It is both an honor and a pleasure to be invited to speak before this distinguished group of colleagues on the subject of research and dental education. Before continuing, my wife and I wish to express our gratitude to Dr. Ichiro Matsue and the Japanese Association of Periodontology for the outstanding hospitality shown to us since our arrival in Japan. We look forward to reciprocating the warmth of your reception when you visit Boston. About ten years ago, I did have the opportunity to host a modest reception at our Medical Library for a group of touring dental students from Japan. The following picture, which I keep on the wall of my office, was taken during the occasion:

Slide 1

I was impressed by this happy and eager group of students who were willing to travel far from home to learn from and about others. One possible reason for all these smiling faces is the fact that my assistant, Dr. Mulvihill, and I arranged for a Japanese luncheon to be served to our visitors. We assumed that after a week or more in the United States they must have been tired of American food, and we wished to cheer them up. I would be curious to learn whether any of those former students are in the audience today.

There is one other connection I would like to mention - and that is our mutual indebtedness to Townsend Harris. As you know, Townsend Harris was the American Consul-General, who by the Treaty of Yedo in 1858 opened Japan to the world. What you do not know is that the high school I attended as a youth growing up in New York City was named after Townsend Harris; and that school played an important role in my personal education and development.

It has been traditional at the Harvard Medical School to consider the quality of biomedical research, teaching, and patient care as the major yardsticks by which to measure the quality of a medical school and its faculty. However, it is only in the past 30 years that biomedical research has begun to be recognized as a valuable and vital activity within the walls of most dental schools in the United States. Even now, there are schools that carry out little, if any, research, and too frequently the research that is done is performed primarily by individuals in the basic science de-
partments. Unfortunately, many clinical departments are satisfied to limit their activities to teaching and patient care. While teaching and patient care are important responsibilities, they are not sufficient. The role of the University is not only the transmission of knowledge, but it also includes the development of new knowledge. Clearly, the development of new and better methods to treat and prevent oral disease can only come about through research—although the time lag varies greatly from the moment a discovery is made in the laboratory until it results in a practical advance in patient care. Most laboratory discoveries serve primarily to increase our knowledge base and relatively few appear to have an immediate and direct influence on advancing a clinical field.

At this point I would like to share with you some of the research findings that have been made in my laboratory over the past 20 years. Since I am a periodontist, it is natural that my research interests have concentrated primarily on periodontal disease. For me, the most important question has been: “What is the mechanism of bone resorption and how can it be controlled?”

In order to study this question we resorted to tissue culture and devised several systems for studying bone in vitro.

Slide—This photograph shows our principal tissue culture system. It consists of a Leighton tube which has a flattened portion at the closed end. Sitting on the flat portion in the tube is a rectangular glass coverslip containing the calvarium of a 5-day-old mouse. The calvarium is attached to the coverslip by means of a plasma clot. The medium consists of 2 ml of fluid containing horse serum, balanced salt solution, and antibiotics. The tube is gassed with a mixture of 50% O2 and 50% N2, stoppered, and placed horizontally in a rotor enclosed in an incubator. The rotor makes one revolution every 5 minutes, thereby slowly bathing the bone tissue and allowing it to receive its nutrients from the medium and its oxygen from the gas phase of the tube. The metabolites are released into the medium.

Slide—This is a closer view of the end of the Leighton tube, showing the parietal bones, the frontal bone and the sutures. The occipital bone has been removed allowing the tissue to lie flatter on the coverslip. The medium is changed every 2-3 days, re-gassed and the bone is examined under the microscope in the living state. The system has many advantages since it permits us to alter the environment of the bone by adding various hormones, vitamins, or drugs to the medium in order to observe their effect. In addition, specific areas of bone may be removed after culture for light microscopy, or electronmicroscopy, and both the tissue and the medium may be analyzed for chemical changes. Radioactive substances may be added to the medium in order to study their metabolism by the bone tissue. The most important advantage of the in vitro approach is that it permits the investigator to study the direct effect of various factors on the tissue, since no other organs are present to metabolize the compound or give rise to an indirect effect. However, this very advantage of the in vitro approach is also a potential disadvantage because we cannot assume that the results would be the same in vivo.

