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Students take advantage of one of the last great Autumn afternoons, and take a break in the courtyard surrounded by medical school buildings. Meet the class of '84 on page 14.
Consider having an instrument which can: (1) measure a few millionths of one-millionth of a gram of a biological substrate or a drug; (2) perform the measurement accurately in the presence of hundreds of other compounds without interference; (3) give unequivocal evidence that a substance is the same as a known comparison substance using the same minute sample; (4) trace safe, non-radioactive isotope-labeled drugs or metabolites in healthy and diseased humans, and (5) obtain information about the structures of unknown substances occurring in tissue samples or in enzymatic experiments. The instrument which performs all of these functions is a gas chromatograph-mass spectrometer, or GC-MS, which, for the applications described, cannot be considered apart from its associated computer. The combined GC-MS/computer system is one of the most versatile and powerful analytical instruments available to science.

The Washington University School of Medicine GC-MS Facility today operates five GC-MS systems, each with its own computer. The staff is experienced in computer programming and electronics design, and has the engineering skills to maintain these hybrid digital electronic/mechanical systems. The staff also has a wide range of expertise in chemistry, biochemistry and intermediary metabolism.

The origins of the facility go back about thirteen years, to Autumn 1967, when we purchased our first instrument with funds from a National Institutes of Health (NIH) Health Sciences Advancement Award. In the late 50's and early 60's three developments in instrumental methods occurred, each of which was to be highly important in its own right but
which, when combined, created an instrument which had previously only been imagined. These events were the commercial development of the gas chromatograph and its interfacing to mass spectrometers, and an accelerated growth in computer technology.

The technique of gas chromatography was first described by A.J.P. Martin and R.L.M. Synge in 1952, the same year in which these British scientists received the Nobel Prize for their studies on partition chromatography. The technique is fundamentally simple. The equipment typically consists of a heated tube, about two meters long and six millimeters in diameter, containing any of several viscous oil-like substances coated either on the walls of the tube or on some relatively inert powdered filler. (In early work powdered firebrick was used; now we use primarily diatomaceous earth.) The sample to be separated is heated to a temperature at which it vaporizes (perhaps 200°C or higher) and it is passed along the tube in a stream of an inert gas such as helium. The components in a mixture which dissolve least in the oily coating emerge from the tube first; those which are most soluble emerge last, with intermediate cases between. Vaporizing involatile compounds is done by modifying substances so that they become heat stable and volatile at elevated temperatures. In the '60's these devices became commercially available with simple, extremely sensitive detectors for following the chromatographic separation. It is commonly held that any substance which can be vaporized can be separated from any other substance by gas chromatography, given the correct conditions (Figure 1).

Mass spectrometers had been used, by physicists mainly, for many years. The principle of these instruments, the deflection of ion beams by magnetic or electric fields (as in a television set) was known before the turn of the century. Two names, A.J. Dempster (1918) and F.W. Aston (1919) are associated with the invention of the mass spectrometer. In 1941, these devices became commercially available, and Hillman became familiar with the principles of such tissues and gives a measure of the scope of such an undertaking. At first interpreting mass spectra de novo to obtain evidence for the structures of compounds, and later, using catalogs of spectra which become available, Hillman became familiar with the appearance of extracts from tissues of normal patients and those with pathology. Once the baseline information was known, the patterns of familiar diseases emerged and he now does much of the diagnosis from a chromatogram such as that illustrated. His main use of GC-MS now is the verification of a substance in a chromatographic peak, or the identification of a drug. Such a drug, probably an anti-seizure medication, occurs in the illustration at about fifteen minutes.
The GC-MS Facility

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minutes. This illustrates another aspect of Hillman's use of GC-MS. Toxicology is an area which makes extensive use of mass spectrometry in the identification of drugs, toxicants and their metabolites, leading to more rational therapy for toxified patients.

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with the construction of mass spectrometers which were the predecessors of instruments used today.

The function of a mass spectrometer is to ionize a chemical sample — that is, give it an electric charge (usually positive) — and to measure the mass and the amount of the charged particle. Each of these functions occurs in a high vacuum, which prevents the generated ions from colliding with other ions or other molecules. The ionized sample is then analyzed by being separated into groups of ions of similar mass-to-charge ratio. Since most ions have only a single charge, the separation is actually by their mass.

Actually, the situation is somewhat more complex. When a substance is ionized, energy is imparted, and the original molecule may remain as a whole entity only to a small degree. Instead, it usually decomposes to a number of ions, each bearing some part of the original molecule. These “fragment ions,” plus the intact molecule or “molecular ion,” constitute the mass spectrum of a substance. The spectrum is graphically represented as the abundance of each ion and its mass value (actually mass/charge value), as shown in Figure 2.

Several kinds of mass analyzers are used. For example, in the magnetic spectrometer, a charged particle is passed through a magnetic field where it acquires a curved path. The heavier the particle, the less will be the curvature of that path.

Figure 2. Below are pictured the mass spectra of the trifluoroacetyl derivatives of two antidepressant drugs: protriptyline (left) and nortriptyline (right). The spectra are represented as bar-graphs, with the relative intensity of each mass spectral peak on the vertical axis and, on the horizontal axis, the mass/charge (m/e) value of each of these ions. This value is actually the mass of each fragment ion peak since the charge is most often unity. At the high-mass end of each spectrum is a peak which represents the molecular weight of the drug derivative. This is the “molecular ion” represented as M: Note how different the two spectra are, in spite of the fact that the molecular weights and elemental composition of the two drugs are identical. Examination of the structures reveals that they are isomers of each other, varying only in the position of a single C=C group. This is characteristic of the mass spectra of most substances; i.e., they are often remarkably unique signatures and they also contain considerable structural information, which is shown schematically. Under the mass spectral conditions used, protriptyline fragments preferentially at the tricyclic ring, due to the bridging carbon-carbon double bond; in the case of nortriptyline the double bond is outside the ring, resulting in a different kind of fragmentation.

The two main fragment ions are characteristic of protriptyline (m/e 191) and nortriptyline (m/e 232). When the GC-MS is focused on just these ions, it becomes a device for specifically measuring each of the drugs in patient plasma with great sensitivity and drug-specificity.

Using GC-MS, John T. Biggs, M.D., Clinical Associate Professor in the Department of Psychiatry, and Sherman, together with associates in Psychiatry developed methods for measuring all of the tricyclic antidepressants used therapeutically in this country. Biggs has used this method in extensive studies of the relationship between the dose of the drugs and the plasma levels attained, as well as the therapeutic response achieved. This is necessary with these and with many other drugs because the range of metabolic capacity for most substances is highly variable from individual to individual. Thus, a dose sufficient for one person may be either inadequate or approach overdose for another, and an objective method for measurement is thus an aid to therapy. The same rationale is being applied to therapy with anticonvulsant drugs in children by W. Edwin Dodson, M.D., Associate Professor of Pediatrics and...
Neurology. With these agents, it is a more serious problem—the narrow margin between an effective and a toxic dose of a drug.

The separated ions, as in the prism-separated colors of sunlight, are a spectrum with intensity (i.e., the abundance of an ion) and the counterpart of wavelength (the mass-to-charge value). The degree of separation between ions of different mass is termed the resolution of the instrument. We use instruments which separate ions with one mass unit of difference, and with masses of up to 1000 daltons. Hydrogen, the lightest element, has a weight of approximately one dalton. The abundance of the ions is a function of the original sample size, thus it can be used for measuring the amount of a substance in a sample.

Because the mass spectrometer operates in a vacuum of one billionth that of atmospheric pressure, and the gas chromatograph typically functions at about twice atmospheric pressure, there is a basic incompatibility between the two instruments. An ingenious solution to this problem was devised by R. Ryhage and E.W. Becker at the Karolinska Medical Institute in Stockholm, who invented a molecular separator that removes the helium carrier gas while preserving 50% of the sample vapor, which enters the mass spectrometer in a continuous stream.

The need for computers in the laboratory is now taken for granted. However, a consideration of the problems encountered in dealing with the information generated by a GC-MS system can lead to an appreciation of the value of the computer to science. In one important application in our Facility, Richard E. Hillman, M.D., Professor of Pediatrics, diagnoses inborn errors in the metabolism of children by examining the urinary products of the metabolism of, for example, amino acids. The compositional complexity of urine can be imagined and, using a gas chromatograph, easily more than a hundred substances can be separated within an hour. Each of these substances is a potential candidate for the evaluation of an enzyme defect and thus can become a mass spectrum to be evaluated. When we obtained our first GC-MS system in 1969, computers for handling the output from these instruments were not yet commercially available. As a substance emerged from the gas chromatograph (for example, every 30 seconds), we obtained the spectra on light-sensitive paper a yard or more in length. Someone would then have to sit down and locate air—a peak for nitrogen (m/e 28) and one for oxygen (m/e 32). The peaks are obvious because they occur in a 5:1 abundance ratio, the composition of air. We then counted, bridging gaps by interpolation, to the highest mass peak in the spectrum, and measured (with a ruler) the height of each peak and tabulated the whole. This could consume from two to five hours not including the preparation of a bar-graph as shown in Figure 2.

