Inst. of Research - BANGALORE - (BANG-A)

Nov. 1986

Honor & privilege to visit this internationally renowned institution - not previously privileged to visit.

note: 10 years & spec in WHO — travel primarily to areas where smallpox was present. Bangalore's reputation as one of the most beautiful cities in India - well known to me but fortunately for you & regrettably for me — you eliminated spec at an early date before I had a chance to visit.

I should say a word to you about JHUH at Johns Hopkins as its age and size, it is similar to your own Institute although its mission in ~~but~~ research & education is different.

Founded 1916

1st in U.S. - research in health problems & post grad education

Vits A + D / B vitamins

Polio vaccine developed

World's first academic departments of statistics, of epid, of immunology

In our progs. - endeavor to span R+E from basic science to its field application.

Thus of 11 depts. - range from Biochem / Biophysics / Environ H.S. / Computing / field progs. in int'l. health.

Faculty of 300 with some 900 support staff and 900 graduate students from 65 countries and a budget of $ 70 million/year.

All this is done in close collaboration with our sister institution — J.H. School of Medicine.

Vaccines
DA Henderson
Probably Indian Inst of Science
Bangalore (Bengaluru), India
21 Nov 1986

~~(Smallpox + vaccines)~~

~~Honor and privilege to visit this internationally renowned institution~~ / [I'm sure it is for you, science and rep.)

as for me, the most exciting time imaginable to be in the field of biomedical science and where once we struggled to identify potential productive directions for work, we now find ourselves trying to select among a hundred productive directions. increasingly fast-paced)

no less in public health. [To keep up with the field is now all but impossible ~~even if one reads the narrowest literature for even current papers at least two years~~ ~~trying to attend many most of the relevant scientific meetings for one soon discovers that it is hard to date~~. To attend and the most relevant scient. fic meetings has become a full-time task.]

~~do laboratory work while flying in an airplane~~. [Even if one does, one finds in private discussions with colleagues)

[That work has usually progressed far beyond even what is presented at the meetings. Just

during the past two weeks, I learned of two discoveries of sweeping significance which I

might briefly share with you [in illustration) - the first, from an Australian laboratory which I learned about in a

Geneva coffee shop and the second, from one of one Johns Hopkins scientists who described his

work at a ~~student~~ faculty party. You can perceive the type of scientific meetings which a Dean attends. One is applied and the second, very basic.

\+ The first pertains to vaccinia virus (yes - our now discarded albeit temporarily smallpox vaccine). (Use - abandoned under pressure in 1980) Vaccinia

as you know, is ~~among~~ one of the largest viruses but needs only a portion of its genome to replicate. My Three years ago Moss and his

colleagues at NIH, discovered that genes fragments of influenza, hepatitis, ~~malaria~~ malaria and other viruses Which and How many still remains to be worked out)

could be spliced into vaccinia (They found that the virus ~~that it~~ would replicate in vivo) and that protection in monkeys could

be achieved. If this also works in humans (believe it will) one could imagine -

A vaccinia virus carrying many different antigens - advantages, once engineered -

+ Easy to produce & cheap -
+ Stable -
+ Easy to apply -
+ Vaccination from birth.

Expect first trials (in humans) ē dengue vaccine within a year.

Problem - (adults &) children ē immunodeficiency diseases.

However, Ada interleukin-2 splice / results: normal mice & nude mice.

Will not solve all probs ē immunodef dis. but a substantial progress.

What it illustrates, however, are several things:

1) Pace of development (as one scientist noted) biomedical engineering permits one to achieve in 10 months of precise work what formerly took 10 years (of trial and error) to accomplish.

2) We are rapidly approaching the point where we understand what piece of the virus genome does what and are able to design vaccines which will achieve precisely what we want them to achieve "designer genes"

3) Now draw in is the concept of combining several antigens in a single carrier rather than having one vaccine for each antigen ~~or group~~

Vaccines ~~Work is~~ hold a special interest and so work is progressing on many fronts. Why vaccines?

For many diseases now and for many more in the (near) future, a vaccine is the single most cost-effective intervention we have -

Illustrate - smallpox program. Cost in international support = $\$8 \times 10^6$/yr.