Our most important research breakthrough in the beginning was the ability to stimulate bone resorption at will by introducing a bone resorption stimulating factor into the medium. One factor that is strikingly effective is parathyroid hormone, which is known to stimulate bone resorption in vivo.

Slide—This slide shows the gross effect of adding 0.5 units of parathyroid extract per ml of
medium. The nine calvaria shown here came from one litter of mice. They were divided into a control group and a parathyroid-treated group. It may be seen that whereas the control bones are essentially intact after the 15 days of culture, the parathyroid-treated bones are almost entirely destroyed.

Since we had developed a reliable system for stimulating bone resorption, we were anxious to determine what cells were associated with the process. We were particularly interested in determining whether osteoclasts were involved in the process, since at that time there was real controversy as to the role of this multinucleated giant cell. Some authorities thought the osteoclast was actively involved in causing resorption. Others thought it was a result of resorption rather than a cause. Except for the work of Gaillard of the Netherlands who had some low magnification time-lapse cinematography films that showed osteoclasts in the vicinity of resorbing bone, no other direct evidence existed that demonstrated the active involvement of osteoclasts in resorption. To answer this question we placed resorbing cultures in a time-lapse cinematography apparatus encased in an incubator and took time-lapse films of resorbing bone at different magnifications.

The following time-lapse film shows the phenomenon of bone resorption in tissue culture. The early sequences show resorption of bone in the frontal suture area at an original magnification of 125x. There is much cellular activity throughout the calvarium. At the resorbing bone margin the cells appear to be primarily macrophages, and no osteoclasts are distinguishable as the bone is rapidly destroyed.

At higher magnification (375x) active osteoclasts can be distinguished as they appear to burrow their way through the bone. The cell membranes of these osteoclasts are extremely active and the cytoplasm is filled with numerous vacuoles streaming from the bone margin. The last sequence shows a dying osteoclast which suddenly ceases all movement.

(FILM SHOWN HERE)

We concluded from this and other time-lapse films obtained in our laboratory over a period of several years that osteoclasts are actively involved in bone resorption and that they are responsible for the formation of Howship’s lacunae.

We also noted that although macrophages are much smaller than osteoclasts, it has been possible on occasion to distinguish these very motile cells attacking bone spicules and apparently participating directly in the resorption process.

An important step in the development of our thinking was the realization that in our tissue culture system bone resorption is directly dependent not only on the concentration of bone-resorption stimulating factors or cofactors in the environment, but it is also dependent on the concentration of oxygen in the gas phase. In other words, with a decrease of the oxygen concentration in the tissue culture system, the presence of a bone resorption stimulating factor is nullified. With an increase in the oxygen concentration such a bone-resorption factor acts at its maximum potential. This phenomenon may be observed in the experiments shown in the next 3 slides:

Slide—This slide shows the effect on resorption of 0.5 units parathyroid extract/ml of medium and the effect of different oxygen concentrations in the gas phase after 12 days in culture. At 10% oxygen in the gas phase little, if any, gross bone resorption has taken place. At 20%, 30% and 50% oxygen, respectively, however, there is a definite resorption response that increases in intensity as the concentration of oxygen increases. Clearly, the limiting factor has been the amount of oxygen in the gas phase. On the other hand, in control cultures containing no parathyroid extract, the same increasing oxygen concentrations did not lead to any bone resorp-
tion. Obviously, both a bone resorption stimulating factor and high oxygen concentrations are needed for resorption to occur.