William F. Holmes, Ph.D., an Associate Professor in the Department of Biological Chemistry, a biochemist with a special interest in computer science, developed our computer programs and the electronic hardware both to control the mass spectrometer and to process its output. He used a commercially produced minicomputer, a PDP-12, to create a system with which the user, in a dialogue with the computer by means of a keyboard and a television-like screen, decides the conditions for the experiment. It was a thrilling experience that I still recall vividly, to watch the computer acquire the information from a spectrum scan, which takes from three to seven seconds, and without a discernible interval, process the data and display the finished bar graph on the screen. At that time the first on-line computers were being developed for GC-MS applications. Through Holmes' efforts, Washington University became one of the early centers of development.
of computers for use with these instruments. It was through the computer that GC-MS became practical for complex applications, such as those of a biomedical nature. Experiments such as those we perform today could not even have been considered prior to these developments.

Ready access to the power of the GC-MS was the beginning of a remarkable period of growth for us, one in which physicians as well as Ph.D.s came to the Facility and personally performed their experiments, with their own hands. We became the first — and are still one of a few — groups where "hands-on" the instruments was highly encouraged for access to their use. That arrangement created thoughtful users who not only designed their experiments more effectively, but contributed to the Facility through constructive criticism and new ideas.

During the last ten years we have acquired four more instruments, three of them from National Institutes of Health and National Institutes of Mental Health grants. Holmes redesigned the computer system, making it even less expensive and more flexible, and we grew in the size of our user group as well as in the size of our support staff. Today we are looking forward to consolidating all the instruments from two distant locations into one area. When that occurs, we hope to acquire the funds to obtain the ultimate mass spectrometer, a high-resolution instrument with the mass range and sensitivity for experiments which are closed to us today.

An early application of our first computer-controlled GC-MS system was one which I felt was quite amazing but theoretically achievable. I looked on it as one of those experiments upon which you gamble because the hoped-for outcome is so remarkable. My interest for years has been the metabolism, function and distribution of myo-inositol, especially in the nervous system. This substance, which all organisms synthesize from glucose 6-phosphate, is known to be essential for dividing cells. It is present in nervous tissue in very high concentrations. Inositol is known to be metabolically involved in biological processes as diverse (or related?) as nerve impulse transmission and the secretion of insulin. Myo-inositol was long thought to be a vitamin, and in fact it can be considered to be so for the neonate, although all organisms appear to synthesize a portion of their requirement for it. I was interested in the distribution of myo-inositol in the central nervous system, at the level of microscopic anatomy. The techniques for weighing microscopically dissected pieces of dried tissue sections as small as one billionth of a gram (one nanogram) had been developed at Washington University by Dr. Oliver H. Lowry. These methods use the deflection of a fine quartz fiber for the measurement of extremely small weights. In a collaborative effort with Dr. Paul M. Packman, now Clinical Associate Professor, and with Rita Boshans, Research Associate, both at that time in the Department of Psychiatry, we used a technique of GC-MS called ion monitoring along with the Lowry techniques in an effort to measure inositol levels in these tiny tissue segments.

In ion monitoring the analyst selects a fragment ion, from the spectrum of a compound, which is unique to that compound. This specificity is not as difficult to achieve as it might seem because the gas chromatographic procedure is likely to separate similar compounds, thus the uniqueness of an ion at a certain time in the chromatographic pro-
process is the operational criterion. The selected ion is then observed with the mass spectrometer (the instrument is focused on that ion) and its appearance at the appropriate time in the chromatography signals the emergence of the compound of interest. Consideration of this procedure reveals that the mass spectrometer can be used as a chemically specific detector for the gas chromatograph. That specificity removes many constraints about purification prior to analysis, as is demonstrated by the inositol measurement in tissues.

Our first experiment involved the measurement of the myo-inositol in a 15-nanogram dried section of the anterior nucleus of rat brain hypothalamus. The tissue section, too small to be seen without a microscope, was immersed in ten microliters of a reagent which converts inositol to a volatile derivative. After a 48 hour reaction the entire liquid sample was injected onto a gas chromatographic column of the GC-MS. (Stop and think that hundreds of substances were present in the sample.) We had focused the instrument on m/e 318, an abundant ion in the spectrum of our derived inositol, one which is highly unique for these compounds. After two minutes, during which time no other substance appeared on the screen of the computer, an unambiguous peak was observed which was due to myo-inositol. It took many more experiments to convince us that we were really measuring inositol in brain samples. However, when — unknown to me — a sample tube had no tissue placed in it, there was no response. This work culminated in the measurement of inositol in sections of individual rabbit dorsal root ganglion cells weighing 3-7 nanograms. We were thus able to measure the inositol in sections through cells which contained only cytoplasm as contrasted with sections which contained both cytoplasm and nucleus. This revealed that, contrary to some earlier published, and suggestive, data the concentration of inositol in the nucleus of (at least these) cells is no higher, or lower, than in the cytoplasm.

To gain some feeling for the size of the single cell tissue segments, Figure 3 shows the dimensions of a five-nanogram (dry weight) piece of tissue. To me, this is still remarkable testimony to the power of these instruments.

Figure 3. The illustration below shows the approximate size of a tissue sample which has been analyzed for its myo-inositol content by GC-MS. The procedure is an example of the chemical selectivity and great sensitivity of the GC-MS method. The analysis is performed by first treating the entire frozen dried sample, which weighs in the range of 5 nanograms (see text), with a reagent which makes the inositol sufficiently volatile so that it can be separated from the hundreds of other substances present in the tissue. The mass spectrometer is then focused on an ion in the mass spectrum of the inositol derivative, which is highly characteristic of the inositol and largely absent in the spectra of the other substances in the tissue. The analysis results in a chromatogram which shows only the presence of myo-inositol (lower inset) which emerges from the chromatograph at about two minutes. This chromatogram is from the analysis of a single section taken through a large dorsal root ganglion cell. The analyzed section weighed 4.3 nanograms (4.3 x 10^{-9} gram) and the amount of inositol measured represents 16 picograms (16 x 10^{-12} grams). Such slices contain 20.9 ± 1.1 millimoles of myo-inositol per kilogram of tissue (the variance is the standard error of the mean). Thus it can be seen that the method is precise, highly sensitive and chemically selective as well.

It must be said that without the electronic designs and the programs which Holmes developed for the ion monitoring system, and all the other aspects of our computer system, the work
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just described, and in fact, all of the work produced by users of the facility in the last ten years, would not have been done. It is not an exaggeration to say that we are as completely dependent on the computer as we are on the GC-MS instrument itself. As evidence that this is true, the various users of the Facility at Washington University alone have published, in the past ten years, over one hundred papers which depend on these instruments for their data.

What lies ahead for the Mass Spectrometry Facility is almost as exciting as its history. Both computer science and mass spectrometry constantly astound us with new developments. Even gas chromatography seems to be still in an ascending phase — for example, a group in my laboratory has recently developed a method for separating the dextro and levo isomers of sugars by gas chromatography.

This year, we received funds from the Division of Research Sources of NIH to rebuild our computer systems so that users can analyze the results of their last experiment while the computer performs a new analysis, unattended. This strategy alone will double our capacity. We have also begun experiments which should lead to entirely unattended operation for more routine analyses. An automatic sampler will inject samples into the GC-MS, initiate and terminate the run, clean the syringe and go on to the next sample or calibration standard.

Dwight Matthew, Ph.D., Research Assistant Professor in the Department of Medicine, is presently constructing an instrument which will be used to measure nonradioactive isotopes of carbon (13C) and nitrogen (15N) in biological substrates with much greater precision than has been possible before. The device is like a GC-MS in that the complex mixtures are first separated by gas chromatography. However, in this instrument each substance is converted to carbon dioxide and nitrogen gas in a combustion chamber as it emerges from the chromatography column. After combustion, the gases are led to a very stable and precise mass spectrometer where the 13C and 15N isotope content is measured. Using this technique, much greater dilutions of the tracer isotopes can be measured allowing, it is hoped, individual labeled amino acids to be infused into patients, thus permitting muscle metabolism to be evaluated, for example, with biopsy samples.

Several years ago it was found that certain molecules, under special conditions, form negative ions and that these substances could be detected with even higher sensitivities than we have described above. Amounts of material as small as a few femtograms (10^-15 grams) have been detected by this means. (One can reasonably ask how many molecules are necessary for the lower theoretical limit for detection. The answer is that negative ion systems are close to that limit.) We expect soon to begin studies with negative ions.

The most difficult area to move into, because of the initial cost and the decline in Federal science funding, is high-mass/high-resolution mass spectrometry. These instruments, which have resolution on the order of 100,000 as compared to 1,000 on the instruments we now use, cost approximately $500,000, and are capable of even greater selectivity in the case of ion monitoring for quantitative analysis. They also utilize devices which can vaporize large, involatile and unstable biological substances — peptides, such as the interesting opioid enkephalins for example — and can analyze their structures using minute samples. Promising results have also been obtained in connecting liquid chromatographs to mass spectrometers. This allows one to separate mixtures of substances that are not amenable to gas chromatography and to perform either structural studies or quantitative analyses on the purified materials. What lies ahead provides sufficient challenge to make the prospect exciting indeed.
Many readers are aware that the majority of elements are composed of more than one isotope, and are also familiar with the wide variety of artificially produced radioisotopes used in biomedical research, diagnosis, and treatment. However, they rarely consider that the major elements in their body are composed of naturally occurring non-radioactive and radioactive isotopes. Thus, approximately one percent of the body's carbon is composed of the nonradioactive isotope $^{12}$C and an extraordinarily small fraction (perhaps $10^{-9}$%) is composed of the naturally occurring radioisotope $^{13}$C. Measurement of the latter, of course, is the principle of radiocarbon dating. Likewise, approximately one percent of the body's potassium is composed of the naturally occurring radioisotope $^{40}$K. This isotope allows one to estimate body potassium and body protein content. Approximately 0.4% of body nitrogen is $^{15}$N and 0.2% of the body's oxygen is $^{18}$O. These isotopes assume importance because there are no nitrogen and oxygen radioisotopes of sufficiently long half-life to make them easily applicable to biomedical studies.

