, the portal vein and hepatic artery.

Microscopic Structure of the Liver

The lobule itself is surrounded by connective tissue and has 5 to 7 clusters of vessels around its edges.

These vessels include a branch of the portal vein, a branch of the hepatic artery, and a bile duct. A central vein runs through the middle of the lobe and is



surrounded by cords of liver cells that radiate out in all directions. Between these cords, there are wide thin-walled blood vessels called sinusoids. All of the blood drains into a hepatic vein, which then circulates throughout the body.

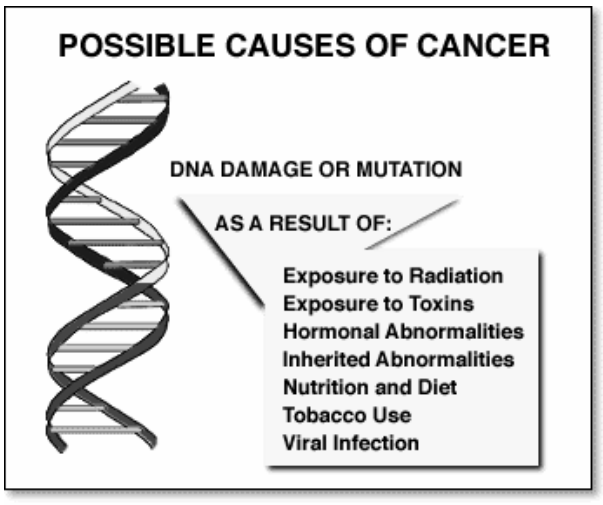
Below is a biopsy from a normal liver. The white arrows demonstrate the hepatic sinusoids and the dark arrow represents the portal pedicle. Blood flows into the liver through the portal pedicle, past the hepatic sinusoids (which contain normal liver cells called hepatocytes) into the central vein and then out of the liver.

How Liver Cancer Develops

Cancer is an uncontrolled replication of damaged cells. This condition usually produces a mass called a tumor. Cancer is the direct result of either a mutation of the cellular DNA or some sort of damage to the cellular DNA. For the cancerous cell to actually develop into a tumor, it must be able to grow and to replicate itself. A cancerous cell that cannot grow or make a copy of it will die or lie dormant for an extended period.

What actually causes genetic mutations or DNA damage is not yet completely understood, but several significant factors that encourage cancer development have been identified.

The liver is a common site of metastases from a variety of organs such as lung, breast, colon and rectum.



When liver metastases occur at the time of initial diagnosis of the primary tumor, they are described as synchronous. If detected after the initial diagnosis, they are described as metachronous. The liver is frequently involved since it receives blood from the abdominal organs via the portal vein. Malignant cells detach from the primary cancer, enter the bloodstream or lymphatic channels, travel to the liver, and grow independently. Till now it is not understood the mechanism of how a tumor cell can leave the primary site and grow in specific organs.

Virtually, the environment of the liver is suitable to the growth of certain tumor cells. Once a tumor begins to grow in the liver, it receives its blood supply from the hepatic artery and develops.

Carcinogenesis

Carcinogenesis is a multistage process.

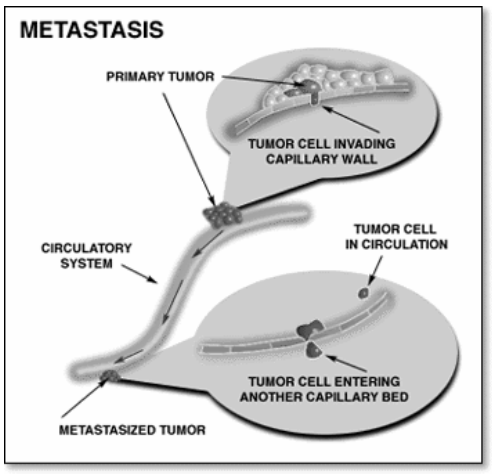
1- **Initiation-** It begins when a carcinogen causes a genetic change or damages the DNA in a normal cell. This makes the cell more defenseless to other genetic changes. This stage is called “initiation.” If the process ended here, and the cancerous cell did not grow and replicate, no cancer would form.

2- **Promotion-** The next stage of carcinogenesis is called “promotion.” This occurs when the initiated cell is exposed to an agent that enhances its growth into a larger mass.

When a tumor actually forms, it has all of the same basic needs as a normal cell. Because the tumor cells are genetically damaged, they are inefficient and deprive normal cells of important oxygen and nutrients. In addition, a malignant tumor grows uncontrollably and can eventually interfere with the function of vital organs, such as the liver.

Growth of Cancer

A small tumor no larger than 1 millimeter in diameter can sustain itself in such a manner indefinitely. But it cannot grow any larger unless the tumor itself begins to generate a network of blood vessels to help supply additional nutrients.

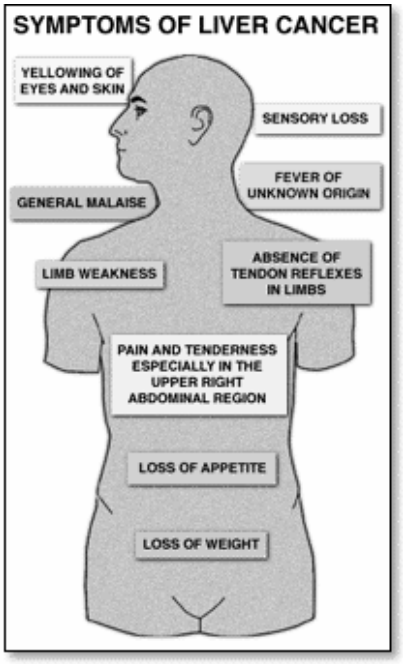


A clinically detectable tumor is about 1 gram in weight and made up of at least 1 billion cells. Metastatic tumors form when large progressive tumors shed off the tumor cells.

These tumor cells must be able to grow and function apart from the primary tumor.

Metastatic tumor cells move throughout the body, usually through the circulatory system or the lymphatic system. These cells often lodge in to a blood capillary, where they may or may not grow. The tumor cells that actually grow are somehow more suited to the new location. Metastatic tumor cells tend to mutate more quickly than normal cells, giving them a greater ability to adapt to their environment as well as a greater ability to resist therapy. These cells are more likely to infect places they can easily reach.

Because the liver is close to or actually connected to several significant organs, and because the liver plays an important role in blood circulation by acting as a filter, metastatic liver cancer occurs in over 75% of all terminal cancer patients.



How Cancer is Detected

Early stages of cancer can be asymptomatic and may go undetected for months or even years. When symptoms do develop, they are most pronounced as pain.

Pain associated with cancer is a result of several possibilities:

1- Invasion or destruction of normal tissue with cancer cells.
2- Stretching of internal tissue by tumor growth.
3- Pressure of tumor on an organ.
4- Blockage of a vital passageway by the tumor.
5- Infection caused by cancer.

Other symptoms may include loss of appetite, loss of weight, fever of unknown origin, limb weakness, sensory loss, or an absence of tendon reflexes in the limb.

Liver cancer, both primary and metastatic, often exhibits symptoms of general malaise as well as pain and tenderness. The discomfort is usually of a moderate degree and most often in the upper or upper right part of the abdomen.

In more advanced cases, symptoms of jaundice, a yellowing of the skin and eyes, may also appear.

Cancer and Homoeopathy

As per above discussion, we can easily understand the role of Homoeopathy in treatment of Cancer.