Slide—This slide demonstrates the resorption stimulating co-factor effect of heparin. The calvaria shown here have been in culture for 7 days at which time the experiment was terminated. The bones were stained with the Von Kossa reaction (which stains the remaining mineralized portion black) to serve as contrast for the clear, resorbed areas. The four calvaria from each of the 4 groups were mounted on slides and photographed in order to compare the amount of bone resorption in each group. The first group showing no resorption was the untreated control. The second group was treated with 10 units of heparin per ml of medium. This, too, showed no resorption. The third group was treated with a suboptimal concentration of parathyroid extract (0.1 units/ml) and showed a slight amount of resorption. However, when this concentration of parathyroid extract (0.1 units/ml) was compared with 10 units of heparin/ml, there was a marked enhancement of resorption leading to almost complete destruction of the calvaria as seen in the fourth group. Because heparin has little or no direct resorption-stimulating effect by itself and because it markedly enhances the effect of a suboptimal concentration of a bone resorption stimulating factor such as parathyroid extract, we refer to heparin as a bone resorption stimulating co-factor. It should be noted that heparin has a similar enhancing effect when used in combination with suboptimal concentrations of any bone resorption stimulating factor.

Slide—This slide demonstrates the interrelation of a bone resorption stimulating factor (parathyroid hormone) a bone resorption stimulating co-factor (heparin) and various concentrations of oxygen.

The first column of calvaria shows the effect of a suboptimal concentration of parathyroid extract (0.025 units/ml of medium) at 50% oxygen and no heparin. This combination gives rise to minimal resorption. The addition of heparin (10 units/ml) to the suboptimal concentration of parathyroid in the presence of 50% oxygen leads to marked resorption. However, this amount of heparin and parathyroid extract in the presence of 30%, 20% and 10% oxygen, respectively, again demonstrates the dependence of bone resorption on the oxygen concentration in the bone environment. As the oxygen is decreased to 20% and 10%, bone resorption is arrested.

How does the osteoclast destroy bone?

Slide—Histological section of human bone showing osteoclastic resorption in patient with hyperparathyroidism. In order to remove the bone substance during resorption, it is necessary to remove both the bone mineral and the collagen matrix. The bone mineral could be removed by the secretion of organic acids, such as citric acid or lactic acid. Collaborative studies carried out by our laboratory and that of Dr. George Martin at the National Institute of Dental Research have demonstrated that citric acid production is significantly elevated in the media of resorbing bone cultures treated with parathyroid extract as compared with non-resorbing control cultures.

Slide—This slide shows an electronmicrograph of a portion of an osteoclast derived from a parathyroid stimulated resorbing bone culture.

One of the outstanding ultrastructural features of the osteoclast (in comparison to the osteoblast and osteocyte) is the numerous mitochondria found in the cytoplasm of these multinucleated giant cells. These
mitochondria are indirect evidence for the high energy requirements of this cell, explaining in part the role of oxygen in regulating the cell activity. In addition, the effect of parathyroid hormone on some of the enzymes involved in the citric acid cycle within the mitochondria also explains the accumulation of citric acid in these resorbing bone cultures and could account for the demineralization phase of the bone resorption process.

Slide—This next slide shows a higher magnification of the area immediately adjacent to the "ruffled border" of the osteoclast. The decalcified collagen fibrils are clearly seen. The question arising at this point is, "How is the bone collagen destroyed?"

We have been working on this problem for approximately 15 years and I would like to share some of our attempts at solving this problem.

The discovery by Gross and Lapiere of an animal collagenase isolated from resorbing tadpole tails led our laboratory, in collaboration with Dr. Melvin Glimcher, Professor of Orthopedic Surgery at the Harvard Medical School, to search for a similar enzyme in resorbing bone cultures. Collagenolytic activity from actively resorbing bone was detected in the media after culturing the tissue with reconstituted radiolabeled collagen fibrils. In addition, by using H-proline-labeled calvaria, other data established that during active bone resorption bone collagen is partially degraded to peptides similar in size and sequence to those produced by the action of bacterial collagenase on collagen.

