Vision Research in the 21st Century

During my 5 years as Editor-in-Chief, I have not written editorials, because I wanted to let the science of vision research speak for itself. It was a joy to assist invited authors with Recent Developments reviews, to supervise the improvement of manuscripts through the review process, to organize each issue, and to write our Inside IOVS summary page. The design and selection of color covers seemed to be universally appreciated by the membership of ARVO.

During a decade as ARVO Secretary–Treasurer and Editor-in-Chief of IOVS, I have seen dramatic change in vision research, both in the content of investigation and the attitude of investigators. There has been an explosion of information and effort; yet the community is affected by uncertainty and pessimism. I would like to review the state of vision research and to make some informed observations.

BASELINE PHASE

Fifty years ago (within my lifetime and that of some of you), there was a comparatively rudimentary knowledge of the eye, its disorders, and their therapy. The types of retinal cells were described, yet their most basic processes were scarcely understood. For example, transduction of light into neural impulses was theorized, but its molecular pathway was known as a conversion of “visual purple.” Cataracts were removed, but postoperative healing required weeks of bed rest, and the aphakic eyeglass correction was functionally inadequate. Retinal detachment was poorly understood and successfully treated largely by chance. The eye pressure and visual field were unquantified, and the basic types of glaucoma were not yet distinguished.

In 1950, the process of vision research was conducted in completely different ways and environments from today. Some investigators made solitary progress on basic vision mechanisms or therapeutics almost as a sideline. There were few organized groups whose principal aim was vision research, and these were limited to a small number of developed countries. The published literature of the time consisted of descriptive laboratory observations and anecdotal clinical summaries. Controlled observations were few, animal disease models were poorly developed, technological applications from other disciplines rarely entered the field, and disease definition was haphazard.

EXPANSION PHASE

By the 1960s, various influences began to change this picture dramatically. Eye institutes within university medical schools were conceptualized as joint venues for doctoral-level scientists and clinicians focused on investigation. In the United States, the development of a separate National Eye Institute (NEI) channeled these groups toward critical mass by funding carefully planned efforts. Other, nongovernmental charitable organizations added financial resources for particular directions, including Fight for Sight, the National Society for the Prevention of Blindness, Research to Prevent Blindness, and the Retinitis Pigmentosa Foundation.

By 1970, the interaction of laboratory and clinical researchers was fostered in an annual, intensive, and informal research meeting in Sarasota, Florida (coincidentally, that was my first ARVO conference). There was an enormous impact of these changes on progress in vision research. The introduction of rigorous research methods and controlled clinical trials brought greater validity to research findings. The major ocular disorders were defined and their prevalence, natural history, and risk factors were initially examined. Evaluations of various treatments were subjected to intensive scrutiny, and anecdotal claims were progressively removed from the publishable realm. In part, these events were the result of improvements in the quality of scientific investigation in all fields. In addition, where clinical researchers lagged in sophistication behind their laboratory colleagues, the interaction fostered by collaborative effort often raised standards. Similarly, wet lab investigators associated with eye institutes benefitted by understanding the population relevance of ocular disorders and were better able to use the disorders of the eye to understand its normal functions.

Because of some dramatic successes in therapeutic interventions, including improved cataract surgery, laser treatment of diabetes and glaucoma, and vitreous surgery, public demand for ocular treatment increased substantially. At the same time, in the United States, Medicare and third-party reimbursement for eye care services (particularly surgery) expanded both the number of persons served and payment per procedure. Ophthalmic institutes became substantial contributors to the rapid expansion of university medical centers, with some faculty serving as clinical cash cows.
Some of the net dollars from clinical income were used to fund research activities and facilities during this time. However, much of the income was used for surgeon’s salaries and expanded bureaucracy to serve the clinical services that developed. Finally, many persons whose successful eye care was delivered in these institutions became substantial financial contributors, motivated by a desire to alleviate suffering from the condition with which they were afflicted.

