The social and scientific value of biomedical research

This article is based on the Lilly lecture given at the Royal College of Physicians on 25 April 1994 and in Bristol on 26 April 1994 by Samuel O Thier, President, Massachusetts General Hospital, Boston.

We ask these questions because...
and the values I have stated thus far would hold that
creative science that generates new knowledge is
valued more highly than derivative science that
relieves human suffering.

But it can also be said that focused or derivative
science that relieves human suffering is more impor-
tant than the most creative science that does not do so.
Such an assertion would appear to contradict my
previous statements. Yet I contend that both valuation
systems are correct; our challenge is to figure out how
to include them both.

Some people expect a payoff on their investment in
research. Payoffs can be quite straightforward: for
example, research can result in an improvement in
health or in the generation of new knowledge. Most
societies accept that generation of knowledge is bene-
ficial, with the promise that some day the knowledge
will be used in people’s best interests. There are also
other payoffs: for example, a pharmaceutical company
that invests in research must get a return on its invest-
ment to continue to invest in research.

Thus we favour not only research that is universal,
creative and generates new questions, but also
research that relieves human suffering. We also accept
that research must have a payoff.

How are we really doing research?

At innumerable Congressional hearings I have heard
the argument that supporting basic research gives the
clinical investigator the opportunity to explore its
application, which will eventually lead to the creation
of new diagnostic methods and new treatments. This
contention seems to me to be one of the great
mythologies of medicine; things have rarely happened
that way. We do not understand sickle cell disease
because we understood protein chemistry; we devel-
oped protein chemistry because of the challenge pre-
sented by sickle cell disease. Thalassaemia challenged
us to develop molecular genetics, and immunisation
spawned immunology and virology, not the other way
around. These new sciences then enhanced our know-
ledge of the diseases. It therefore follows that a truly
linear system of research does not describe biomedical
research. Without the clinical observer and investiga-
tor, the relevant questions that feed back into the
biomedical system will not be asked.

One of my great concerns is that our success with
molecular biology, which has produced superb results,
is inhibiting the development of the next generation
of clinical investigators. This threatens the feedback
loop in the system of biomedical research. Following
the success of vaccines, which led to the development
of immunology, observations in immunology then
helped us to make better vaccines, giving us better
control over viruses through mechanisms that we now
can pinpoint, and that allows further improvements in
the vaccines. There is thus an oscillation, or a loop,
and if one tries to force the process to be linear, or
interrupts it at any point, the system will run down. We
have not made this clear enough to the general public.

It is important to identify and promote the feedback
loop because we have in the development of gene
therapy an opportunity to start with a basic scientific
principle and finish with a means for treating or pre-
venting a disease. Yet I predict that when we begin
somatic cell gene therapy by placing the gene into the
cell, and the gene replaces the missing or damaged
product, numerous other unexpected effects will
occur. Then who will be there to observe these events
and recognise their enormous importance for biology?
We need a cadre of clinicians literate in molecular
biology if we are to take advantage of this enormous
opportunity. It is undoubtedly true that new ideas will
wither if basic science is not supported, and without
new ideas there will be nothing left to apply. But it is
also true that without clinical science, ideas will not be
taken forward, and existing research will not be stimu-
lated and redirected. We have to promote the idea
that this is a connected system, and that all parts of the
system need to be operating and supported if it is to
move forward.

I have heard, over and over again, our faculties and
Congress debate whether it is more important to sup-
port basic research or clinical research. I cannot get
the idea through to them that it is important to sup-
port both. Pasteur said there is no such thing as
applied science—there is only science and its applica-
tions, and one without the other is like a tree without
branches or leaves. Unless people recognise that we
need both, they may well cut back on their support for
researchers who have come to take that support almost
as an entitlement.

Support researchers to do what?