National costs = (basic vaccination) about $\$16 \times 10^6$/yr. or $\$24 \times 10^6$/yr. total.

Savings each year - hospital and OPD care (not to mention death; pain & suffering) = $\$1000 \times 10^6$/yr

Polio in Brazil - total program costs are met by ↓ in rehabilitation costs alone.

Important advantage of vaccine over drug

- Can administer any time - usually only 1-3 doses vs. drug Rx (e.g. years penicillin)
- Mass administration possible
- Most important - individual contacts the virus/bacteria/parasite before infection occurs.

Can I summarize the work going on — no! At last mtg I attended at NAS — we counted a total of 42 vaccines in active stages of development!

<u>But wait — there is more</u> —

Ts'o and Miller at JHU plus collaborators at Cornell, Md, USUS have recently announced yet a new discovery which ~~promises even more~~ is even now under test using a number of different viruses and oncogenes.

What they have done is to synthesize ~~a~~ non-ionic DNA (analogs) which penetrate the cell wall and are totally resistant to nucleases. They bind to messenger RNA and stop gene expression without harming the cell. These compounds are called (MATAGENS) "masking tape for specific gene expression."

In vitro studies show that ~~not~~ only minute amounts of matagen are needed; that it appears to work against many different viruses and oncogenes and <u>now</u> the first animal tests indicate that it is highly effective against Herpes virus I and II.

What does this mean — (whole new class of) effective antiviral agents (antiviral agents have been few and problematic)

Powerful new tool for the study of viral biology & pathology

<u>Note</u>: Like the vaccinia recombinant studies, a ~~[illegible]~~ group of laboratories rapidly exchange reagents and information with each doing that part of the work which he can do best.

Ts'o & Miller are synthesizing the product, developing new refinements ~~[illegible]~~
Group at Cornell is working ~~of~~ on its use in HTLV-III (AIDS)
" " Maryland — herpes and cytomegaloviruses
" " U.S.U. — oncogenes.

With this (type of collaborative work) the pace of progress is almost blinding in speed. Very different from past where one laboratory or investigator and one series of studies

Change in public health from curative to community-based initiatives.

EPI - hq → states

ORT - hq → states

Vitamin A

~~But with all of these positive developments, let~~

We have great cause to be optimistic about the coming decade but serious problems need to be overcome if the promise is to be realized — problems which we solved with SE ~~but they~~ and which offer lessons we must pay attention to.

1967 – have vaccine / the administrative problem to deliver.

We didn't see it this way. Research lab. / in vac. prod. / in the field.

How can the program be executed more efficiently and effectively

1st field studies – every case a failure ↓ persistent of immunity – change in vac. prog. change in strategy

2nd vac. prod. – mfg. of producers; methods of production; improvement of stability

3rd lab. – Search for an animal reservoir (involved epi.; prog. directors and basic virologists) Free discussion of problem

- Monoclonal AB for serology
- Monkey pox virus
- White pox virus – Nobel laureates Nathan/Smith.

Two problems today:

1) (too) little is being done in applied research –

- How best to organize vac. progs.
- Vaccine stability
- Syringe + needle
- New vaccines – e.g. vaccinia-carrier model

2) Communication between basic scientists and field epidemiologists - severely deficient

Another problem (which I see) perhaps most important of all.
~~Support for~~ Need for greater research activity in diseases of the tropics
Almost inevitably, each country supports best ~~the~~ research which is most closest to its own problems and the best scientists work on problems with which they are most familiar.
~~All effort~~ Efforts are in progress ~~has begun~~ to break down these barriers for ~~research and~~ disease problems do not respect national boundaries and the community of science is an international one - not a national one.
Thus, in smallpox eradication, our principal laboratories were in USSR and USA but important work being done in Canada, Netherlands, Australia, UK, India (Calcutta)
Scientists from each of these laboratories, met regularly; they worked in each others laboratories; they shared research observations before publication.
New discoveries were sometimes in widespread use even before results were published in the literature.

Your own institute is an important, world-renowned institution. As we probe further into the frontiers of science, ~~we~~ we welcome a closer collaboration with all of you