Computer Program Simulates Cell Growth, Provides Data for Cytotoxic Drug Studies

A new computer program developed at UT MDAH can simulate and graphically display the simultaneous growth and interaction of two cell populations, such as tumor cells and normal cells. This program, entitled CELLGROW, was developed by Elton Stubblefield, PhD, Department of Genetics. CELLGROW is primarily used to plan drug experiments in tissue culture and to aid in teaching cell kinetics. To operate the program, which runs on an Apple II, II+, or IIe computer, one need not have computer knowledge, only an understanding of cellular growth.

A unique feature of CELLGROW is its ability to display the cell division and multiplication of two cell populations at once. Cells of both populations are shown on the monitor as colored squares that may change color as they progress through the phases of the cell cycle. The program can color code each cell phase so that the color of a cell may indicate its particular phase of growth at a given moment. The two cell populations are usually distinguished from one another by variation in movement or distribution. Simulation data, including tables and graphs of population kinetics, are printed out at the end of the experiment. These show the number of cells in each phase and the total cell population for both populations at any point in the experiment.

Before beginning the simulated experiment, the operator must input for each cell population the cell cycle parameters of time and motion that determine the characteristics of cell growth. Values for these parameters will differ in population 1 and population 2.

The first parameter is time for cell division, which involves assigning a specific time to each phase of the cell cycle. In experiments that simulate the growth of certain types of tissue, the rate of cell division in these tissues will determine the simulated cell cycle time. For example, epithelial cells may require 18 hours for cell division in contrast to fibroblasts, which may divide in 12 to 14 hours. On the average, the G1 phase is approximately 5 hours, the S phase 8 hours, the G2 phase 2.5 hours, and mitosis .5 hours. On the computer, cells proceed through these phases of the cell cycle in a proportional number of minutes. In addition to cell cycle time, the desired number of cell divisions must also be input.

This program also allows cells at specific times to enter and leave the G0 phase, a kind of holding state in which certain cells may remain indefinitely without dividing. In the body, specialized cells may remain in the G0 phase, unless they are recruited into the cell cycle for performing a specialized task. Fibroblasts, for example, reenter the cell cycle from the G0 phase to heal wounds and form scar tissue. After the task is complete, these specialized cells return to the G0 phase.

Another parameter of cell growth that must be given a value is motion. Assigned values from 1 to 10 will determine the degree of cellular activity, whether stationary or active, and the direction of cell movement on the screen, whether random or preferential—up, down, right, or left. Values can be input that allow for the simulation of cellular activity of a certain kind of tissue; this often involves assigning the two cell populations different motion factors. If population 1, for example, is given a value of 0 and remains stationary and population 2 is assigned a value of 3 with movement to the right, a cell kinetic situation is set up that simulates cell growth in the skin. As Dr Stubblefield explained, “Sitting at the base of the dermis are stem cells dividing like population 1 cells, producing cells that migrate out toward the surface of the skin and differentiate into new skin cells, population 2 cells, which eventually die and are washed away.”

Continued on page 7

The computer printouts shown above represent cell populations as they appeared on the computer screen during a simulated experiment at 98 hours (left) and 120 hours (right). As in a comparable tissue culture experiment, the simulated tumor cells (bottom center in both illustrations), which grew from a single cell, are compact and stationary. In contrast, the normal cells (clear squares) are randomly distributed. The experiment was set up so that one out of 1000 normal cell divisions would give rise to a tumor cell.
UT MDAH Code of Ethics Guides Personnel in Making Complex Decisions Concerning Patients

UT MDAH has recently drafted a code of ethics to guide personnel in making professional decisions concerning patients. The code of ethics, the first to be adopted by a comprehensive cancer center, was written by a seven-member committee headed by Charles A. LeMaistre, MD, president of The University of Texas System Cancer Center; Jan van Eys, MD, PhD, head of the Division of Pediatrics; and James M. Bowen, PhD, vice president for academic affairs.

In stating the need for such a code at UT MDAH, Dr LeMaistre said, "We find crucial ethical issues confronting our hospital staff every day. This code will serve as a framework for the staff in managing complex matters constantly arising in the care of patients in a research setting."