Dr. Masaharu Shimizu, who joined our research group during 1966-1968, isolated and partially purified a collagenase from the culture media of actively resorbing mouse tibiae. This enzyme is similar to tissue collagenases isolated from other sources. Dr. Seizaburo Sakamoto and collaborators, who joined our research group after Dr. Shimizu returned to Japan in 1968 further purified and characterized this mouse bone collagenase. During the course of their study it was found that not only did heparin increase the amount of collagenase released into the incubation media by bone explants, but heparin also directly enhanced the enzymatic activity of mouse bone collagenase on solid collagen substrate. Further studies of the interaction between heparin and mouse bone collagenase by Dr. Sakamoto's group in our laboratory revealed that the enzyme could be tightly bound to a heparin-substituted gel at physiological ionic strength and eluted at high ionic strength. This technique, incidentally, provided a method for further purification of mouse bone collagenase with high yield and for isolation and measurement of its activity in our tissue culture media, despite the presence of serum inhibitors such as alpha-2-macroglobulin. Using this technique, Dr. Sakamoto's group has been able to study the quantitative and temporal relationship between the extent of bone resorption and the amount of collagenase activity found in the culture media.

Although these studies demonstrate that collagenase is produced by bone tissue, they do not tell us what cells are responsible for the collagenase production. For this information we must use an approach like the fluorescent antibody technique-using antibodies to purified collagenase.

Recently Dr. Sakamoto's group has succeeded in purifying mouse bone collagenase by use of heparin-Sepharose affinity chromatography. They have subsequently prepared a specific antiserum to mouse bone collagenase and further purified the antibody by an immunoadsorbent method using antigen-substituted Sepharose 4B gel. Using this antibody preparation Dr. Sakamoto's group could not consistently demonstrate the presence of collagenase in osteoclasts. Currently Dr. Sakamoto's group is also conducting fluorescent antibody studies to localize mouse bone collagenase within isolated mouse bone cells and in mouse peritoneal exudate macrophages.
Some years ago I reported that we could stimulate bone resorption merely by placing a small fragment of tumor tissue from a transplantable mouse fibrosarcoma (the HSDM1 tumor named for the Harvard School of Dental Medicine) on the parietal bone of mouse calvaria grown in tissue culture. Despite the absence of parathyroid hormone in the system, marked resorption occurred around the fragment and at some distance away in the suture area of the frontal bone.

Further studies showed that cell-free extracts of the tumor also markedly stimulated bone resorption. This finding was of interest since it dispelled the generally accepted notion that bone resorption due to tumor metastases is due primarily to pressure brought about by the expanding tumor. Our data suggested that the tumor released some metabolite that stimulated bone resorption. This idea was confirmed in a collaborative study with Dr. Armen Tashjian, our Professor of Pharmacology, in which we learned that the tumor released a substance called prostaglandin E2 which is a potent bone resorption stimulating factor.

Along this line, Dr. Matsumoto, who joined us from 1976 to 1978 and worked with Dr. Sakamoto on the bone resorbing activity of the HSDM1 tumor, found that the tumor fragments stimulated the bone to synthesize a large amount of collagenase. Of interest was the observation that the tumor itself neither released nor synthesized collagenase.

In view of the bone resorption stimulating effect of the mouse tumor fragments, we decided to test the effect of human gingival fragments grown in combination with mouse calvaria. To our surprise we found that human gingival fragments were also able to stimulate bone resorption.

Of the 37 gingival samples tested from 28 different patients (22 to 65 years old), 36 induced enhancement of resorption ranging from slight to good. The addition of heparin to the medium of such combined cultures usually enhanced resorption. Further studies showed that the bone-resorption stimulating activity of human gingiva is present both in the epithelial and the connective tissue portions of the tissue. In addition, we found that cell free extracts, as well as the media derived from human gingival fragments growing alone in culture, were potent, too. Apparently, human gingiva contained and released some unknown factor(s) capable of stimulating bone resorption.

Because of our finding that the potent bone-resorption stimulating factor in the HSDM1 transplantable mouse fibrosarcoma is prostaglandin E2 (PGE2), we considered the possibility that PGE2 might be the unknown factor responsible for the bone resorption stimulating activity of human gingiva. The first column shows the untreated control bones without any gingival tissue and no resorption. The second column shows calvaria without gingival tissue but with heparin. Again there is no obvious bone resorption. The third column shows calvaria each of which has attached a small (1 mm diameter) gingival fragment from a 36-year old male patient. Note that some resorption is evident even at gross inspection. The calvaria in the fourth column each contain a fragment of human gingiva and heparin in the medium as well. One can readily see that the combination of gingival fragment plus heparin (our bone resorption stimulating co-factor) has stimulated moderate to advanced resorption.
gingival fragments, extracts, and media.