Furthermore, few physicians who grew up in the era of radioisotopes appreciate that the original tracer studies which demonstrated the dynamic state of body chemical components were performed with nonradioactive tracers. For approximately ten years beginning in the mid-1930's, Rudolph Schoenheimer, David Rittenberg and their colleagues demonstrated, in a now classical series of publications in the Journal of Biological Chemistry, that body protein, fat and carbohydrate are continually being renewed and broken down. These studies were performed using substrates labeled with the stable isotopes deuterium and nitrogen-15, the only isotopic tracers then available for biological investigation. However, the growth of radiochemistry after World War II and the advent of cheaply produced and easily measurable radiotracers in the 1960's brought an almost complete halt to stable isotope studies because nonradioactive tracers, by comparison, were difficult to obtain and to measure.

At the beginning of the last decade, several independent activities sparked a resurgence in the use of nonradioactive tracers for biomedical research. The first was the large scale production of highly enriched carbon-13, nitrogen-15, and oxygen-18 by scientists at the Los Alamos Scientific Laboratory. It is an important, interesting sidelight that this laboratory, which receives so much unfavorable publicity for its weapons research, is a major producer of nonradioactive isotopes for biomedical research. Yet the latter activity receives little mention in the press. The second major development was the commercial marketing of highly sophisticated GC-MS systems to measure nonradioactive isotopes in biological materials. The third event was the growing ethical concern about the use of radioisotope tracers for human research, particularly in children and women of childbearing age. Finally, in relation to the latter concern, research needs in pediatrics and obstetrics had reached the point where important questions could be answered only through the use of nonradioactive tracers. It was this need that started us on our first investigations in the area of nonradioactive tracer studies.

Newborn infants and young children are particularly susceptible to the development of hypoglycemia. This problem had been extensively investigated by Drs. Anthony Pagliara, Irene Karl, and Morey Haymond in Dr. David Kipnis' laboratory when I first arrived at Washington University. However, despite the accumulation of a large amount of important data, several rather basic facts were still unknown. For example, the normal rate of hepatic glucose production in the infant and child were unknown. Furthermore, there were absolutely no data in the human concerning the time of onset of gluconeogenesis in the neonate or on the relative contribution of gluconeogenesis to hepatic glucose output in the newborn or the young child. It was these rather basic, yet important, questions which led us to investigate the use of nonradioactive tracers to study these problems in children. Here (and with collaborators at other universities) employing both $^{13}$C and deuterium labeled glucose, we were able to show that during the growing years, the child produces glucose at a rate approximately 3-fold that of an adult, based on body weight. This rate was achieved even in premature infants as small as 650 g within a few hours after birth. Furthermore, we were able to demonstrate that gluconeogenesis is active in the newborn infant almost immediately after birth and appears to be well established by four to six hours of age. These rather basic data have been used to reference a wide variety of stable isotope tracer studies of abnormal glucose production in various pediatric diseases known to affect blood glucose homeostasis.

Our studies on gluconeogenesis raised additional questions
which, once again, could be approached through the use of nonradioactive, rather than radioactive, tracers. Although amino acids are a major precursor for new glucose production, little was known about the quantitative transport of various individual amino acids for this purpose, particularly in children. Likewise, there was little information in humans concerning the relationships between dietary protein and calorie intake and the breakdown of body proteins to supply such gluconeogenic amino acids for new glucose production. Despite the fact that $^{15}$N-labelled amino acids had been used for many years to study body protein metabolism, most prior methods were capable only of estimating $^{15}$N enrichment in urinary urea because large amounts of material were needed to make the appropriate mass spectrometric measurements. Therefore, little was known about the metabolism of the labelled amino acid itself.

Because of the sensitive and precise GC-MS techniques developed at Washington University, we were able to devise methods to trace amino acid, carbon and nitrogen in plasma amino acids and in intracellular amino acids from very small tissue specimens. These methods have allowed us to quantify the rates of transport and oxidation of certain essential amino acids (notably leucine, valine and lysine) as well as to study the exchange of nitrogen between various essential and nonessential amino acids in humans. With our collaborators at MIT, we were able to study systematically the role of excessive or deficient protein and calorie intake on these processes as well. These data, while also rather basic, are extremely important from the clinical standpoint when one realizes that a large number of the enteral
and parenteral nutritional replacement regimens currently employed in hospital practice are based strictly on empirical data, with very little firm physiologic information.

Stable isotope tracers have other important advantages. For example, obviously there is no problem of radioactive waste disposal. An additional advantage of particular interest to us is that these tracers can be given repeatedly to the same individual, a luxury not generally available in radiotracer investigations. This benefit means that a subject can serve as his or her own control when one introduces various test substances or experimental situations. Furthermore, it has allowed us to study the intrasubject variability in the transport of major metabolic fuels in humans. In other words, we can study how constant the rate of transport is for various important metabolic substances in the same individual over a period of time. Using deuterium labelled glucose, carbon-13 and nitrogen-15 labelled amino acids, and carbon-13 labelled fatty acids, we could study the transport of these substances repeatedly in the same individual, sometimes over a period of years. This type of data allowed us to show that glucose transport is extraordinarily constant in the same individual over a period of time. Amino acid transport, while somewhat more variable, is still reasonably consistent from study to study in the same person. Fatty acid transport, however, can vary remarkably in the same subject studied at different times. This information is important and necessary to define the confidence one can place in changes seen with various experimental or therapeutic manipulations.

In retrospect, after applying nonradioactive tracer techniques to a variety of problems in humans over the last several years, it seems remarkable that we didn't start employing these methods earlier. This realization has also come to pediatric investigators in other medical centers who have now begun to set up similar techniques for their own research problems in children. After learning the methods involved, applying nonradioactive tracer techniques to human investigation is no more difficult (and in many cases, simpler) than conventional radiotracer methods, so there appears to be no real justification for the continued use of radioactive tracers to investigate problems that can be approached with nonradioactive substances, certainly, at least, in the pediatric age group.
Air Pollution May Be Harmful To Cancer Cells

If every cloud has a silver lining, this might be it for the cloud of ozone, a major component of ground-level oxidants in polluted air. Three Medical School faculty members, the wife of one of them, and an alumnus of the School of Engineering, published an article in the August issue of Science concluding that ozone selectively inhibits the growth of human cancer cells when present at levels not harmful to normal cells.

The faculty members, all in the Department of Obstetrics and Gynecology, are: Frederick Sweet, Ph.D., Associate Professor; Ming-Shian Kao, M.D., Associate Professor; and Song-Chia D. Lee, M.S., chief research technician. Wileen Sweet holds a bachelor’s degree in chemistry from Southern Illinois University and is currently working toward a masters degree in civil engineering. She is employed in the air quality program of the East-West Gateway Coordinating Council. Will L. Hagar, who received his B.S. degree in chemical engineering from Washington University in 1952, is Chief of Technical Services for the City of St. Louis Air Pollution Control Division.

Although Frederick Sweet was the chief investigator in the experiment, in which cancerous and non-cancerous cells were cultured in controlled levels of ozone, the chief instigator was Wileen Sweet who persuaded her husband to organize a simple experiment for assessing the effects of air pollution on humans. Sweet explained: "The effects of air pollution on health have usually been assessed by correlating toxic substances present in the air for some time with the occurrence of certain diseases. I thought we could save time by coming up with a system for growing human cells in contact with a pollutant. In tissue culture, changes can be seen in seven or
eight days. If we found good correlation between the pollutant and the growth of cells, we would have a simple way of determining the effect of air quality on human cells." At the outset, they were seeking a laboratory model of the deleterious effects of specific pollutants, rather than the serendipitous outcome published in *Science*.

Will Hagar suggested using ozone as the test pollutant. Ozone levels in the air have been documented by various federal, state and local agencies in the development of air-quality standards. Hagar has worked in air pollution control for the City of St. Louis for more than 15 years. He pioneered in the development of St. Louis' air-quality monitoring system, in conjunction with Charles M. Copley, Jr., a city commissioner, who has an international reputation in the field.

The air-quality monitoring system, developed and used in St. Louis, has served as a model for many urban areas. Hagar has also constructed ozone-generating equipment for use in calibrating instruments which measure ozone in the air. One of these ozone generators was used in the project.

Sweet, Kao and Lee each had tissue cultures, both cancerous and normal, growing in their laboratories for use in various other projects. Thus, identified cells were available for exposure to ozone in the model system. A few square feet of space was made available in Sweet's laboratory, and the use of a dual-chamber incubator was donated by Dr. Kao.

To culture the cells in air containing ozone, filtered ambient air mixed with carbon dioxide was conducted through a calibrated ozone generator and into a sealed environmental chamber located in one side of the incubator. Both normal and malignant cells were also cultured in ozone-free air in the second incubator compartment. The cells were cultured for eight days at ozone levels ranging from 0.2 to 0.8 parts per million (ppm). (Clean air contains less than 0.1 ppm; smog has up to 0.5 or 0.6 ppm ozone.) Ozone levels in the air vented from the ozone chamber were measured with a spectrophotometric ozone analyzer; levels varied less than one percent per day.