The code, drafted for all personnel, helps to set priorities concerning the institution's goals of advancing science and promoting patient care. The code is viewed by many as a statement assuring each patient that staff decisions, whether large or small, will always be made in the patient's best interest. "Our position is not just to advance science, but rather to help people," Dr LeMaistre affirmed.

All codes deal with a balance between meting out mercy and dispensing justice, Dr van Eys explained. He said, "In a sense, our efforts at the basic science level are our efforts toward justice, and our clinical efforts are our gestures of mercy. We must be cognizant of the equal need for all when faced with the problem of cancer."

The code of ethics follows:

CODE OF ETHICS

Preamble

Our institution is a specialized center devoted to the care of patients with cancer and to the prevention and eradication of malignant disease. We strive to combine the activities of patient care, education, and research to benefit not only patients currently receiving care but also future generations. In this diversity, there is often tension; therefore, we hold before us this Code of basic moral principles against which to measure our service and to bond patients and staff together in the difficult task of contending with cancer.

Principle 1

Reverence for the patients for whom we are privileged to care is our primary concern. Such reverence affirms the value and dignity of life.

Principle 2

Acknowledging the value and dignity of life, we dedicate ourselves to provide our best care and to use our knowledge to attempt cure of the disease in each patient while pursuing understanding of the basic biologic nature and eradication of cancer.

Principle 3

The presence of cancer may justify, but not demand, heroic measures. Curing disease, reducing suffering, and sustaining an acceptable quality of life, as defined by the patient with the help of health-care professionals, are central goals of this institution.

Principle 4

All who serve in this institution have specific tasks and roles, yet all are equal as potential friends to patients. Because of these vocational and personal bonds, each of us bears individual moral obligations to each patient.

Principle 5

Knowledge-seeking research and knowledge-disseminating instruction are valued institutional goals. These pursuits require at least three conditions: participants who are informed about risks and benefits; actions that do not undermine the patients' therapeutic needs; the transmission of truthful information that is based on sound evidence.

Principle 6

The diagnosis of cancer is not just an identification of a disease but also carries with it a potential burden for patients, who may...
Epidemiologist Relates Hodgkin's Disease, Testicular Cancer, and Multiple Sclerosis

The epidemiologic similarities among multiple sclerosis, Hodgkin's disease, and testicular cancer suggest that these diseases may be caused by viral agents that have a common mode of infection, according to Guy R. Newell, MD, chairman of the Department of Cancer Prevention.

All three diseases appear to follow the paralytic poliomyelitis model: widespread geographic differences in occurrence of disease with infection by an agent of low pathogenicity. When contracted at an early age, infection with poliomyelitis virus results in lifetime immunity. If infection occurs at adolescence or young adulthood, paralytic poliomyelitis, a different and much more severe disease, develops.

Dr Newell and coworkers, Douglas E. Johnson, MD, Department of Urology, and Paul K. Mills, MPH,* Department of Cancer Prevention, formulated this theory from data suggesting epidemiologic similarities among the three diseases in age at onset, geographic distribution, socioeconomic level affected, racial groups affected, and size of the victim's family.

Data showed that the three diseases have peak occurrences in individuals between 20 and 40 years of age. Individuals generally contract multiple sclerosis around age 30. The peak incidence of Hodgkin's disease is between ages 20 and 30 and after age 50. Peak incidence of testicular cancer is between ages 25 and 34 and, to a lesser degree, between ages 45 and 50.

For both Hodgkin's disease and testicular cancer, histologic type of disease is related to age at disease onset, suggesting the possibility of infection by different agents or disease subtypes in different age groups. In testicular cancer, germ cell tumors account for 95% of all testicular tumors. Choriocarcinoma, teratoma, embryonal carcinoma, and seminoma, which comprises 35% to 71% of these four tumors, are the most common germ cell tumor types. Those contracting testicular cancer at adolescence and in their 20s, have nonseminoma germ cell tumors. The nonseminomatous tumor that occurs at age 15 may be caused by a different agent than a seminoma occurring at age 35, Dr Newell explained.