Since Homoeopathy deals with patient as a whole, as a specific individual, the altering nature of normal somatic cells into the trophoblastic one, can be checked and hence the so called malignancy. To understand this fact, we must know what Homoeopathy is.

What is Homoeopathy

Any person may raise this question. To answer it is not so simple. To well comprehend it, we must first know the fundamentals of life science.

The word Homoeopathy is derived from combination of two Greek words, 'Homoios' means 'like' and 'Pathos' means 'disease'.

This unique system of treating diseases was founded by German Dr. Christian Frederick Samuel Hahnemann (10th April 1755 to 14th April 1843) in late 18th century. This system is based on theory that large doses of drugs that produce symptoms of a disease in healthy human people will cure the same symptoms, hence the disease when administered in small amounts.

It is different from Homoeotherapy, which is the treatment or prevention of diseases with a substance identical with the active causative agent, such as jennerian vaccination.

It is also quite different from allopathy, which is the system of treating diseases by inducing a pathologic reaction that is antagonistic to the disease being treated.

To learn about Homoeopathy, a broad knowledge of life, health, disease, medicine etc. is essential.

Fundamentals of life

What is the basic difference between a living body and the nonliving body? Most of us know the cardinal features of life, i.e.

1- **Metabolism—** the sum of all the physical and chemical changes that take place within an organism including all the energy and material transformations that occur within living cells. It includes both anabolism (assimilation or binding up processes) and catabolism (disintegration or tearing down processes). Metabolism includes all the processes involved in utilization of substances entering the body.

2- **Growth—** the progressive development or increase in size of a living thing. Growth may be normal as in that of an embryo or child, or pathological, as in a cyst or benign or malignant tumor. Growth may be by the synthesis of new protoplasm and multiplication of cells or by the manufacture and deposition of organic substances like fatty acids inside cells.

3- **Reproduction—** reproduction is the process by which plants and animals give rise to their offspring.

4- **Adaptation—** adaptation is the adjustment to a change in the environment.

The thing having any three of the above will be called as living being.

Now what is the difference between a living body and a dead? There is a force, rendering the thing to live. Before being dead, that body was alive. Why does it so happen? Some force, animating that body, escapes out leaving it dead. Yes, true! That is the vital force, which animates the material body. Thus, we can assume that Life is constituted of:

(a) Material parts i.e. the physical body.
(b) Immaterial parts i.e. the Vital Force and/or the soul.

Both these beings are linked together in degrees of precision and fineness.

The energy flowing from the absolute (the soul) towards the physical being and nourishment from physical being to the inner self, thus forming life cycle, and the integrated whole life.

Hahnemann says-

" The material organism, without the vital force, is capable of no function, no self-preservation (It is dead, and now only subject to power of the external physical world, it decays and is again resolved into its chemical constituents), it derives all sensation and performs all the functions of life solely by means of the immaterial being (the vital force) which animates the material organism in health and in disease." (Organon. Aphorism no. 10)

This fact is unanimously accepted worldwide either directly or indirectly. Everybody appreciates presence of this vital force in the name of what he regards viz. Soul, Spirit, Aatma, God, Eishwar etc.

Vital force

This vital force is the dynamic, imponderable, invisible universal force of life energy found in all the living and to some extent in nonliving things also. One can easily appreciate its presence in living things due to visible results. Its existence in nonliving things can only be explained by science.

Every thing consists of small units of molecules. These molecules are made of tiny atoms. Each atom is made of electrons, protons and neutrons (now presence of some more constituents has been proved viz. Positron etc.). Most of these finest particles are electrically charged and are kept together by electromagnetic field of attraction. These ultimate constituents are in the state of certain rhythmical and precise motions, and consequently, whole structure is in a state of harmonious oscillations and vibrations.

Great scientist Albert Einstein says—

'Mass' and 'Energy' are inter-convertible. The ultimate result of divisions of a substance is energy. Whenever anything is tried to divide a matter beyond atomic state, nothing is left except energy, in the form of photons. This energy is nothing but a form of life energy, equivalent to vital force.

Thus, this energy or vital force is omnipresent and is in abundance. Everything uses a very little fraction of this force to exist.

Hahnemann Says-

"In the healthy condition of man, the spiritual vital force (autocracy), the dynamis that animates the material body (organism), rules with unbounded sway,

and retains all the parts of the organism in admirable, harmonious, vital operation, as regards both sensations and functions, so that our indwelling, reason-gifted mind can freely employ this living, healthy instrument for the higher purposes of our existence". (Aphorism no. 9)

Health

Vital force keeps us alive. It always tries to flow very smoothly and harmoniously. This is the state of health. The slightest deviation of vital force may lead one to experience abnormal state.

W.H.O. says—

" Health is the state of mental, physical, and social well being. "

Our body can be divided into two entities, the mind and the physique. The mind governs, and the physique acts.

Mind is an imaginary entity, which is responsible for thinking, feeling, reasoning, will, emotions, intellect and memory.

There are four cardinal functions of mind-

1- Will—the mental faculty used in choosing or deciding upon an act or thought. This is the power of controlling one's actions or emotions.
2- Affection— feeling of love.
3- Intellect— conscious brain function, the mind, or understanding.
4- Memory— the mental registration, retention, and recall of past experiences, knowledge, ideas, sensations and thoughts.

We can define mind as an integration of brain resulting in the ability to perceive surroundings, to have emotions, imagination, memory and will, and to process information in an intelligent manner. This can very easily be understood that mind is the most delicate and sensitive entity in us. It is more dynamic than the physique, hence more liable to get affected and thence sick.

Disease

Now, we must first discuss what the disease and its process is. A particular disease is the particular syndrome of signs and symptoms.

Symptom

Any perceptible change in the body or its functions that indicate its deviation from the health is called a symptom. Symptoms may be:

1- **Subjective—** the sufferings felt by the patient only.
2- **Objective—** the sufferings appreciable to the attendants or observers i.e. visible changes. The objective symptoms are also called signs.
3- **Cardinal—** the principal and necessary symptoms.
4- **Constitutional—** symptoms specific to a particular individual.

Analysis of a symptom

To analyze, complete and qualify a symptom, following points are necessary:

1- **Onset—** date, manner (Gradual or sudden onset), hastening factors etc.

2- **Characteristics and Modalities—** character location, sensation, radiation, severity, timing, modality i.e. aggravating or relieving factors, associated or concomitant symptoms etc.

3- **Course since onset—** incidence, progression, effects of therapy etc.

What makes us sick is the affection of the vital force. Due to weakening or derangement of vital force, it becomes disharmonious. This process results in change in our feelings. Thus, mind is first affected. Will, affection, intellect and the memory, all are affected, leading to a particular group of symptoms. We start feeling various mental symptoms as well as physical symptoms. At primary stage, all are functional. The sensations of sickness may be too violent and tormenting. Afterwards physique also starts suffering. This leads to appearance of various signs, the visible or observable changes.

These deviations from the normal state of health can be noticed by a keen observer.

Ways to Examine a Patient

1- **Inspection—** examination by looking closely into the matter of illness, its manifestations and course of sickness.

2- **Palpation—** examination by touch.

3- **Percussion—** examination by striking of a solid instrument against body parts.

4- **Auscultation—** examination by listening the sounds by the affected organs of the patient.