The researchers found that ozone at 0.3 to 0.5 ppm inhibited cancer cell growth 40 percent and 60 percent respectively, and did not affect the growth of normal cells. Exposure to ozone at 0.8 ppm inhibited the growth of cancer cells more than 90 percent while affecting the growth of the normal cells less than 50 percent. They concluded that the mechanisms for defense against ozone damage are impaired in human cancer cells, an important weakness in cancer cells. Its potential use in treating cancer depends on how well ozone penetrates layers of cells. As the researchers wrote in *Science*:

"These findings lead us to believe that ozone — alone, as a supplement with radiation therapy, or in chemotherapy utilizing electrophilic compounds — may have therapeutic value for patients with certain forms of lung cancer."

No one is recommending that cancer patients rush to Los Angeles for deep-breathing exercises in the smog, however. The experiment raises many questions. "We found cancer cells of all kinds to be more sensitive to ozone than normal cells," Sweet summarized. "But we are eager to continue working on this and have applied for funding to the American Cancer Society."

The next phase, if funded, will be to acquire laboratory mice for use in related experiments focusing on more complex organisms.
Introducing The Class Of '84

by Casey Croy

The Class of '84 moved in during the latter part of August, endured the traditional Autumn rite of standing in lines, and began their studies at the School of Medicine. The 95 men and 27 women were chosen from the 6,278 who applied through the American Medical College Application Service. According to John C. Herweg, M.D. ('45), Associate Dean and Professor of Pediatrics, the School of Medicine usually receives approximately 6,000 applications each year, which is "more than most medical schools receive." Prospective students typically apply to 8 or 10 schools.

The Admissions Committee screens the applications, reviewing the prospective student's academic record and the perceived quality of the undergraduate school, the courses taken and the grades earned. The committee also studies recommendations from the faculty at the undergraduate institutions. Committee members are responsible for being knowledgeable judges of undergraduate colleges and universities, with each member responsible for a geographic region of the United States.

After screening, the committee selects approximately 1,000 students to interview personally. According to Ernest S. Simms, Associate Professor of Microbiology and Immunology and member of the Committee on Admissions, the interview process is seldom simple, for committee members or applicants alike. "Essentially, all of the prospective students are academic successes, but the levels of difficulty they have experienced varies a lot. Assessing academic capabilities is easier than assessing the less defined characteristics which are of importance in selecting future physicians. We are interested in the suitability of the applicant's personality to deal..."
with people, especially in the physician/patient relationship. Concerns and motivations vary a lot, from economics to making real contributions to society,” Simms said. “Sometimes, people present themselves less accurately than the committee would like.”

After the interviews, the committee reviews Medical College Admission Test (MCAT) scores and undergoes the throes of deciding who shall receive notices of acceptance. “Most of the students accepted here are also accepted by other schools,” Herweg said. “In fact, 50 percent last year had at least one offer, 75 percent had three or more offers, and 37 percent had five or more offers.”

The 122 students entering this year represent 28 states and two countries—Trinidad and China. They come from 60 undergraduate schools. Seventeen earned their degrees from Washington University. Seven came from the University of Illinois at Urbana. Johns Hopkins and Stanford each have six graduates in the new class. Four came from the Massachusetts Institute of Technology, and four from Yale. Northwestern, Notre Dame, Vanderbilt and Williams College each sent three. Six students entered with Masters Degrees; 54 with Bachelor of Science degrees, and 67 with Bachelor of Arts degrees. One entered with no degree, after only three years of undergraduate work. Some entered several years after having received bachelors or masters degrees and having worked in other fields.

According to Herweg, “we start with 120 or so in the entering class and increase to 140 during the third year. There are medical schools in the United States which admit more students for the first two years than they can handle in the third, or clinical clerkship, year. With six hospitals and almost 2,000 patient beds in the Washington University Medical Center, we can accommodate additional students for the third and fourth years. We feel that we are fulfilling a national need, and we know that we get excellent students from other schools for the third and fourth years.”

“This entering class is going to be a lively group,” said the man who has met them all in Anatomy lectures and lab—Roy R. Peterson, Ph.D., Professor and Acting Head of the Department of Anatomy and Neurobiology—sharing an anecdote. In honor of the debut of a lecturer from Texas, a contingent of the class showed up wearing cowboy hats. Peterson describes the class as “communicative,” adding “they let me know about problems in a way that is considerate, but not demanding. There was more of an aggressive, demanding attitude in the Sixties and Seventies. Now, they make logical presentations and stimulate discussion, leading to a response, not a reaction.”

Peterson, who came to Washington University as an instructor in 1952, enjoys contact with the students and observing the classes through the years. “A class develops a personality that is different, somehow, from other classes around it. The students come together from a lot of different schools and backgrounds, and the personality of a class evolves from the interactions among the students and from the ways and times in which they were brought up.” Peterson, a former Teacher Of The Year, says that frequently the people with the strongest influences on the personality of a class are not the visible spokesmen or spokeswomen.

Among the many forms to be completed by the entering class during registration and orientation is the Outlook Magazine Survey. Not all of the students completed all sections of the survey, but among those who did there is ample proof of Professor Simms’ comment that prospective students “are academic successes.” Thirty-seven members of the entering class are members of Phi Beta Kappa; seven are in Phi Kappa Phi; four are in the Bronze Tablet society, and three are in Sigma Xi. Thirteen graduated Summa Cum
Entering Class Profiles:

Martin Arkin

In a school with many musicians, people like Martin Arkin will probably be in great demand. "When it comes to music," Martin says, "I like to listen." He is from Lathrop Village, Michigan, a suburb of Detroit, and he earned his B.S. degree, with honors, in cellular and molecular microbiology at the University of Michigan in Ann Arbor. Martin became interested in MST programs and applied to ten schools. He was accepted by three which offer the combined M.D./Ph.D. The head of neurology at the University of Michigan recommended Washington U. to him. During the interviews, he talked to many people doing research here and found great variety and a wide range of opportunity. He has some experience in laboratory work in biochemistry and neurosciences, which he described as "challenging and frustrating," and wants to devote time to both clinical and basic neuroscience research.

As an undergraduate, he worked on some grassroots political campaigns and enjoyed racquetball. To keep in shape, he runs three miles a day in Forest Park. His major hobby has been cross-country motorcycling, which he has been doing for seven years. "I bought a bike to ride on some open land near our house," he says. "Then I wrecked it and bought another." He claims that cross-country motorcycling is not as dangerous as either street-bikes or motocross, an obstacle race. "In cross-country, we have a variety of terrains to cross and need more skill than speed. It's a good way to stay in shape."

He plans to bring his motorbike to St. Louis, probably in the spring. In the meantime, "the workload is incredible!"
Fred Barr

The "Special Interests" line on his questionnaire reads: "theatre, soccer, penguins" in a clear, block-style lettering that a technical illustrator or drafter would envy. "Penguins" is the name of a hockey team, isn't it? But Fred Barr was not referring to a team. He really meant penguins, the funny, formal, flightless birds that walk like Charlie Chaplin in the old movies. Fred's collection, variations on a theme, includes penguins in practically every form imaginable, except living. He has penguins depicted in books and on posters, towels, shirts, sheets and soda cans. He has ceramic and plush penguins, a pinata penguin, a custom-made sand-painting terrarium depicting a penguin (made by a friend), and an antique penguin given to him by the father of a former girlfriend.

Fred first became interested in penguins while writing a paper on them for a fourth-grade assignment. He bought a small ceramic penguin, and he and his family and friends expanded the collection through the years. The Barr family lives in the suburbs of Baltimore, Maryland. Fred's father, Harold Barr, is an engineer, and his mother, Barbara Barr, is a vice-principal at an elementary school. Fred received his B.A. degree in Chemistry from Williams College in Massachusetts, graduating summa cum laude with highest honors in Chemistry. At Williams, Fred also wrote and directed musicals; he plans to be active in class skits here. St. Louis is the farthest west he has ever traveled. He describes the city as comfortable and "fathomable" in comparison with the sprawling megalopolis of the East Coast area. When he first began applying to medical schools, his parents tended to remind him of how far away they were in terms of hours or half-day drives. Washington U. was the farthest, but at decision time, distance was not a major criterion.

"In high school, I began leaning toward medicine or science," he said. "In college, I knew that I wanted to stay in academia, and I have hopes for a medical school faculty position eventually." He applied to nine medical schools, withdrew from two and was accepted by six. He chose Washington U. because of its Medical Scientist Training Program (MSTP). The hobby that began with an essay also led to Fred's approach to his essay for acceptance at medical school. "I talked about penguins in the first paragraph because it was a good way to individualize myself."

Bob Burgerman

With an engineering degree that launched most of his peers into careers, Bob Burgerman entered medical school. "I knew when I was in high school that I wanted to go into medical school," he said, "and I thought that electrical engineering would be a good background for the kind of medicine I was interested in -- neurosciences."

Bob came from Bethesda, Maryland, to study at Washington University School of Engineering because he could combine engineering with pre-med courses. He admitted that having an engineering degree "was an ace in the hole" in case he was not accepted into a medical school. He describes himself as more comfortable with the theory, mathematics and systems analysis aspects of electrical engineering than with circuit design, breadboarding and practical applications. Bob is a cum laude graduate and member of Tau Beta Pi, the honorary society for the engineering disciplines. He was more successful in college than in high school. "I didn't have much of a goal until I was in college. In high school, the future seemed very distant. Then, in college, I knew that it was time to make decisions and do my best. Some people do the opposite, getting motivated in high school so they can get into college. Then, they seem to be less motivated because they have made their goal."