The histologic types of Hodgkin's disease also tend to be age-related. Hodgkin's disease is divided into four histologic groups: (1) lymphocytic predominance, (2) nodular sclerosis, (3) mixed cellularity, and (4) lymphocytic depletion. Nodular sclerosis often occurs in persons around 30 years of age and older; the remaining three histologic types usually occur in older Hodgkin's disease patients. In young adults, Hodgkin's disease appears to be caused by a virus of low pathogenicity, but in the elderly the disease may have a nonviral cause similar to causes of other malignancies, Dr Newell explained. Current epidemiologic studies of these histologic types indicate that Hodgkin's disease may actually be two or more diseases that affect individuals at different ages.

Data suggesting similarities in geographic distribution of the three diseases show a decline in occurrence of each from north to south. They appear more frequently in countries with temperate climates, except for Japan where these diseases, especially multiple sclerosis, are rare. Incidence rates for all three diseases are high in the U.S. and in European countries; these diseases occur infrequently in Africa and among black populations in general.

The three diseases also occur more frequently in economically advanced areas and high socioeconomic groups where early exposure to disease is less common than in impoverished areas. As Dr Newell explained, "In developing countries with poor sanitation, infection is widespread at an early age. However, children may escape infection in economically advanced societies, often having home environments more protective against disease. Not having acquired an early immunity, older children or young adults are susceptible to these diseases." Although Japan is economically advanced, its low disease rates might be attributed to early exposure of the population to disease-causing agents in "night soil," a widely used fertilizer containing human excrement, Dr Newell speculated.

Family size appears to affect risk as well; the greater the number of children in a family, the greater the likelihood of early exposure to infection. Children of small families are, thus, less likely to be exposed and will be more susceptible to disease at a later age.

Evidence linking Hodgkin's disease to several diseases of the central nervous system, similar to multiple sclerosis, lends support to Dr Newell's infectious disease theory. Recent studies have found a predisposition to Hodgkin's disease and other lymphomas in relatives of patients with Alzheimer's sclerosis, one of the presenile dementias. Like Hodgkin's disease and multiple sclerosis, Alzheimer's sclerosis has been associated with a slow-virus etiology. Hodgkin's disease has also been linked with progressive multifocal leukoencephalopathy (PML), PML is a...
Leech Gland Extract Inhibits Metastasis

Table 1. SGE* Effect on Cyclophosphamide-Induced Enhancement of Metastases in Mice Injected with Tumor Cells

<table>
<thead>
<tr>
<th>Treatment of tumor cell recipients</th>
<th>Sarcoma†</th>
<th>Fibrosarcoma‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of mice with metastases/total no. of mice (range)</td>
<td>Median no. of lung nodules</td>
</tr>
<tr>
<td></td>
<td>Mediastinum</td>
<td>Lung</td>
</tr>
<tr>
<td>HEPES buffer, day 0</td>
<td>4/10</td>
<td>10/10</td>
</tr>
<tr>
<td>SGE, day 0</td>
<td>0/10</td>
<td>2/10</td>
</tr>
<tr>
<td>CY, day -1</td>
<td>10/10</td>
<td>10/10</td>
</tr>
<tr>
<td>SGE, day 0</td>
<td>3/10</td>
<td>4/10</td>
</tr>
<tr>
<td>CY, day -4</td>
<td>10/10</td>
<td>10/10</td>
</tr>
<tr>
<td>CY, day -4 + SGE, day 0</td>
<td>5/10</td>
<td>10/10</td>
</tr>
<tr>
<td>CY + SGE, day -4</td>
<td>not administered</td>
<td></td>
</tr>
</tbody>
</table>

* Salivary gland extract from Haementeria officinalis, 3 doses of 500–800 µg given every 2 hours.
† Lung tumors were counted 19 days after i.v. inoculation of 5 × 10⁴ sarcoma cells.
‡ Lung nodules were counted 14 days after i.v. inoculation of 2 × 10⁴ fibrosarcoma cells.
§ Mann-Whitney U test.
‖ Cyclophosphamide (CY) 200 mg/kg body weight i.p.

