

U. of KY - 1982 / JAN
AOA

Special pleasure for me today to be invited to address you at a school which, although comparatively young, has ~~already~~ compiled an enviable record in many fields of medical scholarship and education. ~~Although this is a first visit for me, I feel it is a school I know~~

In an area of special interest to me, I am especially mindful of the fact that this was the first school to establish a Department of Community Medicine - an innovative program developed by an old friend and respected colleague, Kurt Denochle, ~~who~~ ^{whose program} and ~~we~~ ^{we} all followed closely ^{ad.} with administration. In fact, it was Kurt who posed to me the question as to what was most important ~~to~~ ^{you} learned from the program.

It was just 18 months ago that the World Health Assembly ^{passed this resolution}

① Declares solemnly

② Smallpox vaccination.

Over 4 years have now elapsed since October ²⁶ 1977 when a 23

③ year old cook in Morke, Somalia became ill with smallpox. He represented the last case in a continuing human-to-human chain of ~~the~~ ^{to the best of our knowledge,} infection dating

back more than 3000 years. Today, ^{the virus resides under high security}

in just four laboratories - CDC/Atlanta; Porton Down/England;

Institute of Virus Pop./Moscow; and in South Africa.

Much has been written about the S-E-P ^{explicitly} from different

vantage points but little has been said about the role of research in this program. In fact, because of a rather contentious and meaningful interlude at the commencement of the program in 1967, it is ^{important} ~~critical~~ that ~~I~~ ^{ask} ~~of you~~ ^{explore with you today} what role, if any, did research play

~~Science - "They are going to produce a vaccine"~~ ^{Supra} ~~①~~

~~Although much has been written about the S-E Program from different vantage points, ^{explicitly} ~~nothing~~ has yet been written about the role of research played, ^{which} ~~in fact~~, ^{the} ~~little~~ for my discussion originates ^{from} a meaningful interlude ^{at} the commencement of the program in 1966/1967.~~

④ + WHA - ^{May} 1966 - $\cdot \$2.5 \times 10^6$ -
 $\cdot$ ~~SD~~ SD countries $\times \$50,000$
 $\cdot \leq 5\%$ of WHO Budget
+ Pic was sliced in various ways by the senior staff
→ 1967 - Prog began ~~to Region~~
~~to HQ~~

+ DAA arrived in November, 1966.

No funds identified for research

Good vaccine - drop on skin - scratch.

Purely an administrative problem - vaccinate all the people (then something over 1 billion in the endemic countries and 'Voila' - no smallpox) $\cdot$ purely admin prog

Lesson from the past - malaria 1955 - DDT ~~No stop research.~~
^{in knowledge of smallpox} ~~epidemiological malinvestments & malinvest into people.~~

$\therefore$ argue for research funds. No clear idea as to what we needed funds for but ~~not~~ a conviction that however "simple" all this was - ~~it~~ ^{they} would ~~be needed~~ ^{to do research}

Argument lasted over almost a year -

Finally - $\$40,000$ to be administered by the Director of the Div. CD - DAA was too young to be entrusted with a sum so large!
We couldn't even pay indirect costs.

+ Before the program finished, few of the eternal verities of 1966 remained unchanged ~~unchanged~~ and, even as the ~~program~~ ^{last} cases of smallpox were occurring, new questions were arising from the research, ^{which} yet today are unexplained.

Conclude ~~this~~ ^{chapter} on smallpox "Further research is required."

In some areas of Central Europe - child not named until after recovery.

(12) - ⑥ Jenner - milkmaid complexion

(13) - ⑦ ~~⑦~~ complex preventative

- ⑧ ~~⑧~~ James Phipps

- Vaccine spread - arm to arm - later flask of calf
~~Problem~~

- Refrigeration introduction - gradually from U.S. + Europe
over 50 10,000 cases in USA in 1939

- Collier - Lister Institute - 1950's commercially feasible method.

- Disease was a problem to all countries 5 or 5 per

U.S. - 15×10^6 vac.

U.K. / Germany - Hospitals.

Quarantine.

(14) - 1959 WHA - 80% vac. - not very successful Now Delhi.

(15) - ⑨ 1964 Expert Com.

- 1966 - WHA - One last ~~attempt~~^{try} - optimistic rhetoric but no behavior

Malaria was fading

Eradication a doubtful concept - yellow fever - yaws

Coordination of progr. in 50 countries (poor) + > 1 billion people

(16) ⑩ 1967 Program status

Theoretical basis for eradication -

- interruption of transmission

- complete recovery/death - no carrier

- no animal reservoir.

In brief, once the last human case ~~is~~^{is} isolated and does not transmit infection - eradication is achieved.

Program was two-fold: Vaccination + containment

① Vaccinate 80% to increase immunity -

② Develop a reporting system to detect remaining outbreaks + eliminate them.