Slide—This diagram shows that prostaglandin $E_2$ biosynthesis is derived primarily from the essential fatty acid arachidonic acid in the presence of the enzyme system called prostaglandin synthetase.

Slide—This diagram indicates that prostaglandin biosynthesis from essential fatty acids is blocked in the presence of indomethacin or aspirin due to interference with the prostaglandin synthetase system. This property of indomethacin or aspirin provides the investigator with an indirect probe to determine whether prostaglandin biosynthesis is involved in a particular biological process.

Slide—This slide shows the effect of various concentrations of indomethacin on bone resorption stimulated by parathyroid extract or gingival fragment medium. Whereas all concentrations of indomethacin were ineffective in inhibiting parathyroid-extract induced bone resorption, there was an excellent dose response to indomethacin added to the gingival fragment media cultures. This finding suggests that the bone-resorption stimulating factor released into the medium by human gingival fragments in culture acts on bone through a mechanism different from that of parathyroid extract and involves the biosynthesis of prostaglandin $E_2$ by bone cells. Direct measurement of prostaglandins in these cultures supports this conclusion.

Because both indomethacin and aspirin inhibit gingival media-stimulated bone resorption in our tissue culture system, it was deemed worthwhile to test the effect of other compounds used in the treatment of rheumatoid arthritis. We were especially interested in the use of gold salts because we felt they might be useful as markers. This form of therapy (chrysotherapy) has long been used for the treatment of rheumatoid arthritis, appears to be gaining in popularity, and is reported to be helpful. Only limited attempts have been made to explain the mechanism of action of gold salts. Persellin and Ziff have demonstrated that sodium aurothiomalate (SATM) inhibits two lysosomal enzymes from guinea pig macrophages, namely acid phosphatase and $\beta$-glucuronidase.

Sodium aurothiomalate (SATM) was tested in our bone resorption culture system in an attempt to determine whether this gold salt could inhibit parathyroid extract-stimulated bone resorption.

Slide—This slide shows the effect of various concentrations of sodium aurothiomalate (SATM) on parathyroid extract-stimulated bone resorption. The wide bars represent the mean resorption values as measured morphologically through the microscope. The solid narrow bars represent the mean values of calcium released into the medium over the course of the experiment. The first set of bars shows the low basal values for the untreated control group. The second set of bars is the positive control treated with parathyroid extract. About 60% of the calvaria in this group has been resorbed, as measured morphologically. The calcium released into the medium reflects the high resorptive activity. SATM added to the parathyroid extract containing media inhibits the resorptive response. At 100 $\mu$g/ml bone resorption is reduced to the amount exhibited by the untreated control, despite the presence of parathyroid extract. With 50 $\mu$g/ml of SATM/ml bone resorption due to parathyroid extract stimulation is reduced to about 50% of the PTE group without SATM. At 10 $\mu$g/ml SATM/ml there is virtually no inhibition of the PTE-stimulated resorption.

Using another tissue culture system that gives rise both to bone resorption and bone formation it was possible to demonstrate inhibition of bone resorption by these same concentrations of SATM without preventing good new osteoid formation after 14 days of culture.
Slide—This slide shows the healthy layer of new osteoid that has formed over the original, darker-staining bone, indicating that the SATM is acting specifically on the resorption process rather than as a generally toxic compound.

The most striking observation, however, was the conspicuous number of macrophages scattered throughout the section, many of them filled with yellowish-brown particles, inferred to be ingested gold. Preliminary studies revealed that SATM (100 μg/ml) not only inhibits bone resorption, but also inhibits osteoclastic acid phosphatase activity, as visualized histochemically.

Slide—Excellent acid phosphatase staining in osteoclasts of control resorbing culture in the remodeling system.

Slide—Poor acid phosphatase staining in SATM (100 μg/ml) treated culture.