Salivary gland extract (SGE) from the Mexican leech, Haementeria officinalis, has been found to inhibit in mice enhancement of lung metastasis caused by treatment with cyclophosphamide or local thoracic irradiation. This finding is the result of a study conducted by Gabriel J. Gasic, MD, PhD, and coworkers at Pennsylvania Hospital in Philadelphia, in collaboration with Luka Milas, MD, PhD, chairman of the Department of Experimental Radiotherapy at UT MD. Radiation and cytotoxic drugs, by causing normal tissue damage, are thought to promote metastasis to these tissues if they do not first completely sterilize the source of circulating tumor cells. This may occur when chemotherapy or radiation destroys more normal tissue than tumor tissue, as in prophylactic irradiation when the primary tumor is still uncontrolled and in the use of chemotherapy or irradiation for tumors later found to be drug- or radiosensitive. “Tumors resistant to treatment continue to shed tumor cells into the circulation, which may find normal tissues preconditioned by radiation or chemotherapy for the establishment of secondary growths,” Milas said. Tumor cells are thought to lodge more easily in such damaged tissues.

Lung tissue, a common site of metastasis, has been studied to determine the metastasis-enhancing effect of these modalities. In one study, when tumor cells were injected into mice pretreated with cyclophosphamide, lung colonization increased 1000 times that occurring in untreated animals. In these animals and others treated with local thoracic irradiation, susceptibility to lung colonization persisted for months. Although the clinical implications of these findings are uncertain, such agents may have a similar metastasis-enhancing effect in humans, Milas explained.

SGE was investigated in the present study as a possible metastasis inhibitor because of its anticoagulant and antiplatelet aggregating activity thought to prevent tumor cell lodgement and to enhance release of these cells from the lung.

The effects of SGE were compared in mice inoculated with syngeneic mouse tumor cells and either pretreated with cyclophosphamide (200 mg/kg of body weight) or local thoracic irradiation (1000 rad) or not treated prior to tumor cell inoculation. Cyclophosphamide was administered 1 or 4 days before inoculation with tumor cells, and local thoracic irradiation was given 1 day before. Lung metastases were generated by inoculation of 2 × 10⁴ to 6 × 10⁴ mouse sarcoma or fibrosarcoma cells; 2.5 × 10⁴ sarcoma cells generated growth in the mediastinum.

For further comparison, mice in each treatment group were divided into those who received SGE (three doses of 500 to 800 µg of protein in 0.2 ml of Hepes CaCl₂ buffer per injection) and those who did not. SGE was administered by intravenous (i.v.) or intraperitoneal (i.p.) injection on the day of local thoracic irradiation, cyclophosphamide administration, or tumor cell inoculation. Fourteen or 19 days after tumor cell inoculation, mice were killed, and results were determined. SGE almost totally abolished metastasis formation in the mediastinum and lungs of control
mice inoculated with sarcoma or fibrosarcoma cells (Table 1). SGE also greatly inhibited cyclophosphamide enhancement of metastasis at both sites: SGE totally abolished sarcoma metastasis enhancement by cyclophosphamide and reduced fibrosarcoma metastasis enhancement by about 50%. The greatest reduction of metastasis enhancement occurred when cyclophosphamide was administered 1 day before sarcoma cell inoculation and SGE on the day of inoculation (Table 1). SGE also greatly reduced enhancement of tumor metastases induced by local thoracic irradiation whether SGE was given on the day of fibrosarcoma cell injection or the day of local thoracic irradiation, administered 1 day before tumor cell injection (Table 2).

SGE, administered on the day of tumor cell inoculation, also reduced the size of the sarcoma lung colonies measured in normal mice and in mice pretreated with cyclophosphamide. It reduced the average size of sarcoma nodules from 2.4 ± 0.4 mm to 1.0 ± 0.1 mm in control mice; in those receiving cyclophosphamide 4 days prior to tumor cell inoculation, average sarcoma nodule size decreased from 3.3 ± 0.3 mm to 1.7 ± 0.8 mm.

Similar findings were obtained when the weight of tumor tissue removed from the mediastinum of control mice and of mice treated by cyclophosphamide was compared. The total weight of tumor masses from five mice that received the sarcoma cells only was 862 mg; in five mice that received cyclophosphamide only 4 days prior to sarcoma cell administration, total mediastinal weight was 1230 mg; tumor masses of five mice receiving SGE on the day of cyclophosphamide injection weighed 710 mg. Thus when comparing the reduction in size and weight of the sarcoma tumor in control and treatment groups, SGE totally abolished cyclophosphamide-induced metastasis enhancement, Dr Milas explained.