By the late 1980s, other forces began to affect the vision research community. First, the considerable number of those interested in eye investigation from around the world began to participate in large numbers, in part due to more rapid electronic communication. One third of ARVO’s members now live outside the United States. Second, the rapid inflation of medical care costs, and the recognition that more physicians had been trained than were needed, led to a downward trend in clinical reimbursement and an upward revaluation of primary medical care over specialty medicine. Third, the reorganization of medical care delivery has affected not only the United States but other countries as well. In the United States, health maintenance organizations with no ties to eye institutes or medical schools garnered large market shares of a commodity called capitated lives (formerly known as persons). There is now a catastrophic loss of clinical income for some departments of ophthalmology in the face of large institutional commitments to expensive patient care facilities. In many other countries of the developed world, changes in national health systems to improve efficiency and to “privatize” aspects of care are simultaneously ongoing.

We stand, then, at a watershed reached after a rapid increase in research accomplishments and institutional development. From the baseline phase of research, we experienced a professionalization and coordination of investigation unparalleled in previous history (the expansion phase). If we are to believe the many pessimistic voices now assessing the situation, it is likely that our present research activity will lose its momentum. There is an increasing loss of funds from clinical activity to support research and only a modest expansion of the National Institutes of Health (NIH) – NEI budget. Both are occurring at a time of increased competition among researchers for funds, combined with higher costs for the latest research technology. The brightest young people may choose other high-technology fields instead of medical research. Rapidly developing molecular biology methods require constant re-education, which is difficult to accomplish when multiple grants must be written to remain fully funded. Tenure is threatened or effectively eliminated at some institutions. And the public is clamoring for a cure-of-the-week in the media, while showing no sympathy for what are viewed as highly paid specialists. Clinicians’ shrinking reimbursements now make them liabilities to the university at present salary levels. Their loss would end the productive interaction with laboratory scientists.

Are decline and disorganization inevitable? Or are there paths that can lead to a third phase of vision research, what might be called a mature phase? I will outline some ideas for how to continue our progress and some of the means by which it might be achieved.

EYE INSTITUTE MODELS

To continue productive vision research, we require well-trained, dedicated senior investigators and sufficient new trainees to replenish the ranks. Financial resources derived from various sources are vital. Vision researchers must continue to seek new developments in fields outside their own that will drive innovation, including basic techniques from non-vision science laboratories, as well as clinical observations and techniques from ophthalmologists. Societal support of the endeavor is important to guarantee public funding and private philanthropy. Among researchers, both cooperation and healthy competition must continue, along with generosity to share ideas and materials, integrity at the highest level, a spirit of controlled risk taking, and requisite good luck. We need organizations that foster cooperative interaction and that focus efforts in a planned approach to the vision problems that are most important and that are most amenable to solution. For research to be applied to the real world, industrial firms must participate at various levels in the development and implementation of ideas.

How can we fulfill these ideals in bricks and mortar, as well as in direct and indirect costs? First, in our conceptualization of eye institutes of the 21st century, we must avoid what might be called the Sarasota syndrome. For several years, ARVO agonized over whether to move its annual meeting site from its perennial home town. Nostalgia among many members nearly outweighed the signals that scientific interchange was suffering from a lack of facilities and increasing costs at upscale resort hotels. Those who dared to call for change were considered unfaithful to ARVO tradition. The relative success of our Fort Lauderdale meeting site and its improved scientific interchange show that inertia must be overcome and that some scorched earth is, at times, needed. Similarly, the time has come to reconceptualize the eye institutes of the next millennium without being mired in past glories.

Priorities

We should begin by agreeing on the priorities for an eye institute. Foremost is the generation of new information about the normal and abnormal func-
tions of the visual system. Second is the training of those who will participate at various levels in vision research and patient care for visual disorders. And finally, there is clinical patient care at the tertiary and investigational level. For some, patient care is felt to be the most important element. Certainly new information and training have as their rationale the improvement of the quality of life through medical care. But an eye institute must aspire to be much more than a large group practice. Its first dollars and its most secure endowments must be devoted to research and teaching; who else will do so?