When the sickness advances, temporary or permanent changes start to occur in physique. These changes can be observed by one or more methods as described above. To confirm and recognize the result of derangement of vital force, laboratory, radiological or surgical tests etc. may be performed. These tests may assist in diagnosis of the disease and to ascertain the prognosis.

Hahnemann says-

"If the physician clearly perceives what is to be cured in diseases, that is to say, in every individual case of disease (knowledge of disease, indication), if he clearly perceives what is curative in medicines, that is to say, in each individual medicine (knowledge of medicinal powers), and if he knows how to adapt, according to clearly defined principles, what is curative in medicines to what he has discovered to be undoubtedly morbid in the patient, so that the recovery must ensue - to adapt it, as well in respect to the suitability of the medicine most appropriate according to its mode of action to the case before him (choice of the remedy, the medicine indicated), as also in respect to the exact mode of preparation and quantity of it required (proper dose), and the proper period for repeating the dose:- if, finally, he knows the obstacles to recovery in each case and is aware how to remove them, so that the restoration may be permanent : then he understands how to treat judiciously and rationally, and he is a true practitioner of the healing art.

He is likewise a preserver of health if he knows the things that derange health and cause disease, and how to remove them from persons in health". (Organon, Aphorism no. 3)

Thus, this can be understood very well that the deviation of vital force or that of health from the norm results in sickness.

1- This deviation from the norm may be like a pendulum or sometimes one-sided only. (The disease affecting only a single part of the person is known as one-sided disease.)

2- This deviation from the norm may be of various degrees. It may be reversible or irreversible. The reversible displacement may either be easily recoverable or difficult according to the strength of negative force of the disease power, or morbid agent or morbific process applying on the vital economy.

The individuals having strong vitality are easier to recover from illness than those are with weaker vitality. No two persons are alike. Every person has its own identity or individuality. To learn this fact, we should understand theory of Individualization.

Individualization

The general characteristics of every individual cannot be exactly similar. The two may differ in several ways, viz. difference of mental and physical makeup, difference of their cardinal features of living being or their reactions to the environment. One may be morbidly irritable or other rarely irritable or another may be too mild even towards very agitating conditions. A person may be fat and flabby while another lean and thin. One may be too insensible or indifferent to very intense pains and may even sacrifice his limb or body part to please his God or Goddess while another one may faint seeing the syringe in the hands of a doctor!

No two persons are alike. This makes theory of individualization, which plays not only a prominent but sole part in art of healing through Homoeopathy. The individuality of a person is the characteristic feature or group of characteristic features, making him identifiable from all other persons.

"Sufferings are not always felt alike by all men, everyone suffers according to his own peculiar nature. Illness appears sometimes in acute form; at other times they take on a chronic course according to the duration and violence of the existing causes….

The diversity of chronic diseases is sufficiently evident from the external symptoms. The disease is reflected in the totality of the symptoms. These phenomena of the diseases (the symptoms) are perceptible to the patient himself through his senses and by sensations of the changes in the bodily and mental state (subjective symptoms). They are also to be observed by those who surround him and by the physicians, partly obvious and partly to the determined by investigations (objective symptoms)". (Dr. Richard Haehl, M.D. in 'Samuel Hahnemann, His Life and Work' 1992)

Now, this becomes the first duty of the healing artist to identify the individual and his characteristics and thence the degree of curability of a disease in the affected individual.

Susceptibility

This degree of curability will depend upon Diagnosis, Prognosis, and Susceptibility of the Individual towards disease and the medicine.

Susceptibility is the general quality or capability of the living organism of receiving impressions; the power to react to stimuli. It is one of the fundamental characteristics of the life. All the functions occurring in our body viz. Digestion,

assimilation, nutrition, repair, secretions, metabolism, catabolism as well as all disease processes arising from infection with microsms or infestation with parasites and the destructive action of poisons as well as curative action of medicines depend upon this susceptibility or the power of organism to react to specific stimuli.

Susceptibility is directly proportional to the chances of getting sick as well as to be affected by the medicines, hence affecting prognosis or curability of a case.

Diagnosis

After a keen study assisted with clinical, social and laboratory findings, the knowledge about the individual, cause and type of affection, disease and the prognosis can be ascertained and this conclusion is known as diagnosis.

Prognosis

The prognosis is prediction about the duration and ends of disease, and the estimation of the chances for recovery. To treat a sick person properly, one must know the prognosis and what is curable in disease in that particular individual at that very time. Depending on prognoses, the diseases may be of various natures and henceforth the plan of treatment may be programmed. Viz.—

1- **Cure—** the course of treatment to restore health i.e. restoration of health from the state of illness with the aid of measures inducing and supporting the act of restoration to health.
2- **Relief—** the alleviation or removal of a distressing symptom.
3- **Palliation—** is to ease or reduce the effect or intensity, especially of a disease; to allay temporarily, as pain, but without curing.
4- **Suppression—** is the repression of the external manifestation of a morbid condition.

Types of disease conditions

The diseases affecting only a single part of the person are known as one-sided diseases.

There may be some conditions while the same person may be affected by more than one disease at a time.

It is frequently seen that a person suffering from a stronger disease is scarcely affected by minor ones.

A. In case of two dissimilar diseases, if-
   1. The pre-existing disease is equal or stronger than the approaching disease, the former will repel the latter and it will not affect at all.
      Viz. “Those suffering from pulmonary consumption are not liable to be attacked by epidemic fevers of a not very violent character, according to Von Hildebrand.” (Organon, 6th edition)
   2. The pre-existing disease is weaker than the new one, the latter will suppress/suspends the former and once the stronger one has completed its course, the original disease will reappear. Viz. if mania occurs in a consumptive patient, the former removes the phthisis with all its symptoms but if that go off, the phthisis returns immediately and proves fatal.

3. The newer disease may combine with original disease and may behave like a newer disease.
   Viz. Psoriasis and veruccosis often combine with each other and appear like a new disease.
4. The two dissimilar diseases after running a considerably long time simultaneously, in the same individual, may run parallel to each other occupying the parts or organs most suitable or adaptable to them.
   Viz. Psoriasis and rheumatism often make the diagnosis of psoriatic arthritis.

B. In case of two similar diseases, if-
   1- The former one is equal or stronger; the newer one will not attack at all.
      Viz. A person suffering from small pox is not attacked by measles.
   2- The former one is weaker than the newer one; the latter will cure the former.
      Viz. Measles often cures cutaneous eruptions if attacking a person suffering with dermatitis.

   This last point is the nature's universal law of cure.

Law of Cure

"A weaker dynamic affection is permanently extinguished in the living organism by a stronger one, if the latter (whilst differing in kind) is very similar to the former in its manifestations." (Organon of Medicine, Aphorism no. 26)

This is the ultimate, eternal and immutable law of cure.

Based on all these facts, Dr. Hahnemann thought to discover some device to apply this law to treat the diseases. He used to administer drug substances orally to the healthy human beings and studied their effects. This process is known as 'Drug Proving'.

Drug Proving

When a drug substance is given to a healthy human being, it develops some signs and symptoms peculiar to its effects. The person on whom the proving being carried out is called subject. It is of two types:

1- **Blind Proving -** When the subject does not know about the drug taking for proving, the condition is known as Blind Proving.
2- **Double blind proving -** When the prover and subject both are unknown about the drug to be proven, it is known as Double blind proving.

Proving is carried on both the sexes and different age groups. The effect of the drug on subjects are noted down and collected in book form. This collection of the signs and symptoms in systematized form is known as 'Materia Medica'.