The results of these recent tissue culture studies with SATM suggest that the gold salt picked up by the macrophages alters their function, thereby interfering with the resorptive process. It is appealing to hypothesize that macrophages and osteoclasts work as a team to bring about bone resorption. Perhaps the osteoclasts first remove the bone mineral and the macrophages then provide the collagenase to remove the bone collagen. An alternative hypothesis would hold that either the osteoclast or the macrophage could resorb bone independently. Further studies are needed to clarify this issue.

About six years ago we proposed a scheme as to how some of the factors we have described in tissue culture may play a role in patients with periodontal disease and how they may influence bone metabolism to enhance alveolar bone loss. According to that scheme, an increase in gingival inflammation could lead to three local alterations within the gingival tissue that would favor resorption of the underlying alveolar bone:

1. increased local heparin availability due to the disruption of gingival mast cells and the discharge of their contents into the local environment,
2. release of an unknown bone resorption stimulating factor(s) present in human gingiva,
3. increased local oxygen supply due to an increased local vascularity.

Increased local heparin release due to inflammation probably does occur, but it will be difficult to prove.

The bone resorption stimulating factors in human gingiva are probably numerous, and probably include endotoxin, prostaglandin E₂ and its precursors. With regard to the third point concerning local vascularity, we have finally made some headway by utilizing nuclear medicine techniques to obtain some quantitative values for blood flow in the gingiva and alveolar bone of healthy and periodontally diseased beagle hounds. This study was carried out primarily by Dr. Michael Kaplan and Dr. Marjorie Jeffercoat.

Slide—From this slide it may be seen that in preliminary studies using ¹⁴¹Ce-labeled microspheres it was possible to determine blood flow in ml/min per gram of tissue. In periodontally diseased dogs the gingival blood flow was about twice that found in healthy gingivae. Although alveolar bone blood flow is much less per gram of tissue than it is in gingiva, the blood flow in the alveolar bone of periodontally diseased animals is about 3 times that of the healthy animals.

Perhaps the most exciting results coming out of our nuclear medicine research on periodontal disease is the observation that there is an increase in the alveolar bone uptake of a bone seeking radiopharmaceutical (technetium-99M-tin-diphosphonate) in dogs with chronic destructive periodontal disease, when compared to health dogs.

Slide—Shows the anesthetized dog being scanned with a rectilinear scanner 4 hours after the injection of the radiopharmaceutical.
Slide—Shows the lateral scan image of the head of a healthy control dog and that of a periodontally diseased dog.

It can be seen that the uptake in the jaws of the diseased dog is much heavier than in the jaw of the healthy dog.

Film density values for the mandibular joint area of each image were used to normalize the data in order to correct for variations among dogs with respect to skeletal uptake and clearance rate of the radionuclide from the blood.

Recently, our nuclear medicine group has been utilizing a miniaturized semiconductor probe to measure alveolar bone uptake of the bone-seeking radiopharmaceutical. Not only were they able to confirm that dogs with alveolar bone loss have higher uptake of the radiopharmaceutical as compared to dogs with healthy alveolar bone, but they found higher uptake in both jaws when only one jaw showed bone loss. This finding suggests that a generalized alteration in alveolar bone metabolism exists once alveolar bone resorption has occurred around one or more teeth.

More recently, using this probe in beagles, we have obtained evidence showing a correlation between high radiopharmaceutical uptake around healthy appearing teeth (as determined radiographically) and future bone loss around these teeth 2 years later.

Slide—Graph showing correlation between probe values and subsequent bone loss around specific teeth.

These findings indicate that the use of nuclear medicine techniques will provide the researcher with a powerful tool to study alterations in alveolar bone metabolism in whole animals during the onset, progression and treatment of periodontal disease. It is not too speculative to assume that in the future nuclear medicine techniques will play an important role in the diagnosis and monitoring of periodontal disease and other oral conditions as is currently the situation for many medical problems.

To start my review of dental education in the United States, particularly the events that have occurred at Harvard, I would like to take you back more than a century ago, around the time of Townsend Harris.