I will suggest two possible identities for ophthalmic centers: the research institute model and the clinical excellence model. Individual eye institutes can take stock of their priorities, as well as their resources and goals, in choosing one of these models or aspects of both. Some may choose to focus their efforts on particular areas of visual science, whereas other groups may be large enough to study multiple areas. Feasible program areas should be matched to the available faculty and collaborators. The education of medical students and eye care professionals is an important function of ophthalmology departments and should continue in the context of the health care system. It is not necessary and may be undesirable for every department to carry out laboratory research in collaboration with PhD colleagues. Rather the investigation of new modes of care delivery and participation in clinical research seem a more appropriate role for those who choose the clinical excellence model. I would expect that fewer departments will choose the research institute model. The attempt to accomplish both model goals may be an unreasonable strain on the capabilities of most departments of ophthalmology.

Research

The NEI has long championed the individual, investigator-initiated R01 grant as its predominant funding mechanism. A well-conceived project carried out by one or more researchers is an efficient and effective means to generate new information. The high level of competition in the R01 peer-review mechanism and rigorous peer review before publication are desirable but demanding selective pressures. However, threats to the lone wolf laboratory are becoming more obvious. First, it is impossible to fund fully the career of individual researchers in this way on a long-term basis. Complete funding through grants is virtually precluded: Shorter grant funding periods and lack of secretarial funding are only some of the mounting problems. Investigators in the ideal institute have teaching and other administrative duties that must be compensated through other mechanisms. Furthermore, it is increasingly difficult for each investigator to span the breadth of subject matter, research techniques, and clinical relevance that is needed to optimize research output in the next century. Teams of investigators with complementary talents will fare better and compete more effectively to produce the best data. Although this can, in some cases, occur in parallel, individual laboratories, maximum success will logically occur through shared effort in projects and grant submission among those with additive laboratory expertise and among grouped laboratory-oriented and clinically oriented researchers. The research institute model will conduct both laboratory and clinically based projects through these mechanisms.

There is an important place in both institute models for the researcher who actively carries out investigations and who also conducts patient care. There are many observations of clinical disease that have or will point to important research directions. The difference in prevalence among various ethnic groups in macular degeneration or glaucoma leads directly to genetic and cell culture hypotheses. The potential feasibility of proposed disease mechanisms and therapies is most appropriately weighed by persons experienced in dealing with the disorder. One cannot appreciate the nature of a disease by library study alone. Clinicians who are not actively collaborating in research will be less likely to observe interesting leads. The wisdom of continuing support for an essential cadre of clinician-scientists seems obvious. However, fiscal constraints are increasingly directing the clinician toward efficient and effective care rather than investigation. As time constraints increase, there will be a tendency toward less communication between full-time clinicians and full-time laboratory researchers. Clinician-scientists can serve a bridging role between the two groups, and some must be included in the eye institute of the future. Furthermore, the clinician-scientist is an important communicator to the health care community of the findings and applications of new research. Someone who is known to be personally familiar with a disorder and its treatment can command the respect of clinicians for consideration of new directions and can also help to convince private donors of the value of research. Clearly the clinician-scientist is, by some measures, quite inefficient. Unlike a “full-time” researcher, he or she cannot devote 6 days a week to the grant work (and still maintain a clinical practice). Similarly, he or she will not be a cataract surgeon performing 1000 cases per year or a vitreoretinal surgeon with the largest practice. And there are simultaneously important teaching roles that this triple-threat personage must fulfill. Thus there may be only a few such persons in an eye institute.

Funding

The present sources of research funding must be aggressively nurtured. ARVO contributes to national ef-
forts to maximize congressional support for the NIH. The research community should provide active oversight for the efficient use of the funds provided to the NEI. It would be potentially useful to have a major, national review of the present use of grant funding. This could be carried out under the auspices of a consortium of groups, including ARVO, private foundations, lay organizations, university representatives, governmental officials, and others.

In addition to maximizing funding and efficiency through NIH and other government sources, support from private foundations and individual donors must increase substantially. Already several foundations aim to foster information on specific disorders that are of particular interest to their founders. Some of these were the product of the clinical practice of an ophthalmologist. We must present the opportunity to similar donors to support investigations of interest to them. Effective development programs should be a part of each institute. Ophthalmology professors, like professors of English, need to be valued by their institutions sufficiently that their endowed support reduces the anxiety of short-term termination. This will require the continued interaction with patients whose gratitude for ophthalmic care motivates them to provide such support. We must provide these persons with the opportunity to help now, while our contact with them is assured.