The collected record about each medicine is known as drug picture. When the signs and symptoms of the diseased individual are matched with a drug picture of this Materia Medica, that particular medicine becomes the remedy to that particular individual and cure him as per Homoeopathic principle.

Since, the number of drug pictures increased beyond the limit of memory of a person, the thesaurus of Materia Medica i.e. medicine after the signs and

symptoms, which are now called rubrics was prepared. This device is called Repertory and the process of preparing drug picture similimum to the sick individual is known as Repertorization.

Forces affecting State of Health

Now, we may just think over the above facts and concludes that there is some force, rendering chemical and physical constituents to remain united in certain order and style to work in co-ordination and harmony to perform the vital or lively activities.

There is always a fixed type of configuration of all the chemical and physical constituents peculiar to particular individual creature; and this kind of force (Vital Force) is interlocked as an most essential element because only this force is capable and therefore responsible to keep this characteristic configuration fixed and stable, thus maintaining all the fundamental and salient features of the formed creature.

Since the very unit stage of life i.e. haploid units of genesis viz. Ovum and sperm or other units, this vital force is inseparable ingredient because it is essential to keep them persisting. After fertilization, the mitotic divisions get start to develop a particular organism. This life force continuously acts to function, configure and stabilize according to life principles and thus getting solely integrated within organism.

Now this can be well understood that the slightest derangement of vital force will affect the whole system and develop certain signs and symptoms which can be clearly distinguished from the normal state of health of that particular one. This force is dynamic and hence must be affected by some another kind of force.

Types of Forces

There may be three states of life. First, the normal state of health the norm, second, the negative pole the direction of deterioration or disease condition and third, the direction of extra energy state or supreme health or exhilaration, the positive pole. Both the extremes are right away from the norm i.e. health state and therefore the disease state.

There may be three kinds of forces.

1- The Vital force, that keeps us animating (Neutral Energy) and always tries to remain in neutral state of balance or health.
2- Morbid or disease force, that tries to get us sick (Negative Energy) by injuring the norm and to disbalance the vital force towards the negative pole causing illness.
3- Curative force, that tries to correct derangement of vital force and to combat morbid force (Positive Energy) by pushing / pulling the vital force towards the positive pole, i.e. towards the state of balance or health.

The signs and symptoms are identical in either condition whether the derangement is away from the norm (center) towards negative or positive side.

The negative or morbid force may affect the health in several ways. It may either simply alter the normally running bodily and mental functions or lead to extra growths or degeneration leading to ulceration and deterioration of the body parts or sometimes complex of any two or all of these processes.

These diseased states are not reached spontaneously. There is always some factor or morbific noxious agent, which is responsible for the same. This agent is known as 'Miasm'.

According to the nature of the disease process viz. simple indisposition or alterations in normal functions, extra growths or destruction of the parts, etc. five groups of sickness are made-

1- **Psora-** this is the basic group of affections, including indisposition or only functional deviations of the normal health state in mental and physical planes. Viz. Itch, mania, alopecia (Hair falling) etc.
2- **Sycosis-** this is the second miasm that includes all the diseases having extra or over growths. Viz. Warts, tumors, arthritis OA etc.
3- **Syphilis-** this miasm includes all the degenerative conditions, viz. ulcers, gangrene, osteoporosis, atrophy etc.
4- **Pseudopsora-** this is the combination of Psora and syphilis and is also known as tubercular miasm. Viz. epistaxis, diabetes, leprosy, tuberculosis, piles etc.
5- **Cancerous miasm-** when all the three miasms are combined, this miasm is developed. Viz. all the malignancies.

Mode of action of Homoeopathic Medicines

When a medicinal substance is applied into a sick person according to homoeopathic principles, it applies similimum but stronger positive force on the vital force deranged due to negative or disease force. This phenomenon sometimes enforces it to shift towards positive pole, in the opposite side of its affection, causing a little bit exaggeration of the sufferings, which soon returns to the normal, neutral state of health. This is the process of cure.

This exaggeration is not always seen. It is often observed in some chronic diseases.

Now a question arises what is the inherent power of the Homoeopathic medicines, and how does it stored in tiny globules or tablets or drops of distilled water or rectified spirit, and how does it acts on tongue in such a minute quantity?

Homoeopathic medicines act on basis of principles of atomic physics. The substances used as medicine (viz. Milk sugar, distilled water, rectified spirit etc.) are called 'vehicles'.

These all the vehicles have OH— (Hydroxyl ions). The free electron of hydroxyl ion has particular amount of static energy, peculiar to it. The amount of energy controls the revolving motion of the electron around the nucleus of an atom and in an ion, in a certain class, known as energy level. The higher the energy retained by this free electron, the higher will be the energy level of this electron. This free electron is also known as valant electron. The number of electrons in outermost class of an atom or ion is known as valancy of that atom or ion. This electron is free for physio-chemical reactions and can bind up other atoms or ions to form larger elements. This outer most free or valant electron has capacity to store more and more energy and remains revolving around the central unit or nucleus.

The amount as well as characteristics of the energy being stored can be controlled by some methods so that the store of the desired energy can be used

at times. Homoeopathy uses these methods to store the particular amount and peculiar type of the energy in this free electron of OH— ion.

When the selected medicine is put on the tongue, the energy stored in the OH— ions of the medicine is released to the nerve endings of the tongue surface and the nervous system of the body starts functioning according to the characteristics of the medicine applied.

Preparation of Homoeopathic Medicines

The process to store the desired amount and type of energy into the vehicles is called 'Potentization' or 'Dynamization'.

This process is different for the soluble and insoluble substances to be used as medicine, termed as Succusion and Trituration respectively.

Succusion- The method applied to make medicine from substances soluble in water or alcohol is termed as succussion. In this process, the crude medicinal substance is dissolved in a medically inert solvent, called vehicle, viz. purified water or rectified. This saturated solution is called 'Mother Tincture'.
One part of this mother tincture is diluted with vehicle according to the scale used. Now ten strong downward strokes are given to the container for decimal scale and hundred strokes for centesimal scale.
Here some conditions are essential. Each stroke must end in a jerk and next stroke is given after the bubbling of the fluid has been stopped in the container. All the strokes must be equal in power.
Trituration- The method applied to make medicine from substances insoluble in water or alcohol is termed as Trituration.
In this process, one part of the crude drug substance is mixed with nine parts of sugar of milk powder and grinded in uniform direction to form '1x' potency. In the same way, 2x, 3x etc. potencies are prepared.
The same process is adopted to form centesimal potencies, but the ratio of crude drug substance to the vehicle becomes 1:99.
This process of Dynamization arouses the inherent and latent powers of crude and inert drug.

Scales to prepare Homoeopathic Medicines

There are three main scales to prepare medicine potencies.

1- **Decimal Scale—** in this scale, one part of the medicinal substance is mixed with nine parts of the vehicle (solvent). The prepared potency of the medicine is called '1x'. To prepare 2x potency, 1 part of the '1x' potency is mixed with nine parts of the vehicle and ten down ward the ready potency is called '2x'. In the same way, further potencies viz. 3x, 4x etc. are prepared.

2- **Centesimal Scale—** in this scale, one part of the medicinal substance is mixed with ninety-nine parts of the vehicle. The prepared potency of the medicine is called '1c' or '1'. To prepare '2c' potency, 1 part of the '1c' potency is mixed with ninety-nine parts of the vehicle and the ready potency is called '2c'. In the same way, further potencies viz. 3c, 4c etc. are prepared.