Between 1860 and 1865 there were three types of dental practitioners in Boston:
1. graduates of medicine.
2. graduates of dental colleges established in 1840 and later.
3. apprentice-type dentists who set themselves up in practice (these were in the majority).

In 1867, the Harvard Corporation voted to establish a separate Dental School despite the fact that there was strong sentiment amongst a number of dentists that Dentistry should be established as a department of the Harvard Medical School. The Harvard Dental School thus became the first dental school connected with a university and closely associated with its medical school. It should be noted that this decision set the pattern within universities for the formal separation of Dental Schools in the United States.

Initially the curriculum was two years long and consisted of four months in each year. Subsequently, the academic year was extended to five months, then to seven months, and now is ordinarily nine months.

In 1891 Harvard moved to a three year curriculum. The purpose of this change was not merely to increase the amount of time spent in restorative dentistry, but it was also for the purpose of developing the biological background of the students. In 1917 the dental course at Harvard was increased from three years to four years in conformity with the recommendation by the National Association of Dental Faculties. Between World War II and the Korean War, Harvard instituted a unique curriculum aimed at producing graduates who received degrees both in Dentistry and in Medicine. The program required the dental students to spend the first two years at the Medical School, taking basic science courses together with the medical students. This
was followed by two years at the Dental School, studying clinical dentistry. At the end of this period the students received the Doctor of Dental Medicine (D. M. D.) degree and were given the option of continuing for another two years in clinical medicine if they wished to obtain the M. D. degree. On paper the plan was superb. The objective was to produce a medically qualified dentist. Unfortunately, the program did not work, since almost all of the dental graduates who decided to continue for the M. D. degree at the Harvard Medical School remained in Medicine and abandoned Dentistry. As a consequence, the Faculty of Medicine was forced to pass a rule that forbade graduates of the Dental School from returning to the Medical School after 1954. It seems obvious that for many dental students of that time Medicine was more attractive than Dentistry and their commitment to Dentistry was superficial or negligible. During the past twenty years at Harvard the development of postdoctoral training programs combining advanced clinical dentistry with biomedical research has served to provide a much needed intellectual stimulus to clinical dentistry. By setting our goals at producing leaders for the dental profession, we constantly sought new and better ways to educate our students. Our losses to Medicine became minimal.

About ten years ago, in an effort to understand the reason why in many hospitals oral surgeons were having a difficult time interacting with plastic surgeons and otorhinolaryngologists, I held an informal meeting with representatives from these different surgical specialties. I learned to my surprise that the objection to the oral surgeons was not that they lacked the M. D. degree, but that oral surgeons were the only surgical specialists functioning in hospitals who did not have general surgery training. Coupling this revelation with the fact that advances in oral surgery appeared to be originating abroad, in countries like Switzerland and England where the oral surgeons also had medical degrees and advanced surgical training, we immediately set up a new oral surgery program for graduates from the Harvard School of Dental Medicine. The length of the program is five years in comparison to the three years that are ordinarily required. The main components of the program include 21/2 years of oral surgery at the Massachusetts General Hospital and other Harvard teaching hospitals, 1 year at the Harvard Medical school to obtain the M. D. degree, and 11/2 years in General Surgery. These various components are interdigitated and sequenced in such a fashion as to provide the maximum benefit to the student. Perhaps you are wondering how these students can receive the M. D. degree after only 1 year at Harvard Medical School. That is because our dental students still spend the first two years of dental school primarily with the medical students at the Harvard Medical School. For this they receive two years credit towards the medical degree. The first year of the 5-year oral surgery program is an oral surgery internship. The second year is spent exclusively at the Harvard Medical School (actually the Harvard Teaching Hospitals) where they receive their training in clinical medicine. These two years are both credited towards the M. D. degree, making a total of four years which is required for the M. D. degree. Upon receipt of the M. D. degree, it is then possible to offer these oral surgery students training in general surgery.

The program has been in operation for about 7 years and I am told by Dr. Walter Guralnick, our professor and Head of the Oral Surgery Department, that the individuals completing this program are superbly trained. Most of them have assumed key positions in hospital dental departments and are able to interact effectively with the plastic surgeons and otorhinolaryngists. To date, we have lost none of these oral surgeons to Medicine.