Similarly, partnerships with industry should maximize the likelihood that sound diagnostic and therapeutic ideas reach the marketplace. This will require more effort by researchers to use their knowledge of disorders and therapies in coordinated efforts with technology firms, with the aim to increase income and knowledge.

**Training**

The appropriate place to train a new generation of visual science investigators is beside senior researchers. Intimate contact during the process of generating research plans and their implementation is the most effective means to impart the approach to investigation. Eye institutes now have two pathways for training: (1) residency and brief subspecialty fellowship leading to clinical practice, and (2) postdoctoral research training. In many programs, it is resident training that is seen as paramount.

The eye institutes of the next decade must change the approach to residency training. There is general agreement that the United States now has more ophthalmologists than are needed. The care delivery systems are now stressing primary care, not superspecialty medicine. Already the additional reimbursement to hospitals that train residents is being reduced in some areas, with specialty residencies particularly targeted for reduction. It is time to change resident training, yet there are few programs undergoing any dramatic change. It is anticipated that most persons who obtain care through medical assistance will soon be capitated to HMO delivery systems. Despite these changes, chairpersons appear to feel that the larger their resident class, the better the program. Many institutions depend on resident caregiving to provide service to associated hospitals and clinics, many with a high proportion of indigent persons. If resident programs are cut back dramatically, who will fill these roles? In some institutes, residents serve as extenders of faculty practice. Again, if there are cutbacks, who will do this work?

An institute concentrating on clinical excellence must redesign its program to produce an appropriate number of ophthalmologists who will interact effectively with the health care system as it will exist. This includes stress on efficiency, outcome assessment at a personal and collective level, knowledge of public health and epidemiology, and effective use of available and new screening techniques. Interaction with technical personnel and other eye care professionals should be defined and optimized. This does not mean the production of primary eye care physicians, but rather eye care physicians whose primary aim is to prevent avoidable visual impairment. Several of the areas described here are not part of the present training environment.

The research institute model should strive to develop a residency program that maximizes the opportunity for its students to become investigators. Although this includes an experience similar to that of residents in a clinical department with respect to knowledge of visual disorders, the 2 or 3 clinical years should be followed by 3 or more years of research training with senior research faculty. This should be a time when the physician develops the necessary skills to become an independently functioning and funded investigator. The present K08 Clinician–Scientist grant program is an excellent model for funding of this training. Other sources of support must be developed and given sufficient priority in fund-raising. This research training should follow clinical training, because if it comes first, there is too much time for the student to miss actively developing fields. Subspecialty training and surgical development can occupy 1 or 2 days per week of this time, providing in sum the same total clinical subspecialty training as the present 1-year fellowship. For most departments, this will mean that fewer residents are trained in total as the length of the program is increased. It is anticipated that not all entrants will choose to continue during the research phase of training.

To replace the role residents now serve in various portions of department functions, I suggest two alternatives. First, we should use the abundant eye care
professionals already trained and board certified in each community to perform care. Graduate physicians need the work and would do at least as good a job at community, public, and veterans hospitals (certainly with greater experience). If extended contracts were written, continuity of care for the clients would be improved. Residents should be placed in efficient training settings where their ability to learn is maximized. They could retain positions within those portions of the care system in which their education could be conducted. The role of physician-helper within faculty practices might be better fulfilled by ophthalmic technicians, whose salaries are presently less than those of residents and who need not be retrained several times per year, as residents do.

Physical Facilities

Many eye institutes have adequate physical space, due to investment during the boon 1980s. In fact, to make institutes more efficient, we should redesign and consolidate existing space to save on fixed costs. More and more, the individual institutes can communicate through high-speed, internal and external computer networks. This would allow maximum use of existing large equipment throughout a medical complex (such as confocal microscopes and image analysis devices) and it would facilitate collaboration among eye institutes. Furthermore, electronic means should be used to foster collaboration with nonophthalmic colleagues. Research can be carried out by national collection of data, such as patient outcomes and genetic disease databases. Collaboration among eye research institutes should be actively encouraged by immediate discussions among chairpersons, seeking methods to expand research through interaction. The multicenter clinical trials of the past 20 years show that joint effort can provide valuable information. It is now time to find cost-effective means to generate much more information with a cross-institutional approach.