3- **Fifty Millesimal Scale—** in this scale, one part of the medicinal substance is mixed with fifty thousand parts of the vehicle. The prepared potency of the medicine is called '0/1'. To prepare 0/2

potency, one part of the 0/1 potency is mixed with fifty thousand parts of the vehicle and the ready potency is called '0/2'.

In the same way, further potencies viz. 0/3, 0/4 etc. are prepared.

Application of Homoeopathic Medicine in Liver Cancer

From above discussion, it is clear that mode of Homoeopathy is quite different from all other systems of medicine. Through very keen observations and inquiries, the most similar i.e. similimum Homoeopathic remedy is administered to the patient. It more or less always does, as we want i.e. improve the patient in general and often cures.

There is no consensus regarding the optimal treatment of patients with liver tumors. This contributes to the pessimistic attitude that many have regarding the treatment of liver cancer. Aggressive treatment strategies can cure or significantly prolong the life of many patients with liver cancer.

There are some wonderful drugs for liver cancer as I have frequently verified in daily practice-

1- Cholesterinum (ALLEN)- Description: - Ameke claimed to have derived great advantage from its use in cases diagnosed as cancer of the liver, or in such obstinate engorgements that malignancy was suspected. Burnett claims to have twice cured cancer of the liver with it, and "in hepatic engorgements that by reason of their intractable and slow yielding to well-selected remedies make one think interrogationally of cancer." In such conditions, where the diagnosis is in doubt, especially if the patient has been subjected to repeated attacks of biliary colic, Cholesterinum, he claims, is very satisfactory and at times its action even striking for cancer of the liver.

Cholesterinum (BOERICKE)- Obstinate hepatic engorgements. Ameke, who did much to introduce the proximate principles of the tissues as remedies, anticipating the practice now so much in vogue in the old school, recommended Cholesterine as a remedy in cancer of the liver.

Cholesterinum (CLARKE)– Characteristics: - Burnett has recently adduced conclusive evidence in support of the correctness of this assertion; and I have myself cured, mainly with this, a case described to me (I did not see the patient, a man over 50) as in the last stage of liver disease.

He had been given up by his medical attendant, who ordered him to make his will without delay.

Burnett uses the 3x or the 3 trit. and substantial doses.

He commends it in "obstinate hepatic engorgements, which by reason of their obstinacy make one think interrogatively of cancer," also in "cases in which there appears to be a semi-malignant affection, involving the left lobe of the liver and what lies between it and the pylorus and the pancreas."

In such cases Burnett gives alternately Cholest. 3x and Iodoform 3x.

Like many other "yellow" medicines, it has a marked action on the liver, causing jaundice and liver enlargement.

Cases of cancer of the liver have been reported cured by it.

Fulness, goneness, and constipation are the leading indications.

Mohr (H. R., xiii. 210) gave Nit. ac. 3x to a man who suffered from cancer of the liver with bloody diarrhoea, followed by constipation; violent pains in stomach and liver; unable to sleep; or unable to take any food without much pain, mostly vomiting. "Burning in liver region" has led to the cure of abscess and even cancer of that organ.

2- Theridion curassavicum (CLARKE)- Characteristics - The symptoms are < by touch; pressure; on ship-board; riding in carriage; closing eyes; jar; least noise.
Lying = pain deep in brain; >> flickering before eyes. < Stooping; rising; motion; exertion, going up or down stairs; walking.

Left : slight heaviness in half of forehead; half of forehead feels higher than right; pain in temple; pain in eye; cancer on side of nose; pain in half of tongue; hard lumps in hypochondrium; pain radiates to shoulder; pain in epigastrium; lobe of liver attached to tumors; fossa supraclavicularis, indurated lymphatic glands; crack in angle of mouth; tumor in breast; dull, heavy pain in scapula; pain in shoulders; tingling in fingers while writing; pimples side of nose.

Continuous vomiting and straining to vomit.

3- Kreosotum (HERING)- Hiccough, Belching, Nausea and Vomiting- Sympathetic vomiting, as of phthisis, of cancer of liver or uterus, of pregnancy, and of chronic kidney disease.

Hepatic region painful to touch. Severe burning pain in cancer of liver (relieved).

Burning: in occiput; in cancer of liver; in abdomen and rectum; in palms and soles; in hypogastrium and uterus; leucorrhoea; in carbuncle on side of chest; in abscess on back of neck; in anthrax between shoulder blades; all over body, irritable spine; of skin.

The application of Homoeopathy in various forms of cancer depends upon signs and symptoms of the patient. It will absolutely depend on complications caused by cancer in different ways, which will manifest themselves in the form of requisite disease picture.

Oncologic Emergencies

Four primary etiologies underlie most emergencies that occur in the field of oncology. Each of the causes may result in an additional emergency, i.e., pain, which is best reviewed independently. This article is organized according to the underlying pathophysiology of the oncologic emergency as follows:

1. Metabolic emergencies
2. Hematologic emergencies
3. Infectious and inflammatory emergencies
4. Mechanical emergencies

1- METABOLIC EMERGENCIES

Multiple metabolic and endocrinologic problems can potentially occur in patients with cancer. Tumor lysis syndrome (TLS) is the most common of the problems found in the pediatric population, and it frequently requires emergent therapy despite substantive prophylactic treatment. Hypercalcemia, hyponatremia, hypoglycemia, adrenal failure, and lactic acidosis occur less commonly.

Tumor lysis syndrome-

TLS is defined as a metabolic triad of hyperuricemia, hyperkalemia, and hyperphosphatemia. Renal failure and symptomatic hypocalcemia are associated secondary complications. The primary triad results from rapid release of intracellular contents into the bloodstream and is most likely to occur in the setting of large tumor burden, rapid cell turnover, and rapid tumor response to therapy. These conditions frequently are present in the context of acute lymphoid leukemia (ALL), acute myeloid leukemia (AML), and high-grade lymphoma (e.g., Burkitt lymphoma) and following initial chemotherapy treatment for some large solid tumors.

a. **Hyperuricemia-** Uric acid is derived from the breakdown of nucleic acid and results from catabolism of hypoxanthine and xanthine by the enzyme xanthine oxidase. Potassium and phosphate are present naturally in the cytoplasm of tumor cells at concentrations significantly higher than in the extracellular space. Hyperuricemia, hyperkalemia, and hyperphosphatemia result from the release of these intracellular substances from the tumor cell. Also released, but not considered part of the TLS triad, is lactate dehydrogenase (LDH). Secondary hypocalcemia results from compensatory down-regulation of calcium in the context of hyperphosphatemia.
b. **Hypercalcemia-** Abnormalities in calcium levels may be sufficiently severe to constitute a metabolic emergency. Hypercalcemia is encountered more frequently than hypocalcemia.

Clinical manifestations of hypercalcemia

I- **Neuropsychological signs-** includes confusion, psychosis, seizure, obtundation, stupor, and coma.
II- **Neuromuscular signs-** includes fatigue, lethargy, muscle weakness, hypotonia, and hyporeflexia.
III- **Gastrointestinal tract signs-** includes anorexia, nausea, vomiting, constipation, obstipation, and ileus.

IV- **Cardiac signs-** includes prolonged PR interval, shortened QT interval, wide T wave, bradycardia, and atrial or ventricular arrhythmia.