There is a lot of ongoing discussion in the United
States about priorities for resource allocation. It is
important to recognise that one cannot forecast who
will come up with a creative impulse. What may be pos-
sible, however, is to establish an environment in which
creativity can flourish. As an example, I am on record
as saying (incorrectly) in the 1970s that the war on
cancer, which was started with the funding of the
National Cancer Institute, was going to be an enor-
mous waste of resources. What actually happened was
that scientists were drawn into cancer research and
began to ask questions that were at least remotely
related to cancer. If one looks at what has been
learned since then about oncogenic viruses, about
oncogenes, about the regulation of cell growth and
its importance in abnormal cell growth, one can see
that the whole paradigm of the control of cancer has
shifted dramatically within 15–20 years. The change
can be attributed to research conducted by people
drawn into the field by the availability of resources for
studies in an expanding field of biology.
The sciences of health care

The fundamental sciences of medicine are biology, molecular biology, cell biology and genetics; there are also the behavioural sciences, computer sciences, chemistry and mathematics. They represent the components of all life sciences, and are the disciplines in which the universities and the medical schools should be coming together. These collective fundamental sciences need to be supported and strengthened, yet we have allowed our medical schools to grow apart from our universities at a time when their intellectual bases should merge.

The integrative sciences of physiology, pharmacology, and system sciences that focus on the disease process have been virtually abandoned. In the United States, Harvard, for example, does not even have a department of physiology. Although physiology is not seen to be as important as molecular biology, it is nonetheless fundamental if we are to understand how a gene codes for a protein that inserts itself in the membrane and traverses it, how that particular protein communicates with other constituents in the membrane, how that cell communicates with other cells, and how that organ communicates or functions within an intact or defective organism. Currently there is little active research in these integrative sciences which connect the fundamental sciences into the functioning systems that we see as physicians.

Increasing support for the management of disease—diagnoses, treatments, clinical trials—has come largely through the interests of pharmaceutical and biotechnology companies. However, funding for clinical behaviour modification is limited; enormous strides could be made in this area by dealing with such health-related issues as smoking, drinking or AIDS, but we do not know how to change behaviours because we have not adequately studied how to achieve these changes. This subject has not been seen as worthy of inquiry.

We must also expand vital population studies. We did a foolish thing in the 1920s in the United States when we separated public health from medicine. As a result, we had one group of physicians who, although doing fine mechanism-based care, had no idea whether their ideas would work effectively in 100 people, and another group in public health who could ask superbly designed but clinically irrelevant questions. Now when people ask what works, what does not work, and what should be included in a basic benefits plan, we cannot tell them. We have not collected adequate data to select among multiple choices. It is our own fault because we have not developed biostatistics and epidemiology as fundamental elements of the education of physicians.

We also need to look at health care practices: the measurement of quality, the generation of practice guidelines, and the application of outcomes research. The whole area of practice and technology assessment and outcomes research is critical and will determine health policy into the next few decades.

Technology and policy development must also go hand-in-hand with science and medicine. One thing I learned in Washington is that a bad policy can easily undo any good that we attempt to do. If Congress, out of ignorance, produces a bad policy, we often have ourselves to blame for not keeping its members adequately informed. They listen instead to the information from people who represent special interest groups and do not necessarily have the interests of patients at heart.

Looking into the future

This is a good time to begin thinking about how we would like to see our health care develop over the next couple of decades and to understand what we can expect from the research that underpins those possibilities. I am speaking of research from the broad base of sciences for health that includes the fundamental sciences, the integrative sciences, the evaluative sciences, and the study of policies to bring them all together. It is an interesting challenge. We have allowed some exciting advances in biology to distract our investment in clinical and behavioural science, and we have to make some course corrections. We can certainly marshal our resources and take off again. We can serve our patients better than anybody has ever served patients in history, even though the insurance companies and the government keep interfering. I think we will win in the long run if we become engaged, but if we sit back and simply defend our current position we will lose a wonderful opportunity, not only in the United States but also in many countries around the world.

So, from time to time we should get together and share our experiences, because one thing is clear—we are all interested in what is best for our patients.

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