Faculty

Overall faculty size will almost surely contract. As I have said, some prolific surgeons will choose not to remain within institutes whose salary structure will no longer provide the incomes of the past. Support for clinical faculty will need to be similar to that of research faculty, who are supported by long-term, endowed funds that provide some stability. Clinical faculty are vital to the teaching of a next generation of eye surgeons. But from where will the patients come? Eye patients consist (simplistically) of many with common disorders of low complexity and a smaller number with complex problems requiring high-technology treatment. The institute of the future can choose to work in one or both environments.

Health Care Delivery and Institutes

At present, HMO structures appear to be hungrily devouring the health care system. Patients need to perceive that quality is important in their choice for care. Yet they and we who deliver care seem to have taken a passive stance toward the onslaught of care at the lowest price. Our message to those served must be loud and clear: Reductions in quality are unacceptable. Quality care may cost more. This approach demands evidence to support the initiative; otherwise it simply sounds to the cynic like defense of home turf and current salaries. Outcome research must expand to demonstrate where the line must be drawn for quality of care. At the same time, we must become as good at cost-efficient care as we are at higher cost, high-technology care. Not all institutes will choose to compete as caregivers for the mass audience. They can specialize in solutions to difficult problems.

There will still be the need for tertiary care that is linked to complex interdisciplinary problems (e.g., the acquired immunodeficiency syndrome, genetic disorders) and expensive care systems that are carved out of the routine care. The institute can associate its tertiary care with efficient, community-based offices that deal in issues needed by most of the population for their eyes. Screening systems must be designed to identify those with serious disease, and these represent an important area of potential research for eye institutes of both models. We frequently hear of the dilemma posed by the availability of a complex, expensive therapy such as bone marrow transplantation for advanced breast cancer. Hundreds of thousands of dollars can be spent for what may be minimal extension of life, yet the demand for coverage from those with the disease is great. How can we not offer potential treatment? Yet how can the cost of therapy with questionable benefit be justified? We might include recurrent vitreoretinal surgery in a similar discussion. Research institutes can serve both patients and health care delivery systems in this difficult situation. Patients can be offered such expensive treatments, but only within the confines of controlled clinical trials conducted by experienced researchers. In this way, the high cost of treatment is being used to determine its efficacy, but no person willing to participate in such trials is denied therapy. The proper role of complex treatments would therefore be clarified and the societal commitment would not be open-ended, but rather directed. Eye institutes can assist in solving ethical dilemmas while generating support for research.

We must convince the governmental control mechanisms and private payers that research support is good business and good politics. An excellent example is the ongoing study of medical testing before cataract surgery. If we ask whether detailed physical exami-
nation, laboratory blood studies, and electrocardiograms are needed before eye surgery, various answers are obtained, from a variety of perspectives. Patients dislike the inconvenience, internists and anesthesiologists like their apparent security, and some ophthalmologists feel they are obligated by medicolegal concerns to test. We will soon have the result of a detailed study of the utility of such testing in nearly 20,000 cataract operations in a research program funded by a tiny proportion of the federal dollars expended for cataract surgery each year. The results will provide scientifically valid measures of the utility of testing that transcend anecdote and self-serving professional viewpoints. When costs are justified by estimated safety increases, testing will continue. Savings are to be anticipated by eliminating tests that are useless. It is estimated that the money spent on such testing each year is of the same magnitude as the annual NEI extramural budget. Our representatives in Congress should be encouraged to earmark a proportion of appropriations under all public and private medical care plans to research.

There are several aspects of our research endeavor that I hope will not change and that justify our best efforts to improve and maintain our community. The joy of investigation must be nurtured. The generosity of those who teach the next generation of researchers must have a home and be valued. The high standards of peer review and the scientific method cannot be diluted. And the ultimate desire to improve health must have a higher priority than any other.

Harry A. Quigley

Editorial Transition: Where to Send Your Manuscripts

Gerald J. Chader, PhD, the incoming Editor-in-Chief, has established his editorial office at the address below. All new and revised manuscripts should be sent to Dr. Chader at this address.

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