V- **Renal signs-** includes polyuria.

Pediatric patients with hypercalcemia also may present with bone pain. Bone pain may result from significant bone marrow infiltration by disease, pathologic fracture of severely demineralized bone, or direct osteolysis of bone caused by metastatic disease.

Pathophysiology of hypercalcemia

The principal pathophysiology underlying malignant hypercalcemia is excessive osteoclast-mediated bone resorption resulting from direct dysregulation of normal calcium homeostasis. Normal bone resorption is stimulated by parathyroid hormone (PTH), prostaglandin E2, osteoclast-activating factor, other polypeptide growth factors, and osteoclasts derived from mononuclear phagocytes.

Although blast cells from patients with ALL and AML have been shown to produce PTH in vitro, in vivo neoplasms are associated more commonly with elevation of a similar compound, parathyroid hormone-related polypeptide (PTHrP). PTHrP binds the PTH receptor, but it is immunologically distinct from PTH. Hibi and coworkers reported hypercalcemia and elevated PTHrP levels in vivo in 4 of 83 (4.8%) pediatric patients with early pre–B-cell ALL.

Hypercalcemia also has occurred in the context of elevated prostaglandin E2 levels in infants with mesoblastic nephroma or malignant rhabdoid tumor of the kidney.

Although an increased level of osteoclast-activating factor frequently is associated with the hypercalcemia of multiple myeloma, it has not been associated with pediatric malignancy. Multiple other cytokines are involved in bone resorption and may be related to malignancy-induced hypercalcemia. Transforming growth factor b is released as a result of osteoclast activity and increases PTHrP production by tumor cells. Tumor necrosis factor and interleukin 6 (IL-6) levels often are elevated in the context of malignancy and have been shown to increase osteoclast production and differentiation.

c. **Hyponatremia-** Severe hyponatremia, which is defined as a serum sodium level of less than 125 mEq/L, is a known complication for pediatric patients with malignancy and can result from systemic illness, syndrome of inappropriate secretion of antidiuretic hormone (SIADH), or iatrogenic factors acting individually or collectively. Symptoms primarily are neurologic, but no significant symptoms of early mild hyponatremia exist. Anorexia, nausea, and malaise are the first overt findings, which then progress to headache, confusion, lethargy, seizure, coma, and death. Although a gradual change in serum sodium concentration may be tolerated by the central nervous system (CNS), rapid changes of 1-2 mEq/L/h lead to cerebral edema and neurologic dysfunction. Severe life-threatening symptoms are seen almost uniformly at a serum sodium concentration of less than 105 mEq/L, but these symptoms also may be seen if the level falls to 120 mEq/L within 24 hours.

Pathophysiology of hyponatremia

Hyponatremia most often results from water retention combined with administration of normal or excessive amounts of fluid. Water retention is a consequence of antidiuretic hormone (ADH) release induced by decreased effective circulating intravascular volume.

Hyponatremia can occur both in edematous states and in true volume depletion. Hyponatremia associated with edematous states is more common in patients with cancer and may result from liver disease, veno-occlusive disease, infection, drug toxicity, or multiple other etiologies. Hyponatremia associated with true volume depletion is less common and typically is consequent to identifiable fluid losses, such as severe diarrhea, bleeding, and drainage of effusions or ascites. In either situation, hyponatremia results from disproportionate accumulation of water from administered hypotonic fluids. Abnormal release of ADH also may result in hyponatremia, as in SIADH.

Hyponatremia is secondary both to dilution of sodium from retention of free water and to progressive increase in urinary loss of sodium.

Hyponatremia also is a frequent iatrogenic result or consequence of underlying systemic illness. Overhydration with hypotonic solutions frequently results in mild or moderate hyponatremia. Failure to administer stress-dose levels of glucocorticoids to patients who are adrenally suppressed also results in hyponatremia. Alternatively, patients with suprasellar tumors or Langerhans cell histiocytosis may self-hydrate with hypotonic fluids in the setting of diabetes insipidus and cause hyponatremia.

d- **Other metabolic emergencies**

Metabolic emergencies such as hypoglycemia, adrenal failure, and lactic acidosis are significantly less common in the pediatric population than in the adult population.

I- **Hypoglycemia-** often is defined as a serum glucose level of less than 40 mg/dL; however, initial symptoms may occur at higher levels, particularly if the blood glucose level is decreased rapidly. Symptoms often are worse in the early morning and may include weakness, dizziness, diaphoresis, and nausea. Symptoms may progress to diffuse neurologic deficits, seizure, coma, and death. Hypoglycemia most commonly results from insulin-producing islet cell tumors that occur alone or as part of multiple endocrine neoplasia syndromes. Symptomatic hypoglycemia also may result from tumor production of compounds with low molecular weight with nonsuppressible insulinlike activity. Although excessive glucose use by large tumors is a possible cause of hypoglycemia, few data support this as an etiology in pediatric patients with malignancies.

II- **Adrenal insufficiency** in pediatric patients with cancer is rare and usually is secondary to adrenal suppression resulting from extended use of glucocorticoids at supraphysiologic doses combined with abrupt termination of therapy. Symptoms of adrenal insufficiency are exaggerated in the setting of physiologic stress and can

manifest as mild acidosis, hyponatremia, and hypokalemia. Severe circulatory collapse and shock are uncommon.

III- **Lactic acidosis** in pediatric patients with malignancy is rare and most frequently is associated with hypoperfusion and tissue hypoxia, as seen in patients with sepsis, low cardiac output, or extreme anemia. Lactic acidosis resulting from rapidly progressive hematologic malignancy or extensive liver involvement is documented best in adult patients with cancer.

2- HEMATOLOGIC EMERGENCIES

Hematologic abnormalities that require emergent treatment result from abnormal hematopoiesis or coagulopathy. With respect to hematopoiesis, underproduction of specific cell lines is more common than overproduction. Underproduction is consequent to disease infiltration of the bone marrow, syndromes of bone marrow failure, or treatment-related myelotoxicity. Underproduction results in anemia, thrombocytopenia, neutropenia, or a combination of the three. Overproduction of hematopoietic tissue primarily is observed in the form of leukocytosis associated with acute leukemia. Coagulopathy manifests as hemorrhage, thrombosis, or both. Coagulopathy is a primary consequence of disease, results from a primary toxicity due to treatment, or is secondary to other known complications.

Depression of bone marrow activity- results in anemia, thrombocytopenia, and neutropenia. These signs are best treated with supportive care, regardless of etiology. Supportive care often includes transfusion of individual blood components, which requires the following considerations in the context of the immunosuppressed patient with cancer: All blood, platelets, and granulocytes administered to immunosuppressed patients must be irradiated to prevent the lethal complication of graft versus host disease.