To determine the mechanism of action of SGE, researchers tested SGE’s ability to accelerate tumor cell clearance from the lung. This experiment involved measurements of lung radioactivity in mice inoculated with 125I-UDR-labeled sarcoma cells and pretreated with cyclophosphamide 4 days before; these mice were given a single injection of 1500 µg protein SGE 2 hours before tumor cell injection. In addition, radioactively labeled tumor cells were injected and retention determined in mice that received cyclophosphamide alone or SGE alone and in control mice receiving Hepes buffer only. The radioactivity of the lung was measured at 10 minutes and 2, 4, and 8 hours after tumor cell injection. Initially at 10 minutes, 85% to 95% of tumor cells were retained in the lung in all groups. Thereafter, however, at 8 hours the control mice retained 42% ± 3% of cells, and the cyclophosphamide-treated mice not receiving SGE, 68% ± 8% of cells. In those receiving SGE alone, retention of tumor cells was reduced to 18% ± 1% at 8 hours. In mice pretreated with cyclophosphamide and receiving SGE, tumor cell retention was reduced to 38% ± 12% at 8 hours. SGE (500 µg protein) also reduced lung retention of tumor cells in cyclophosphamide-treated animals when the extract was given in three injections 2 hours before and 2 and 4 hours after tumor cell inoculation.

Further testing indicated that increased tumor clearance was not due to any cytotoxic effect of SGE or augmentation of natural killer cells by SGE. Instead, SGE was found to reduce metastasis enhancement by interfering with factors responsible for the cyclophosphamide effect. This was concluded because SGE reduced lung nodules when administered alone on the same day or 1 day before tumor cell administration, but not when given alone 4 days before tumor cell injection. However, SGE was similarly effective whether given several hours before or after cyclophosphamide or 4 days after cyclophosphamide. In addition, when SGE was given with cyclophosphamide on the same day but 4 days before tumor cell injection, the number of metastatic nodules decreased. SGE, then, had no effect when given 4 days before tumor cells unless administered with cyclophosphamide and, therefore, must have interfered with the cyclophosphamide metastasis-enhancing effect.

Investigators attributed several factors to SGE’s effect. Because SGE exhibits strong anticoagulant and antiplatelet aggregating activities, it may interfere with the accumulation of platelets around tumor cells and the formation of fibrin clots that facilitate vascular lodgement by tumor cells. In addition, because local thoracic irradiation and cyclophosphamide damage capillaries, causing gaps in the capillary endothelial lining, tumor cells

### Table 2. SGE* Effect on LTI-induced Enhancement of Lung Metastases in Mice Injected with Tumor Cells

<table>
<thead>
<tr>
<th>Treatment of tumor cell recipients</th>
<th>Experiment 1</th>
<th>Experiment 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median no. (range)</td>
<td>Median no. (range)</td>
</tr>
<tr>
<td>Heparin buffer, day 0</td>
<td>46 (43–71)</td>
<td>3 (0–10)</td>
</tr>
<tr>
<td>SGE, day 0</td>
<td>9 (3–16)</td>
<td>0 (0–3)</td>
</tr>
<tr>
<td>LTI, day -1</td>
<td>134 (31–158)</td>
<td>9 (3–20)</td>
</tr>
<tr>
<td>LTI &amp; SGE, day -1</td>
<td>not administered</td>
<td>&lt;.05†</td>
</tr>
<tr>
<td>SGE, day 0</td>
<td>66 (32–85)</td>
<td>2 (1–16)</td>
</tr>
</tbody>
</table>

*Salivary gland extract from Haemonectes officinalis, 3 doses of 600 µg given i.v. every 2 hours.
† Local thoracic irradiation, 1000 rad.
‡ Lung nodules were counted 14 days after i.v. inoculation of 3 x 10⁵ (Exp. 1) or 6 x 10⁴ (Exp. 2) fibrosarcoma cells.
§ Mann-Whitney U test.
¶ 8 of 10 mice had metastases.
# 3 of 10 mice had metastases.
†† P-value for LTI, day -1 and LTI, day -1 + SGE, day 0.