Bob is the son of a physician, Arthur Burgerman, M.D., an endocrinologist in private practice in Washington, D.C. He has an older sister and a younger sister. He enjoys rock, jazz and blues, and plays saxophone, clarinet and guitar.

He was accepted by three medical schools and put on the waiting list at two more. He chose Washington U. because of the opportunities in neurosciences. His major interest at this point is biomedical engineering applied to neurology, and he hopes to become involved in a neuroscience research project. He worked one summer and one semester in an ophthalmology lab at the School of Medicine, and also worked for a time as an engineer in the Water Division of the City of St. Louis.
Mark Cooper

He entered medical school (the first in his family ever to attend graduate school) with no degree at all, just a string of honors and a straight "A" average after three years at the University of Oklahoma in Norman, in the chemical engineering and pre-med program there. Before assuming that a young man from a small Oklahoma town (Pryor, population 9,000) would be impressed with a city like St. Louis, be informed that Mark Cooper has played alto saxophone in a band concert in Carnegie Hall and several concerts in Europe. The band, America's Youth In Concert, was part of the Bicentennial celebrations and auditioned musicians from all 50 states. Mark also played alto sax in the marching band at Oklahoma, and enjoyed trips to the Orange Bowl.

He said that he has wanted to be a doctor "from the time I was a little kid and people would ask what I wanted to be when I grew up." He enjoyed science classes in high school, and enrolled in pre-med in college. He took the MCAT test in his sophomore year, and the following summer worked at a state hospital in Norman, on the geriatrics ward. "It was a wonderful experience, with a lot of personal contact with the patients there."

It was this experience which led him to apply to medical schools. In his junior year, he learned that he had been accepted by several medical schools, so he took liberal arts courses during the second semester, rather than following chemical engineering. "I called up several physicians in the Norman area and introduced myself and asked their opinion about the schools that accepted me," Mark said. "They were nearly unanimous about Washington University and recommended that I come here."

His experience on the geriatrics ward continues to be an influence on Mark, who hopes to "look deeply into geriatrics as a specialty." Knowing that the U.S. population is aging faster than it is reproducing and believing that many elderly do not have adequate health care, Mark says: "It would be a hard specialty to handle on the personal level. You can't cure old age. I wonder if I could handle the feelings of being so limited in what can be done for the elderly."

Mark's father and mother, Clomer and Avil Cooper, own a wholesale pipe and fittings business in Pryor. "My father started the business, and all along, it was sort of expected that I would take it over," he said. However, his older sister is a certified public accountant and she and her husband are involved in the business. I'm glad that it will stay in the family." Mark says that his older sister, a former Junior Miss and first runner-up in a Miss Oklahoma pageant, "was a great role model for me in her success. I'm proud of her." He credits his parents with motivating their children to make the most of whatever talents and abilities they have.

Kaya Sila

Kaya Sila was born in St. Louis while his parents, Basri and Ulgan, were serving their residencies here. They had received their M.D. degrees at the University of Istanbul, Turkey. Kaya doesn't remember much from his early life in St. Louis, except for having his leg set in a cast at Barnes Hospital. He spent some of his early childhood in Istanbul, but has lived in Baltimore, Maryland, since the age of six. His parents are in private practice there. Basri Sila, M.D., is a child psychiatrist; Ulgan Sila, M.D., is a pediatric allergist.

Growing up in a family with both parents practicing medicine "doesn't seem to be any big deal," he says. "I'm surprised that there aren't more in the class from households like that." One benefit, he says, is "there were always plenty of interesting things to talk about in the evenings." Kaya says he never considered being anything but a physician, but that his younger brother, now a sophomore at the University of Pennsylvania, doesn't seem oriented toward medicine. Kaya earned his B.A. degree in biology at Swarthmore College, and is glad to have a liberal arts background. "Specialization comes later. I think you get a balanced outlook with a liberal arts education and benefit from being with people majoring in something other than science. It is a good opportunity to expose yourself to diverse subjects." He particularly enjoyed ethnology studies.

Kaya applied to fourteen medical schools, "and I made it clear to my parents that I did not want to come here. At least at first." He was accepted at five schools, and the more he learned about Washington U., the more interested he became. "There were good friends here, very supportive and warm, and they influenced my decision."

For relaxation, he lifts weights. "I used to spend as much time as I could on the beaches back home. I will miss them." On the other hand, there is some good to be said for some of the nearby rivers.
Ronald G. Evens, M.D., Director of the Mallinckrodt Institute of Radiology, and A. Everette James, Jr., M.D., Professor and Chairman of the Department of Radiology and Lecturer in Legal Medicine at Vanderbilt University, who presented the ninth annual Wendell Scott lecture.

Wendell Scott, M.D., a 1932 graduate of Washington University School of Medicine, served his internship and residency at the Washington University Medical Center, at Barnes Hospital and the Mallinckrodt Institute of Radiology. A distinguished member of the faculty, his honors included the Gold Medal of the St. Louis Medical Society and the American College of Radiology, the President's Medal of the American Roentgen Ray Society, and the National Award of the American Cancer Society. He served as president of the Washington University Medical Alumni Association, the St. Louis Radiological Society, the American Roentgen Ray Society, and the National American Cancer Society. He died in 1972, and friends and colleagues established the lectureship as a living memorial to his loyalty and excellence.

The ninth annual Wendell G. Scott Memorial Lecture was held in the Scarpellino Auditorium in the Mallinckrodt Institute of Radiology on September 8. A. Everette James, Jr., M.D., spoke on law and medicine. James received his M.D. degree in 1963 from the Duke University Medical School. He served in the U.S. Army for two years, including duty in South Vietnam. During his military service, he received a law degree from the Blackstone Law School. He trained in radiology at Harvard Medical School and the Massachusetts General Hospital, later receiving a post doctoral degree from Johns Hopkins. He received an honorary fellowship of the Royal Society of Medicine, and studied physiology at University College. After five years as a member of the faculty of Johns Hopkins Medical School, he was named Professor and Chairman of the Department of Radiology and Radiological Sciences at Vanderbilt University, where he also serves as Professor of Medical Administration and Lecturer in Legal Medicine, and as a research associate in The Institute for Public Policy. He is president-elect of the Society for Chairmen of Academic Radiology Departments. He is consultant to the Smithsonian Institutions, National and Regent's Zoological Parks, National Institutes of Health and Armed Forces Radiobiological Research Institute. James is a member of the National Council of Radiation Protection, Explorer's Club, National Health Lawyers Association, International Platform Association, American Veterinary Radiology Society, and the National Trust for Historic Preservation. James has authored over 200 manuscripts, 50 chapters, and 9 texts.
I am most honored and appreciative of the opportunity to present the Wendell G. Scott Lecture at a time in which many facets of my intended discussion appear to be of compelling interest and immediate concern. In the general context of our society, medicine, and more specifically, the discipline of Radiology and Radiological Sciences, represents a microcosm of the predicted external forces of the 1980’s.

In this communication, I would have us consider the current circumstance of American medicine and its relation to the field of law. We should reflect upon an appropriate response to various societal trends and public policies which appear to be profoundly influencing our chosen profession. I hope to characterize some of the basic and fundamental qualities and positions of the fields of law and medicine. This exercise is intended to demonstrate that, although at any particular point of reference or inquiry, these disciplines may seem to be in conflict, their ultimate goals are similar.

The practice of medicine grew from man’s basic instinct to heal and assist fellow beings. Law was designed to provide persons living in a social circumstance with a structured methodology to protect, preserve, and maintain their rights. Both of these honored professions have origins in laudable instincts and are certainly praiseworthy in their concepts. One would believe that compatibility and mutual purpose would be a natural result of the activities of these practitioners who are characterized as concerned, dedicated and highly skilled.

The increasing complexity of our society appears to stress the differences among certain professional groups, even though the differences may be small compared with similarities. I suggest that a significant factor is that the approach and techniques of achieving the purpose of these two professions are fundamentally disparate.

Conceptually, medicine emphasizes the use of a body of proven data to deduce the proper course of action and to encourage collaboration and goodwill among colleagues. Group activities and attitudes to incur good favor among peers are emphasized throughout a career of medical practice.

The law promotes utilization of a body of rules, facts and opinions as guidelines for professional conduct which is, by its nature, adversarial. Attorneys are trained to use these data to establish the truth of a particular line of reasoning. The lawyer’s responsibility includes dealing with similar data leading to different conclusions, often weighed in a public forum. Attorneys are trained to emphasize the validity of the available data to benefit their clients. In so doing, they may deemphasize cooperation and collaboration with their adversarial colleague in any particular and specific litigation procedure. Thus, we must accept the fact that although both professions have a purpose and investment in public welfare, the differences in attitudes and approach may be manifest by a lack of acceptance by each group for the activities of the other.

To examine the concept of differences between law and medicine from another aspect, these professions are those of well-being; the law for the well-being of society in general terms, and medicine for the well-being of physical and emotional health in a more individual context. The law is directed toward process whereas medicine is directed toward effort. The fundamental principle of medical practice is the relationship of trust between physician and patient. In legal terms, the patient is the jury while the physician is the initiator of thought and provider of evidence. Medicine approaches patients and their ailments as a scientific endeavor generously laced with human compassion.