Anemia- usually, anemia in pediatric patients who are not critically ill is well tolerated and does not require transfusion unless the hematocrit level is less than 20-25%, with no evidence of recovery, or if transfusion is necessary for symptomatic improvement. Transfusion of packed red blood cells (PRBCs) also may be necessary to maintain optimal intravascular volume in a patient who is critically ill or who has acute hemorrhage. The use of recombinant erythropoietin is limited by the weeks of therapy necessary to increase hemoglobin (Hb) levels significantly. Once developed, severe anemia usually requires transfusion.

a- **Common Transfusion Reactions-** Fever 0.1-5 in 100 Commonly results from recipient antibodies to WBCs or platelets present in transfused blood products and subsequent release of pyrogens (interleukin 1, IL-6, tumor necrosis factor). Rarely, fever is secondary to bacterial contamination of transfused blood products or is an initial symptom of an acute hemolytic reaction.

b- **Thrombocytopenia-** in pediatric patients with cancer results from underproduction of platelets or from excessive consumption of platelets.

c- **Neutropenia-** is the most common toxic result of myelosuppressive chemotherapy, but it also may result from either failure or suppression of the bone marrow. Absolute neutrophil counts lower than 500/mL are associated with increased risk of infection. Neutropenia extending beyond 2 weeks is associated with increased risk of systemic fungal infection.

d- **Hyperleukocytosis-** is the most common hematologic overproduction syndrome necessitating emergent treatment of pediatric patients with cancer. Hyperleukocytosis is defined as a peripheral leukocyte count greater than 100,000/mm3. Hyperleukocytosis is a poor prognostic indicator in the setting of either ALL or ANLL because it is associated with metabolic and hemorrhagic complications. Respiratory complications are a more prominent feature of elevated leukocyte counts in patients with ANLL. When present, clinical manifestations of hyperleukocytosis result from anaerobic metabolism and proliferation of blast cells within the microvasculature. Physical findings result from the increased viscosity associated with blast cell aggregates and thrombi in combination with damage to vessels and secondary hemorrhage. Resultant clinical findings primarily include respiratory and neurologic signs. Respiratory signs include dyspnea and hypoxia. Neurologic signs include focal deficit, ataxia, agitation, confusion, delirium, and stupor. Other signs include plethora, cyanosis, papilledema, and retinal artery or retinal vein distension.

e- **Coagulopathy-** Pediatric patients with cancer are subject to have significant abnormalities in procoagulation, inhibitors of coagulation, and fibrinolysis. The abnormalities result in hypocoagulable and hypercoagulable conditions that manifest as hemorrhage or thrombosis. Hemorrhage and thrombosis are significant problems in the setting of hyperleukocytosis. Bleeding predominates in this setting secondary to the relative excess of fibrinolytic proteases, compared to prothrombotic thromboplastic materials, released from blast cells. Hemorrhage also may result from consumption of coagulation factors in the setting of chronic activation of the procoagulation cascade, or it may result from underproduction of necessary coagulation factors in the setting of severe systemic illness and relative hepatic insufficiency.

f- **Disseminated intravascular coagulation (DIC)**- is characterized by excessive activation of blood coagulation with consumption of clotting factors. DIC causes hemorrhage, microangiopathic hemolytic anemia, and thrombosis of varying degrees. DIC may contribute to hemorrhagic and thrombotic events. In children with cancer, DIC is associated most commonly with ANLL induction chemotherapy in which thromboplastic materials are released from leukemic blast cells. DIC also occurs in patients with sepsis or, less frequently, widely disseminated solid tumors.

g- **Thrombosis-** is a less common oncologic emergency in children than in adults. Clinical presentation of thrombosis of the sagittal sinus varies and ranges from asymptomatic to life threatening.

3- INFECTIOUS AND INFLAMMATORY EMERGENCIES

Children with cancer are at increased risk for acute life-threatening infection and acute inflammatory processes as a direct result of the underlying disease, treatment, or both. Infectious emergencies include infections resulting from bacteria, parasites, mycoplasmata, viruses, and fungi. Pneumonitis, pancreatitis, hemorrhagic cystitis, enterocolitis, and tissue necrosis from extravasation of chemotherapeutic agents are representative of the severe inflammatory states that may occur. Patients with both infectious and inflammatory conditions may require emergent treatment, and the conditions are considered independently.

a- **Infectious emergencies-** Immunosuppression is the primary underlying factor that predisposes patients with cancer to infectious complications. Patients are variably subject to quantitative and qualitative decreases in granulocyte function (neutropenia), B-cell function (hypogammaglobulinemia), T-cell function, splenic function, and normal immunologic and integument barriers. In addition, alteration of typical body flora can result in overgrowth of pathogenic organisms. Individually and in combination, these factors increase the risk of serious systemic infection by bacterial, viral, fungal, and other opportunistic organisms. Patients are primarily susceptible to systemic dissemination of endogenous bacteria and fungi that colonize the skin and gastrointestinal tract, reactivation of endogenous viruses (e.g., herpes simplex virus), or reactivation of latent cysts (e.g., Pneumocystis carinii). Secondarily, patients are at increased risk of systemic infection from aerosolized viruses, Legionella species, and fungal spores. Relative risk for infection with a particular agent is influenced by the degree of compromise in specific arms of the immune system.

   I. **Bacterial infections-** Bacterial pathogens may induce focal or systemic infections, and the incidence of bacterial infections increases as the absolute neutrophil count (ANC) decreases from 1000/mm3 to 500/mm3 to 100/mm3. The most common etiologic agents are bacteria that colonize the skin and gastrointestinal tract of the host. Neutropenia is the primary risk factor for bacterial infections, and fever is the most common presenting symptom.

   II. **Fungal infections**-Fungi are categorized broadly by morphology as either yeasts or filamentous molds. Candidal organisms are the most common invasive fungal pathogens in pediatric patients with cancer and account for approximately 65% of documented fungal infections. Although Candida albicans is the most common pathogen historically, infection with other species is increasing and accounts for approximately 50% of candidal fungemias. The most common organisms are Candida tropicalis (23%), Candida glabrata (8%), Candida parapsilosis (6%), and Candida krausei (4%). Molds account for approximately 35% of all invasive fungal infections, 65% of which are caused by Aspergillus species. Fusarium species, members of the Mucorales order, and other molds also infect severely immunocompromised hosts. Unlike yeast and bacterial pathogens, molds are not part of the typical body flora and usually are not acquired via person-to-person contact. Therefore, exposure to spores remains a significant risk factor for patients. Aspergillus species and other molds principally cause pneumonia, sinusitis, and cerebral abscess formation.

b- **Inflammatory emergencies-** Pneumonitis, pancreatitis, hemorrhagic cystitis, and extravasation of vesicant chemotherapy products are significant noninfectious inflammatory conditions that require emergent treatment in pediatric patients with malignancy.

   I. Transfusion-related acute lung injury (TRALI)- is characterized by noncardiogenic pulmonary edema variably associated with respiratory distress and hypoxia following transfusion of a blood product. TRALI results from granulocyte-agglutinating anti-HLA antibody-induced pulmonary leukoagglutination. TRALI typically occurs within 6 hours of transfusion.

II. **Pancreatitis-** Pancreatitis is a complication of immunosuppressive therapy, and approximately 18% of all pediatric cases occur in the context of antineoplastic therapy.

III. **Hemorrhagic cystitis-** is hematuria that results from an inflammation of the bladder. The condition is defined as painful urination with leukocytes and erythrocytes or clots in the urine. Cyclophosphamide and ifosfamide are the most common chemotherapeutic agents causing hemorrhagic cystitis via an acrolein dye byproduct of metabolism. The byproduct is a chemical irritant of the bladder mucosa and renal collecting system. Clinical symptoms may occur hours, days, weeks, or years after chemotherapy administration, and once established, recurrent bleeding is a common complication. Cystitis progresses from mucosal edema and ulceration to late fibrosis, reflux, and hydronephrosis. Prior or concurrent pelvic irradiation is a risk factor for the development of hemorrhagic cystitis, and a significant positive association is found between hemorrhagic cystitis and infection by both adenovirus (primarily type 11) and the BK virus.