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Epidemiologist . . .
Continued from page 3

disease of the central nervous system that is caused by a papova virus. Some patients with PML have underlying malignancies such as Hodgkin's disease that impair cell-mediated immunity. These malignancies may, in fact, predispose patients to PML. Hodgkin's disease is also associated with subacute motor neuronopathy (SMN), which may develop late in the course of Hodgkin's disease or other lymphomas. SMN causes neuronal degeneration primarily of the anterior horn cells of the spinal cord, producing lesions very similar to those seen in paralytic poliomyelitis. Since Hodgkin's disease and paralytic poliomyelitis are epidemiologically similar, this finding may provide a valuable clue to the interrelation of these diseases.

Hodgkin’s disease, multiple sclerosis, and testicular cancer, then, may each be explained in terms of an environmental infectious agent or agents of uneven worldwide distribution that generally have low levels of pathogenicity. Each disease occurs infrequently and in response to a given set of host factors that are not yet clearly understood. Testicular cancer and Hodgkin's disease each may be caused by several different agents working in combination or by a diverse histologic response to a single agent. Myxoviruses, slow viruses, and enteric and respiratory viruses are presently being investigated as possible causes for the three diseases.

A comparison of similar epidemiologic features is of value because it suggests a plausible hypothesis that, after further epidemiologic, clinical, and laboratory studies, may shed some light on the causes of these diseases. As Dr Newell explained, “Such studies may enable us to identify the etiologic agent involved and then take the intervening steps to prevent the disease.”

(Physicians desiring additional information should write or call Guy R. Newell, MD, Department of Cancer Prevention, MDAH Box 189, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030 (713) 792-3020.—ED)

Code of Ethics . . .
Continued from page 2

feel stigmatized, and for those close to them, who share the impact. We must understand their perceptions and help them to come to terms with their altered lives.

Principle 7
Patients justly expect personal information to be confidential, yet their medical records are accessible to all health-care providers. All information must be recorded responsibly. Access also confers a moral obligation. Access must be justified and not harmful to the patients' interests.

Principle 8
Since our specialized roles result in varying levels of function and decision-making, we affirm the need to demonstrate mutual respect and to acknowledge interdependence as coworkers responsible for the welfare of patients.

Principle 9
The immediacy of patient care tends to obscure the relevance of basic biologic research. We affirm that research, responsibly conceived and scientifically sound, establishes an environment of learning, encourages exacting practice, fosters new knowledge, and creates realistic prospects of eradicating cancer, thus promoting a favorable balance of risks and benefits.

Principle 10
Cancer therapy and research are expensive endeavors demanding conscientious stewardship; however, financial considerations should never dictate the quality of care offered to each patient.

The University of Texas
M. D. Anderson Hospital and Tumor Institute
at Houston

2nd Annual Administrative Conference

Administrative Aspects of Home Health Care

February 1, 1985

Four Seasons Hotel
Houston Center
Houston, Texas

Chairperson: Donald B. Wagner, MA, associate vice president for patient care operations

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Computer Program . . .  

Continued from page 1

The means by which population 2 cells arise must also be determined before the simulated experiment begins. There are four methods of creating population 2 cells. In one, a fraction of daughter cells from population 1 can become population 2 cells after mitosis. In a second, a fraction of G0 cells from population 1 may reenter the cell cycle as population 2. This method may be used in simulating drug experiments with tumor cells in culture. Tumors often have cells in the G0 phase that may reenter the cell cycle at any time. These G0-phase cells can influence the effectiveness of a drug and, therefore, must be included in a simulated drug experiment. In a third method, a fraction of population 1 cells may become population 2 cells after passing through a particular cell cycle phase. This method is useful in simulating drug experiments in which cells in a certain phase are radiolabeled to determine what percentage of the original cell population was killed by a drug that is cytotoxic in that phase. By a fourth method, population 2 cells may be created at the beginning of the experiment as a separate unrelated population of cells.

In addition to the above-mentioned situations, this program can be used to simulate other cell growth experiments in culture, also involving the effects of certain drugs. Many drugs are cytotoxic only in particular phases of the cell cycle, usually when cells are duplicating their chromosomes in the S phase or in mitosis. In two cell populations, normal cells and tumor cells, for example, if a drug is used that kills cells in S phase and if the normal population 1 has a much longer G1 phase and shorter S phase than the cancerous population 2, then by simulating these circumstances, the length of time of S-phase cell kill for maximal kill of tumor cells and minimal harm to healthy cells can be determined. This information then indicates how long a drug should remain in culture to achieve the most effective results.