The legal profession focuses upon the complaint of the client as if it were a fundamental truth and accepts the adversarial mode as the appropriate process. Often it seems as if we are dealing with two sides of the same coin, but struck from a different mold. The law must be accepted as part of the ecology of medicine much in the same way as nutrition, cleanliness, and immunization are. This communication will explore one particular facet of the interaction of the disciplines to emphasize the effects of the activities of each profession on the other. Additionally, the public responsibility they share will be emphasized. Certain public policies will be examined under the considerations of antitrust policy.

The relevance of antitrust law to the practice of medicine would have escaped both professions only a few years ago. Now, however, antitrust is assuming an ever-increasing role in the delivery of health care. This is in large part due to three fundamental developments to be considered here. Until the U.S. Supreme Court’s decision and opinion by Chief Justice Burger in the case of Goldfarb vs. the Virginia State Bar, it was generally accepted that the “learned professions” of law and medicine were exempt from antitrust considerations. This traditional concept was clearly put to rest by an opinion in which the court held that there was no intention in the initiation and application of antitrust policy to provide such an exemption. Traditional wisdom had also noted that antitrust laws apply only to interstate commerce; it had been successfully argued that the delivery of health care if considered a business at all, was most certainly an intrastate business. Today, several federal agencies, and more importantly the courts, do not seem inclined to accept that position. A landmark example is generally considered to be the holdings and opinions expressed in Hospital Building Company vs. Trustees of Rex Hospital. In this case it was found that if, in the conduct of normal activity, there is a potential for use of goods, services, or assistance rendered to persons or firms that reside outside of a state, then interstate commerce is involved.

The Federal Trade Commission has recognized that the delivery of health care is a major industry involving some 10% of the gross national product, with a current expenditure of approximately 200 billion dollars. Beginning in approximately 1976, the FTC launched a major investigation of the degree of competition prevailing within the industry of medicine.

Any policy analysis and interpretation of antitrust law is significantly compromised because of an absence of a general consensus as to the underlying purposes of antitrust legislation and the accommodations that seem most reasonable for present and future applications. The most commonly suggested considerations that support an antitrust policy are allocative and productive efficiency, wealth transfer or redistribution, economic deconcentration, and a sense of business ethics. One might suggest that consumer welfare — and in the medical context, patient welfare — is the most appropriate antitrust objective.

The general considerations of antitrust law should begin with the Sherman Act of 1890, which has two important sections. Section one proscribes contracts, combinations or conspiracies in restraint of trade. This mandate is rather broad and at times undefined. Section two is more circumscribed and forbids all activities which lead to monopolization. The Clayton Act of 1914 forbids certain marriages,
Hospitals have traditionally been accorded to physicians who apply with little inquiry as to the policies and due process afforded to the applicants by the facilities. Because the physician is seeking a position in the marketplace, the health-care facility, exclusive-privileges contract law appears to be most applicable. The problems with applying this concept to the complexities of a health care delivery system is clearly elucidated in several well-known cases that have particular importance to the discipline of medical imaging. In *Harron vs. the Union Hospital Center, Inc.*, there was a consolidation of hospitals in a small community. For a period of time, two radiologists were allowed entry into the hospital with unconstrained practice privileges. Subsequently, one of these radiologists was given a contract and made “the” radiologist for that hospital. Thus, Harron, in an antitrust context, was eliminated from the marketplace. This case is a consideration of the delivery of a service and not a product; thus it is excluded from the Clayton Act which applies only to arrangements involving goods, products and supplies. Recently, however, radiological consultation has been interpreted as a product in some jurisdictions. The logic applied is that the activity results in an image (most often a film with data upon it). This line of reasoning appears inconsistent with applications in both business and other areas of medicine.

The Sherman Act would be invoked under considerations of service. An exclusive-dealing contract of the type described in *Harron* has not been deemed a *per se* violation under the Sherman Act considerations. Therefore, one could apply the rule of reason and use of evidence to support the concept that public (patient) welfare is best served by having an exclusive-privileges contract with a single radiologist. If successful, this action would be upheld by the court. One might question what is the marketplace which could be considered.

In the case of Harron, with only one hospital in that community, exclusion would represent a market foreclosure of 100% if the locale were chosen as the standard of reference. One might propose however, that the market for radiological services should be considered national in scope, and exclusion from a single hospital should have an insignificant effect on the health care system.

A very important case in an analysis of antitrust considerations in the discipline of medical imaging is that of *Datillo vs. the Tucson General Hospital*. Datillo was denied staff privileges at the Tucson General Hospital in a closed-staff arrangement in which the hospital had secured the services of another radiological group. Applying the rule of reason, the defendant attorneys demonstrated to the court’s satisfaction that the public welfare was best protected by the type of closed-staff arrangement which had been applied. This posture was found to be necessary in order to standardize practice procedures, to allow the Board of Trust to monitor professional activities, to determine professional standards at all levels in the radiology department, to have increased efficiency due to more appropriate scheduling of procedures and to provide consistency of radiological consultation. The court concluded that the restriction by Tucson General Hospital was a reasonable one and relied, in large measure, upon the testimony of various hospital administrators and the chairmen of radiology departments in that locale.

The particular characteristics of an academic radiology or clinical department can have antitrust implications. In a university center and teaching hospital, the particular form of closed-staff policy and the division of professional responsibility have numerous parallels in the business world. The landmark decision involving an academic department of radiology is contained in *Bland vs. Palo Alto Stanford Hospital Center*. The department, on the advice of other academic centers, decided to subspecialize in the discipline of radiology. Thus, each staff member was to have a specific area of expertise (such as neuroradiology, pediatric radiology, etc.) and each was, in large measure, to orient professional activities accordingly. Under a staffing arrangement of this type, the general radiologists were not particularly welcomed members of the permanent full-time faculty. This professional arrangement policy was challenged by a practitioner of the discipline who did not wish to confine himself to what he believed to be such a narrow field of expertise.

The court relied upon the testimony of academic radiologists and hospital administrators to determine whether the closed-staff policies were necessary in this circumstance. They applied the rule of reason to decide whether this was an illegal group boycott. The courts sought to determine whether or not the contract with the hospital had as its primary purpose the creation of a monopoly, and if a monopoly were so created, whether this circumstance was attended by any dominant social or economic justification. The “social” justification here was considered to be that of training of students, residents and fellows, as well as consultation with other subspecialty faculty members. Boycott case law has a number of important precedent decisions. One of the more famous was that of the *United States vs. Terminal Railroad Association*, in which there was a question of access to the city of St. Louis. It was held that exclusion of some firms from participating in a joint venture to acquire terminal facilities was illegal by virtue of the importance of access routes to that city. A number of cases are equally important, but the finding in each appears to have rested upon whether or not the defendant controlled some resource necessary to the success of a particular trade or business. One
of the fundamental issues in these cases, with regard to medicine, is to determine whether the analysis should fall under an exclusive dealing contract or a group boycott. Group boycotts would be deemed per se violations of antitrust law, and thus the courts need not determine whether or not public welfare is protected by the activity.

These recent cases have involved the question of physicians providing consultation for practitioners of chiropractic. The cases of Slovek and Wilk specifically involve consultation by radiologists at the request of chiropractors. The more general case is that of the American Medical Association's Principles of Medical Ethics. Many believe that these considerations hinged upon whether or not concerted refusal to deal case law was relevant, or whether these cases be considered under group boycott. If group boycott is held to be of primary concern, the rationale of the boycott participants would be irrelevant. Even if it could be established beyond any doubt that the activity was predicated on a reasonably held belief to insure the best health interests of patients by not consulting with chiropractors and that the activity was not intended to be anti-competitive, a decision for the plaintiff chiropractors would still be forthcoming.

Even with concerted refusal to deal as the primary antitrust policy, anti-trust implications can still be established. Among the landmark cases is that of Fashion Originators Guild of America in which the per se principle is applied. The Fashion Originators Guild refused to deal in a business sense with persons and firms that either stole or copied patterns. Although these activities were immoral or possibly even illegal on the part of the "style pirates," the group quality of the action of the Fashion Originators Guild made this a group boycott and illegal on per se grounds. A somewhat more complex case is that of Blalock vs. the Ladies Professional Golf Association. Ms. Blalock, because of alleged cheating during tournaments, was dismissed from the ladies golf circuit by a group of her peers. In determining the methodology by which Blalock was excluded, the court felt that due process had not been respected and that the criteria applied may have been specifically created for this determination. The major policy question that arises from this decision is whether or not a private association can engage in boycott activity to insure quality and honesty in the performance of its members.

A case related to Blalock is that of Deesen vs. the Professional Golf Association in which Deesen challenged the methodology of qualifying rounds to determine whether a professional could participate in any given tournament. In analysis of the methodology employed, the courts felt that this was a reasonably uniform standard in which the number of strokes in the qualifying rounds determined whether one could play in a given tournament. The Professional Golf Association demonstrated that if tournaments were held open to anyone who wished to participate, the facilities would never permit com-
The conduct of these specialty board examinations has come under analysis by the Federal Trade Commission. It has been suggested that such practices, but also the inherent motivation. We must accept the mode, procedure, and process of our attorney colleagues as one characteristic of their profession and have them, in mutual accord, accept the efforts and practice of an industry based upon the fundamental physician-patient relationship.

The courts will have to determine whether or not the mandate given the hospitals and their trustees by certificate-of-need legislation is superior to the interest of individual patients and their physicians. Hospital privileges in this context would be a necessary scarce resource and would be considered as an asset essential for the conduct of a particular activity. Under the supremacy clause of the federal Constitution, the presence of a federal mandate has been historically considered sufficient to insulate what appears to be an anticompetitive program from the scrutiny of antitrust laws. One would predict that, in the immediate future, a rather inhomogeneous application of this type of logic will be seen.