IV. **Extravasation-** of chemotherapy products is reported to occur in 0.1-6.5% of chemotherapy infusions and may cause severe, irreversible, local injury. Chemotherapeutic agents may be classified as irritant, vesicant, or nonvesicant based on the local toxicity to subcutaneous tissues

4- MECHANICAL EMERGENCIES

Mechanical emergencies in pediatric patients with malignancy refer to acute events that result from direct compression, obstruction, or displacement of vital tissues by a neoplastic process. These emergencies are conveniently classified according to the affected organ system. Neurologic, respiratory, cardiovascular, gastrointestinal tract, and urologic mechanical emergencies require immediate medical attention.

a- **Neurologic emergencies-** The principal neurologic mechanical emergencies requiring acute medical treatment manifest as spinal cord compression, increased intracranial pressure (ICP) in association with cerebral herniation, and status epilepticus.

b- **Spinal cord compression-** refers to impingement of the spinal cord or cauda equina, which may occur via an intramedullary mass from a primary CNS tumor or compression of the thecal sac from a tumor in the epidural space. The latter occurs most commonly by direct extension of metastases in the vertebral bone, but it also may result from tumor growth through intervertebral foramina. Pain is the first symptom of spinal cord compression and may occur hours or months prior to neurologic dysfunction. Pain associated with epidural spinal cord compression is exacerbated when the patient is recumbent and improves with the patient in the upright position. The pattern of pain is opposite that experienced with a herniated disc or degenerative spinal disease. Radicular pain is a less common but excellent localizing symptom. Weakness usually occurs after the onset of pain, and sensory complaints follow shortly thereafter.

c- **Cerebral herniation-** may result from a mass expanding within the cranial vault or from an obstruction of cerebrospinal fluid circulation. Either process may result from tumor mass, hemorrhage, thrombosis, abscess, or infarction. Classic clinical findings suggestive of impending herniation

include impaired consciousness, abnormal extraocular movements, pupil size abnormality, nausea, emesis, and stiff neck. Papilledema is a more common finding if the presentation is subacute. Cushing reflex of hypertension and bradycardia are late signs of increased ICP.

d- **Status epilepticus-** is defined as prolonged or recurrent seizure activity lasting over 30 minutes in which the patient never regains consciousness. Seizure may result from mechanical or metabolic perturbation of the CNS consequent to a tumor or tumor therapy.

e- **Respiratory emergencies-** Airway obstruction is the primary mechanical emergency of the respiratory system in pediatric patients with malignancy. Obstruction can occur at the level of the larynx, trachea, or bronchi. Airway obstruction is the most common complication in pediatric patients presenting with a mediastinal mass and has been reported in 60% of patients. Leukemia, lymphoma, Hodgkin disease, rhabdomyosarcoma, and neuroblastoma are the most common diagnoses in these patients. Laryngeal obstruction is uncommon in pediatric patients with cancer, but it is most likely to occur in the context of vocal cord paralysis. Airway compromise in the absence of mediastinal mass or adenopathy also has been reported in pediatric patients presenting with hemangioma, lymphangioma, teratoma (cervical and mediastinal), respiratory papillomatosis, thymoma, and a variety of head and neck tumors. Clinical symptoms depend on the level of obstruction. Stridor is associated with extrathoracic obstruction, and a hoarse voice suggests unilateral vocal cord paralysis. Increased obstruction of the trachea or mainstem bronchi may be manifested as wheezing, dyspnea, orthopnea, or increased effort of breathing.

f- **Cardiovascular emergencies-** Mechanical emergencies of the cardiovascular system in pediatric patients are uncommon, but they may result from compromise in cardiac function or vascular flow.

   I. **Cardiac tamponade-** Cardiac tamponade is defined as the inability of the ventricle to maintain cardiac output because of extrinsic pressure or intrinsic mass. Clinical findings of impending tamponade are similar to heart failure and include chest pain, cough, dyspnea, hiccups, nonspecific abdominal pain, and a pulsus paradoxus greater than 10 mm Hg. Chest radiographs may reveal the classic water-bag cardiac silhouette. ECG may demonstrate low-voltage QRS complexes and flattened or inverted T waves. Echocardiography is the best single study used, and it demonstrates pericardial effusion and atrial or ventricular collapse with hemodynamic compromise. Percutaneous catheter drainage is the treatment of choice and may be performed under echocardiographic or fluoroscopic guidance. Pericardial fluid may contain malignant cells and should be evaluated accordingly.

   II. **SVC syndrome-** SVC syndrome results from obstruction of the SVC by external compression or internal thrombosis. Symptoms include cough, hoarse voice, chest pain, dyspnea, and orthopnea and progress to headache, confusion, altered vision, and syncope. Symptoms are aggravated with patients in the supine position or performing the Valsalva maneuver. Signs of SVC syndrome are swelling and plethora of the head, neck, and upper extremities.

   III. **Gastrointestinal tract emergencies-** Gastrointestinal tract obstruction, pseudo-obstruction, and ileus are much more common

in adults than in children with cancer. Although uncommon, gastrointestinal tract obstruction in children is reported most commonly secondary to intussusception in which a neoplasm within the bowel wall creates a lead point to initiate the process. Burkitt lymphoma in the terminal ileum frequently comes to medical attention in this manner. In addition, intussusception has been reported in patients with adenomyoma of the Meckel diverticulum, hamartoma of the ileum, acute lymphoblastic leukemia, leiomyosarcoma, and following resection of a Wilms tumor. Gastrointestinal tract obstruction also has been reported following a volvulus resulting from a mesenteric lymphangioma. A temporary ileus also may be precipitated by typhlitis, sepsis, or other severe illness.

IV. **Urologic emergencies-** Similar to many other mechanical emergencies, urinary obstruction is a more common complication in adult patients with cancer. Nevertheless, urinary obstruction may occur in the upper or lower urinary tract of children with cancer.

V. **Upper urinary tract obstruction-** With regard to the upper urinary tract, ureteral obstruction may result from direct tumor invasion, compression, or encasement. Most tumors causing ureteral obstruction are genitourinary in origin, such as rhabdomyosarcoma. Ureteral obstruction also is a long-term complication of external beam radiation. Although acute ureteral obstruction often is associated with flank pain and colic, chronic unilateral obstruction usually occurs without symptoms. Acute or chronic bilateral obstruction is associated with decreased urine output and uremia. IV urography, renal ultrasound, CT scan, radionuclide renography, or retrograde pyelogram may be used to diagnose ureteral obstruction. In addition, CT scan best defines extrarenal pathology.

VI. **Lower urinary tract obstruction-** Lower urinary tract obstruction may result from bladder outlet obstruction or urinary retention. Bladder outlet obstruction may result from extrinsic compression from a large pelvic tumor or obstruction from an intrinsic neoplasm at the bladder neck or as a complication of hemorrhagic cystitis. Urinary retention in pediatric patients with malignancy primarily results from neoplasms in the brain, spinal cord, or nerve routes. Clinical findings of lower tract obstruction include suprapubic pain and suprapubic fullness, which result from a distended bladder.

After very keen study of various signs and symptoms produced by carcinoma, by any cause above defined, the correct disease picture can be made and matched with Materia Medica to find the similimum drug to complete the cure.

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