The computer can also be used to simulate experiments in which a drug blocks, or immobilizes, cells in a certain phase to synchronize the cell growth of different cell populations. Vinblastine, for example, blocks cells in mitosis. The program can determine how long vinblastine should remain in the culture to achieve maximum synchronization of cell populations. On the computer screen, all cells passing through mitosis, represented as orange squares, would remain static for the length of time assigned to the cell block. At the end of that time, the cells, or colored squares, would begin dividing again.

When the simulated experiment is complete, a dot-matrix printer prints out population data as it appeared on the screen and in graphs and charts. The total cell population influenced by different variables at different time intervals during the entire experiment is depicted in these illustrations. This ability to immediately assimilate information concerning cell growth is the primary benefit of CELLGROW. As Dr Stubblefield explained, "It may take all afternoon to compile data from an experiment and draw a graph. But the computer does it instantly."

In the near future, Dr Stubblefield plans to develop a computer program to simulate embryonic growth in three dimensions. The computer would be capable of showing a slice through a three-dimensional embryo at any point in embryonic growth. This program, which will require the use of a super computer, should determine the factors involved in cellular differentiation and embryonic development and may help to explain how cancer is a variant of normal growth.

According to Dr Stubblefield, the value of CELLGROW is its ability to make a summary statement of everything known about the growth of certain cell populations. Such a vast amount of information would be almost impossible to assimilate by means other than computer. CELLGROW is also a first step in the development of more complex programs that may clarify the interrelation of cell populations and thus determine how cancer cells arise, Dr Stubblefield explained.

(Physicians desiring additional information should write or call Travis E. Stubblefield, PhD, Department of Genetics, MDAH Box 6, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030 (713) 792-2581.—ED)
Leech Extract . . .
Continued from page 5

can more easily attach to the capillary wall. Once attached, tumor cells, by secreting proteolytic enzymes that destroy components of capillary walls, pass through the walls into extracapillary spaces where metastases usually occur. SGE contains proteolytic enzyme inhibitors, thus reducing tumor cell extravasation.

However, SGE’s action against tumor cell lodgement cannot explain its effect when given on the same day as cyclophosphamide 4 days prior to tumor cell injection, because after 4 days the extract is no longer active and would not have affected tumor cells. One possible explanation cited by Dr Milas is that SGE also contains inhibitors of enzymes associated with tissue injury and thus reduced the tissue damage inflicted by cyclophosphamide and local thoracic irradiation.

According to Dr Milas, these findings may have an impact on the future treatment of patients with cytotoxic drugs or radiation: “SGE or its active component might eventually be used with primary drug or radiation treatment to prevent the possible metastasis-enhancing effects of these modalities, especially in instances in which the therapeutic effectiveness of the treatment is uncertain.”

(Physicians desiring additional information should write or call Luka Milas, MD, PhD, Department of Experimental Radiotherapy, MDAH Box 66, The University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston, Texas 77030 (713) 792-3424.—ED)

Clinical Conference Book On Lymphoma Now Available

Hodgkin’s Disease and Non-Hodgkin’s Lymphoma: New Perspectives in Immunopathology, Diagnosis, and Treatment, a compilation of proceedings of the 27th Annual Clinical Conference held at UT MDAH in November 1983, is now available (Raven Press, New York, 1984, 474 pages, $98.00). The volume, edited by Richard J. Ford, Jr, MD, PhD, Department of Pathology, Lillian M. Fuller, MD, Department of Clinical Radiotherapy, and Fredrick B. Hagemeister, MD, Department of Hematology, presents the most recent findings of basic researchers and clinicians on the etiology, epidemiology, diagnosis, and staging of Hodgkin’s disease and non-Hodgkin’s lymphoma as well as the treatment of patients with these diseases. Major areas of discussion include: the tumor biology and pathology of lymphomas, oncogenes and other cytogenetic abnormalities in lymphomas, new chemotherapy combinations, and immunotherapy with immunotoxins and bone marrow transplantation. Because the lymphatic cancers offer the most instructive human tumor model systems, the editors hope that the studies included in this volume may provide insight into the causes of all malignancies.