We have been so impressed by the success of this program for oral surgeons that we recently petitioned and received permission from our
Medical school to extend this concept to other dental specialities, including pediatric dentistry, oral pathology, periodontology, and general dentist. These fields normally require 2 years of postdoctoral training. According to our new plan the time commitment would be extended to 4 years, the additional time being 1 year at the Medical School school and 1 year for the appropriate medical internship. For example, those in pediatric dentistry would take a one year internship in pediatric medicine after receiving their M.D. degree. If should be emphasized that we do not advocate this additional medical training for all dental specialists. However, such training should be of particular value for dentists involved in dental departments within hospitals or medical centers where medically compromised patients require complex management by several cooperating departments. Furthermore, we anticipate that the additional medical qualifications will help break down any remaining barriers that might exist in such institutions and facilitate more complicated clinical research as well as patient care.

Recently the Executive Committee of our School reaffirmed that the major educational mission of the Harvard School of Dental Medicine should be the production of clinical scholars who could play a leadership role in the dental profession. Furthermore, it was realized that there are other avenues for scholarly pursuits by clinicians in addition to biomedical research. We recognized that better leadership in solving health care delivery problems was essential and would require knowledge and skills far broader than expertise in dental technology per se provides. One need only read the Journal of the American Dental Association to see how complex the practice of dentistry is becoming, particularly with the numerous rules and regulations imposed by the federal government. How will the dental profession in the United States cope with these new areas of concern? How do we develop clinical scholars who can advise and guide the authorities concerning the cost, quality, and distribution of health care, and the national policies and regulations that will control the system of health care delivery in the future? It is becoming too complicated to cope with these problems as amateurs—we will just have to spend the extra time and learn the field formally from the experts. That is why we have developed an additional track at Harvard for our postdoctoral students—the so-called "Health Care Delivery Track."

Slide—This diagram reviews the Biomedical Research Track, the Oral Surgery-M.D.-General Surgery Track and the Health Care Delivery Track. Please note that the Health Care Delivery Track gives the postdoctoral student the opportunity to combine Advanced Clinical Dentistry with either:

a. An additional year at the School of Public Health, studying public health issues;
b. An additional 2 years at the Kennedy School of Government, studying public policy issues;
c. An additional 2 years at the School of Business Administration, studying management issues.

Slide—This diagram indicates that both the Biomedical Research Track and the Health Care Delivery Track may be followed by the M.D.+Internship program, if desired.

Harvard's mission to produce clinical scholars cannot be limited to our postdoctoral programs. What do we do about our predoctoral students who plan on doing their postdoctoral work elsewhere? How do we guarantee that all Harvard D.M.D.'s in the future receive that "extra dimension" in biomedical research or in health care delivery that we have built into our postdoctoral programs? We decided that this could only be done by extending the program from four years to five years, with the last year devoted primarily to either biomedical research or to public health. As a result of this decision, a new 5-year program
for all incoming students will go into effect in September, 1979. For most Harvard graduates who plan to continue their postdoctoral studies at Harvard, no additional time will be involved, as may be seen from the next slide.

Slide—Diagram linking 5-year predoctoral program with Advanced Clinical Dentistry and M.D. + Internship.

The next slide shows the evolution of curriculum length since the founding of the Dental School in 1867 until 1979.

Slide—Evolution of curriculum length at Harvard Dental School

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To summarize this part of my presentation, the Harvard School of Dental Medicine has reaffirmed its primary mission of producing clinical scholars. In charting our course for the next decade or so we have recognized the need for becoming more deeply involved with other schools at Harvard University, such as the Medical school, the school of Public Health, the School of Government and the School of Business Administration, since they have the expertise that our students must obtain.

We have no guarantee that our efforts shall succeed, but we should learn from the experience. What we are attempting to do is merely an extension of what our predecessors have tried to do—to meet the future needs of the public and the profession. Harvard has never been satisfied with the status quo. We must always look for a better way.