Antitrust laws presume that the desirability of a competitive system and the competitive model depends upon the existence of informed and rational consumers. It presumes that consumers are given free entry into the industry. With this type of logic, certification and specialty boards are looked upon primarily as mechanisms for guild protection and not for protection of the public. Therefore, the conduct of these specialty board examinations has come under analysis by the Federal Trade Commission. It has been suggested that such practices and the conduct of board examinations should be changed in their nature to allow the public and consumers a much more important role. Physicians and organized medicine have contended that the formal nature to allow the public and consumers a much more important role.

The rising costs, a number of policies have been enacted. Prominent among these has been certificate-of-need (CON) legislation. Certificates of need pose a significant antitrust problem because of the quasi-monopoly rights created by the limited number of certificates. Consider the circumstances leading to recent litigation involving the combination of granting of hospital privileges and the effects of certificate-of-need application. Certificate-of-need legislation, by its very nature, will limit the distribution of scarce resources. Distribution limitations may also effectively limit access also. These considerations are particularly relevant in the discipline of medical imaging, in which resources would be instruments such as the computed axial tomographic (CAT) scanner, ultrasound equipment, cardiac catheterization laboratories, megavoltage therapy units, and nuclear medicine devices. If certificate of need places these costly and sophisticated technological advances in a specific and particular hospital, then a physician's patients might be denied use of this medical resource by the very fact that the physician does not have privileges of patient admission to that particular hospital.

For organized medicine, the time-honored use of certification and specialty board examination has been employed to insures patient welfare. A more recent development is that of certificate-of-need (CON) legislation to assist in slowing the continued growth of hospital costs. Using antitrust analysis, it has been shown that, by both microeconomic theory and empirical study, restrictions of the available supply of goods or services will result in higher prices than would exist given free entry into the industry. With this type of logic, certification and specialty boards are looked upon primarily as mechanisms for guild protection and not for protection of the public. Therefore, the conduct of these specialty board examinations has come under analysis by the Federal Trade Commission. It has been suggested that such practices and the conduct of board examinations should be changed in their nature to allow the public and consumers a much more important role.
Bruce Allen Bach, Ph.D.,
fourth-year medical student, 
received a SmithKline Foundation 
Medical Perspectives Fellowship 
from the National Foundation for 
Medical Immunology. Bach, who 
holds a graduate degree in im-
munology, will conduct research 
at the Center for Disease Control 
in Atlanta, and at the University of 
London, England, on the use 
of vaccination to control the con-
genital rubella syndrome.

Jean M. Dwyer,
fourth-year medical student, 
was awarded a fellowship by the 
American Association of Univer-
sity Women Educational Founda-
tion. According to the AAUW, 
1,200 women applied for the 100 
fellowships awarded. The AAUW 
was founded in 1882 and now 
has 190,000 members in the 
United States, Puerto Rico, 
Guam and the Virgin Islands.

Irving I. Gottesman, Ph.D., 
formerly Director of the Behav-
ioral Genetics Center at the Uni-
versity of Minnesota, has joined 
the faculty as Professor of Psy-
chiatric Genetics. Gottesman has 
directed research into the in-
heritance of schizophrenia for 
more than 20 years, concentra-
ting on schizophrenic twins who 
did and did not have affected 
co-twins. He has written or 
colauthored more than 90 scholarly 
papers and three books on ge-
netics and personality devel-
opment. In the Department of 
Psychiatry's Clinical Research 
Center for Epidemiological 
Genetics and Family Studies, 
Gottesman will be one of four 
co-principal investigators work-
ing on the causes of the familial 
clustering of many mental dis-
orders. Theodore Reich, M.D., 
is director of the center. In October, 
Gottesman presented a paper, 
"Genetics and Schizophrenia," 
at an international symposium, 
in Montreal, Canada.

Samuel B. Guze, M.D., 
Vice Chancellor for Medical 
Affairs, was installed as Chair-
man of the Board of Directors 
of the Association of Academic 
Health Centers (AAHC) at the 
annual meeting in October in 
Tarpon Springs, Florida. He has 
been a member of the board of 
directors since 1976 and was 
previously chairman-elect. The 
AAHC is a national educational 
association of institutions of 
higher education with teaching 
hospitals and programs in med-
cine and one or more other health 
programs.

Stanley Lang, Ph.D., 
associate professor of physiol-
ogy and biophysics, was one of four 
Washington University faculty 
members honored at the Founders 
Day banquet in October for 
their "outstanding commitment to 
teaching, and dedication to the 
intellectual and personal growth 
of students." Lang came to St. 
Louis in 1954 as a physiologist in 
the surgery department of Jewish 
Hospital and instructor at the 
Medical School. He was appoint-
ed to the full-time faculty in 1966. 
He has published more than 60 
scholarly papers and was named 
Teacher of the Year in 1974.

Michael J. Welch, Ph.D., 
professor of radiology and chem-
istry at Mallinckrodt Institute of 
Radiology, received the Paul C. 
Aaberg Award, the highest 
recognition for science conferred 
by the Society of Nuclear Medi-
cine. Welch is the first hot-atom 
chemist to be involved in using 
a cyclotron to make short-lived 
radiochemicals. He was 
honored for his numerous contribu-
tions to the development of 
short-lived radiochemicals, 
clinical uses of them, and for 
training scientists in nuclear 
medicine.

In Memoriam

A memorial service was held on 
October 11 in Graham Chapel for 
William T. Newton, M.D., Profes-
sor of Surgery, Surgeon-in-Chief 
and head of the Washington 
University Surgical Service at 
Cochran Veterans Administration 
Hospital. Dr. Newton, 53, died 
on September 25, several weeks 
after surgery, at the Jackson 
Memorial Hospital in Miami, 
Florida. Featured speakers at the 
memorial service were Chancellor 
William H. Danforth, M.D., 
C Alan McAfee, M.D., Associate 
Professor of Clinical Surgery, 
and William W. Monafo, M.D., 
Professor of Surgery.

Describing Dr. Newton as "every-
thing a faculty member should 
be," Chancellor Danforth said he 
was "intelligent and curious, a 
true intellectual in the best sense. 
He loved to work with young peo-
lies and to pass on to them the 
knowledge and the insight that he 
had, and... to learn with them."

A colleague and fishing compa-
nion, McAfee shared with the 
audience several memories of fish-
trips, and described Newton as 
a "proud husband and a proud 
father. He was also a historian, 
a gourmet cook, an entomologist, 
a fly-fisherman and an excellent 
dry-fly fisherman." Newton is 
survived by his wife, Patricia, a 
daughter and three sons.

Monafo briefly highlighted 
Newton's youth and career. 
Newton was born in Texas, and 
was an outdoorsman from his 
boyhood days. He served in the 
U.S. Navy, received his B.S. from 
Yale in 1944, and was graduat-
ed with honors from the Yale Medical 
School in 1950. He received the 
Campbell Prize. He scored the 
highest grade in Surgery on the 
examination of the National 
Board of Medical Examiners 
and was awarded an Honor Cer-
cificate. He entered the post-
graduate surgical program at 
Washington University in 1950, 
and in 1958 completed the Chief 
Residency in General Surgery. 
In 1957-58, he was a research 
fellow in the Immunology Labo-
atory of Dr. Herman Eisen. 
Throughout his career, Newton's 
principal research interest was 
in basic immunology and in clin-
ically related problems in tissue 
transplantation, especially renal 
allotransplantation. He initiated 
clinical renal transplantation in 
St. Louis. A member of the full-
time faculty since 1958, Newton 
was appointed Chief of the Wash-
ington University Surgical Service 
at Cochran Veterans Administration 
Hospital in 1961, and was 
He became Professor of Surgery 
in 1972.

"Although he always had numer-
tous teaching and administrative 
responsibilities," Monafo said, 
"he personally conducted scienti-
fic research throughout his 
career. He loved to work at the 
laboratory bench, where he was 
meticulous, patient and clearly 
content. Over the years, he self-
lessly and willingly devoted much of his time to helping others — particularly young investiga-
tors — resolve methodological or other difficulties in their research projects. This important contribution, which was sustained during his 20 years on the faculty, was characteristically often an-
onymous. Despite that fact, his bib-
liography still includes more than 70 different co-authors; it stands as partial testimony to the extent of his scholarly interactions with others in the University. Clinically, he expertly headed a large teaching 
service... in a way that encour-aged maturation of the technical 
and diagnostic skills of his house 
officers, yet appropriately 
emphasized the biological 
basis of surgical practice... He served loyally. He contributed 
significantly."
Former House Staff

Fedor Bachmann, M.D., was appointed acting chairman of the Department of Medicine at the University of Lausanne Medical School in Switzerland.

Roger Brumback, M.D., was promoted to associate professor of neurology at the University of North Dakota School of Medicine.

Paul J. Goodnick, M.D., is on the faculty at Wayne State University, Allen Park, Mich. He presented a paper entitled, “CSF Amino Acids in Aging and Depression” at the annual meeting of the American Psychiatric Association, which was held in San Francisco in May 1980.

Robert F. Owen, M.D., Florissant, Mo., was elected to membership in Sigma Xi, the Scientific Research Society.

Kevin Pranikinoff, M.D., Williamsville, N.Y., completed his urology residency at the University of Rochester, last June. He is currently an assistant professor of urology at the State University of New York at Buffalo.

Jesse Roth, M.D., chief of the Diabetes Branch of the National Institute of Arthritis, Metabolism and Digestive Diseases, was named the winner of the first annual Lita Annenberg Hazen Award for outstanding achievement in clinical research. The $100,000 award was presented to him last November at a dinner held in his honor at the St. Regis Hotel in New York. Dr. Roth also received two other scientific awards last year, the prestigious Diaz Cristobal Prize for excellence in the field of diabetes research, and the third annual Berson-Yalow award for the development of new assay methodology.

Don M. Samples, M.D., New Orleans, reports that the hematology-oncology section at the Ochsner Clinic is staffed entirely by former WU housestaff and a WU alum. They are: William R. Arrowsmith, M.D., George H. Porter, III, and Carl Kardinal, M.D. ’65.

Ralph E. Sweeney, Jr., M.D., writes that he has a private practice in orthopaedic surgery in Elizabeth, N.J.

Wendell H. Yealy, M.D., Williamsport, Penn., retired from his practice in radiology last August.
Class Notes

'20s

Sol Londe, '27, was appointed professor emeritus at the School of Medicine of the University of California, Los Angeles.

'30s

Robert F. Monroe, '31, Louisville, has retired from private practice in obstetrics and gynecology.

Irving L. Berger, '39, has retired from chief of psychiatry at the VA Hospital in Fayetteville, N.C. Dr. Berger will divide his time between Cleveland and Florida. He plans on doing consulting work and fishing.

Howard R. Bierman, '39, Scientific Director of the Institute for Cancer and Blood Research, Beverly Hills, Calif., has been appointed to the Cancer Advisory Council of the State of California by Governor Edmund G. Brown, Jr.

'40s

Fred J. Biggs, Jr., '40, Poplar Bluff, Mo., writes that "he sold his cattle ranch and leased the farmland that he acquired over the last 25 years." Last year, he built a winter home in Harlinger, Texas, on a golf course. "My game has improved," Biggs says.

Charles G. Obermeyer, '40, St. Louis, suffered a myocardial infarction in June, and has retired from active practice.

Joe B. Hall, '48, is the senior member and founder of the Fayetteville Diagnostic Clinic, a group of 9 internists, in Fayetteville, Ark.

'50s

Brig. Gen. Wayne E. Garrett, '53, has been named Mobilization Assistant to the Director of Medical Plans and Resources, Office of the Surgeon General, USAF, Washington, D.C.

Col. Donald H. Tilson, '55, Vancouver, Wash., has been with NW Permanente P.C. (Kaiser) in Portland since retiring from the army in 1977. He is currently chief of orthopaedics at the Interstate Clinic, Portland, Ore.

John S. Meyer, '56, St. Louis, is doing work in breast tumor cell kinetics and steroid hormone receptors, and was elected treasurer of the Cell Kinetics Society.

Donald R. Harkness, '58, has been named chairman of the Department of Medicine at the University of Wisconsin Medical School.

Lucy Jane King, '58, Arlington, Va., is working in the Neuropharmacology Division of the Food and Drug Administration.

Raymond G. Schultz, '59, has been appointed Director, UCLA Hospital and Clinics. UCLA Hospital is a 689 bed facility which serves as the major teaching hospital of the UCLA School of Medicine.

'60s

Floyd E. Bloom, '60, is director of the Arthur V. Davis Center for Behavioral Neurobiology, Salk Institute, San Diego, Calif.

George P. Hoech, Jr., '60, was promoted to clinical professor of anesthesia at the UMKC School of Medicine.

Raymond B. Isely, '61, Public Health Research Physician at the Research Triangle Institute and Adjunct Assistant Professor of Health Education at the University of North Carolina at Chapel Hill has been named Associate Director of a multimillion dollar project entitled, Water and Sanitation for Health, designed to assist developing countries in the planning, execution and evaluation of water and sanitation programs in rural and periurban areas.

Mordecai P. Blaustein, '62, Baltimore, formerly professor of biology and biophysics at Washington University School of Medicine, is professor and chairman of the Department of Physiology at the University of Maryland Medical School.

Anne Bosshard Fletcher, '64, director of the nursery at Children's Hospital Medical Center, and associate professor of pediatrics at George Washington University School of Medicine, has been elected to a six-year term on Clark University's Board of Trustees. Dr. Fletcher received a B.A. degree in biology from Clark in 1960.

Edward F. Ragsdale, '64, Alton, Ill., was a delegate to the Republican National Convention.

Dennis P. Cantwell, '65, internationally acclaimed for his work in behavioral, developmental and emotional problems of children has been named to an endowed professorship at the UCLA School of Medicine. He was appointed the first Joseph Campbell Professor of Child Psychiatry.

Margaret C. Telfer, '65, received the J.A. McCintock Award from the 1980 graduating class of The Pritzker School of Medicine of the University of Chicago. The award was given "for outstanding teaching in the Medical School." She also received the award in 1978.

Neil Valdes, '65, Carbondale, Ill., clinical assistant professor of surgery, Southern Illinois University School of Medicine, has been accepted as a fellow in the American Academy of Orthopaedic Surgeons.

Frank Vinicor, '67, is an associate professor of medicine at Indiana University School of Medicine and co-director of the Diabetes Research and Training Center.

Robert E. Groble, '69, Jacksonville, Fla., has been in private practice for 5 years. He is co-chairman of psychiatry at the Baptist Medical Center, consultant at the Pastoral Counseling Center and chairman of the Professional Advisory Board of the Mental Health Association. Their second child was born Jan. 1.
In Memoriam

'70s

Joann L. Data, '70, will be a senior clinical research scientist with Burroughs-Wellcome, Research Triangle, North Carolina, effective Nov. 1. She also is on staff at Duke Medical School, Division of Clinical Pharmacology.

Richard A. Blath, '71, St. Louis, had a book chapter published in Outpatient Surgery, edited by George Hill and published by W. B. Saunders. Dr. Blath's urology practice is in St. Louis County. He was recently on a local TV channel speaking on vasectomy.

Robert M. Galatzer-Levy, '71, Chicago, reports that his third son was born April 22, 1980.

Robert A. Laibovitz, '71, recently contributed a chapter in Neuro-Ophthalmology 1980 on "Choroidal Osteoma." He has an ophthalmology practice with a retinal sub-speciality in Austin, Texas.

Robert A. Rosenbaum, '72, Chicago, and his wife, Marjorie announce the birth of their son, Andrew born March 10, 1980.

William L. Rohr, Jr., '75, completed his residency in orthopaedic surgery at the Navy Regional Medical Center in San Diego. He is now serving as a staff orthopaedist at the same institution, for his two-year obligation.

Robert L. Lamberg, '76, St. Louis, started practice in ophthalmology by taking over Dr. Lawrence Post, Jr.'s office in Clayton, Mo. He is also working with Dr. James M. Gordon at Christian Hospital, NE, in St. Louis County.

Karen Sumers, '76, is doing a fellowship in cornea and external diseases of the eye at Emory University Medical Center in Atlanta, Ga.

J. Trig Brown, '77, Durham, N.C., received the "Haskel Schiff Award in Clinical Medicine." It is a memorial award presented yearly by the Duke medical house staff to a member of the house staff who is thought to best represent the ideals of Haskel Schiff, M.D., a former Duke Resident who tragically lost his life in an auto accident.

James L. Davis, '77, is in graduate medical training in cardiology at the Mayo Graduate School of Medicine, Rochester, Minn.

Allan L. Goodman, '77, is chief resident in diagnostic radiology at Rush Presbyterian, St. Luke's Medical Center, Chicago, Ill.

Timothy J. Ley, '78, completed his internship and medical residency at Massachusetts General Hospital in June. He is currently a clinical associate at NIH in Bethesda, working with Dr. Arthur Nienhuis, director of clinical hematology.

Harvey D. Bingham, '38 April 7, 1980
Ewan F. B. Cadman, '46 September 28, 1980
Robert W. Crossman, '32 February, 1980
William A. Fuson, '24 May 27, 1980
John E. Gallagher, '40 June 9, 1980
Rodney J. Gray, '26 April 17, 1980
George A. Greenberg March 29, 1980
Edward Kendrick, '76 October 14, 1980
Charles L. Klenk, '05 June 16, 1980
Henry H. Meadows, Jr. '36 March 28, 1980
Robert R. Mensendick, '56 August 11, 1980
Ralph R. Merrill, '33 February 28, 1980
Edward C. Meyer date unknown
Morris Moore, M.D. April 2, 1980
Philip S. Mountjoy, '37 August 5, 1980
John W. Murphy, Jr., '44 April, 1980
Herman J. Roodman, '54 August 17, 1979
Henry P. Rover, '26 June 30, 1980
Phillip M. Stimson, M.D. date unknown
Miles E. Thomas, '47 June 23, 1980
John E. Wattenberg, '17 January 28, 1980
Edward P. Wood, '47 June 12, 1980
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"If I were a Cassowary
On the plains of Timbuctoo,
I would eat a missionary
Coat and bands and hymn-book, too.
Instead, I am a picidae
On an oak in Illinois
Where the grubs I pick today
My munching will annoy.

The first verse is from Bishop Samuel Wilberforce's Epigram.
The photo is from F. Glenn Irwin, M.D. (30), whose hobby is wildlife photography. He is now semi-retired and lives in Decatur, III.
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