Soon found - areas where <80% c. vac. scar + eradication

- " " >95% " + smallpox

STRATEGY SHIFT to SURV. - CONT. - detect outbreaks/contain.

Africa - comparatively simple

• 1970

• 1973

Asia - ? traditional home/reservoir of smallpox - ? possible

> 700 x 10⁶ people.

> Always on the move - trains/buses - religious festivals (Mecca etc.)

> The "Search" - 120,000 people (contact census)

①⑨ 130 U.P.

Problem arises - young Oxford U. couple.

Calcutta - sidewalk dwellers

Markets - >95% of outbreaks in 12 mile radius.

②⑦ ①④ Decreasing incidence

②⑧ ①⑤ Sabine Bance

②⑨ ①⑥ Ethiopia -

Size -

20 x 10⁶

Lighting

①⑥⑦

Pop. dist. person - 50% > 1 day's walk from a

ROAD

①⑦⑧ ①⑨ Last case in Ogaden desert

②⑤ ①⑩ One last chapter Somalia - 3000 cases

②⑥ ②⑩ Ali MAALIN - Oct 26, 1977 (10 yrs. / 9 mos. / 26 days)
on the target

Two year search - reward - Int. Commission - Oct 26 1979 end.

Have ~~discussed some of the~~ ^{epidemiological} ~~little short~~ research as it applied to the program - selected
3 vignettes to illustrate ^{two} problems ~~and state contributions~~ -
① App. Tech. ② ~~Exp~~ ③ Virology - Epi

+ Vaccine application

- (27) (28) { Scratch technique - describe - 25 dose vial.
U.S. multiple purposes technique
Looking for a better way -
- (29) (30) Jet gun - problems
- (31) (32) Needle - used for foot ppx - Wye th / multiple purposes
Multiple punctures / bleeding
Conservation of vaccine
Change in needle for reuse
- (33) (34) Holder
- (35) (36) Cleansing of skin / Contraindications
- (37) (38) Vaccinators package.

+ Airborne spread

- Smallpox hospital isolated / Cases around hospital.
1963 U.K. - fierce debate aged -
- (26) 11 Jan. 1970, 20 yr. old German electrician
Returned from Karachi Afghanistan + hospitalized.
13 Jan Rash
16 Jan. Dx of smallpox made
- (27) 19 cases followed
How were they spread -
Nurses
Food diet.
Priest.
Patient himself
- (28) "The smoke experiment"
Density of rash & cough
Low humidity
Cool temp.

One previous outbreak - but / air borne spread was no longer a volume

The interrelated nature of field + lab research is best illustrated in our quest to answer the

+ Question of an animal reservoir

Only a requisite of these studies is possible the air circulation

Most important question to be answered } Yellow fever program in Americas continued for years in belief, no animal reservoir. ~~There~~
Discovery of simian malaria - not able to be differentiated - but nevertheless there.

Decided as a deliberate policy to find varicella virus in lower animals
1968 - 1st meeting of a working group - ~~scientists~~ ^{virologists} from Tokyo, Moscow, CDC, St. Mary's Hosp (London), Birmingham, Ryke, Inst. in Netherlands, ^{Paris - by telephone} Frank Fenner (Aust.), G. Mathejohn (US) + ~~exp~~ from field programmes. Met q 2 yrs. + agreed on basic directions of study and exchanged working data.

Multiplicity of species specific pox
Difficulties of identifying (monoclonal AB may solve this)
dif. types

Where to begin ^{many pox viruses} - decision simians
von Magnus 1958 - 1st report of monkeypox - around world

+ letters to labs working c monkeys -
10 outbreaks uncovered - NO human cases.
(Monkeys - Africa + 4? Malaysia)

Next step - serum testing to try to identify antibody -
> 3000 serum in Africa 0 significant AB.
480 " " Malaysia "

Look at a group of rodents ~~Studies in Azerbaijan - the Moscow Zoo - heading nowhere~~

Atc ~~but~~ - what to do next - Mysterious cases of smallpox
Zaire 8/4/70 ^{no source import. of source trace} Liberia Sept/Oct. - 4 cases
No contacts - ^{Liberia story.}

Moscow discovery -> Atlanta (Temp. growth)
45 cases since - villages/trop. rain forest/eating monkeys.

Collection of specimens in vicinity of cases
4 in Moscow 1974 to 1975 - ? contamination
2 in Netherlands (1964) - REAL.

"Whitepox" - but really ? smallpox.
How do we find out?

London, Atlanta, Tokyo, Moscow, Netherlands and

Intensive studies begun - } BRIMMINGHAM + RHOODY Aug/Sept 1978

What tell the press, the scientific community? ^{VARIOLEA / M. POX} ^(VAX + M. POX) ^{WHITE POX} ⑦
Characteristics same (but do they infect humans?)

Epidemiology

~~Two~~ ^{Two} years ago - Netherlands technician
Last summer - thanks to Watkins & Smith - genetic analysis possible.

~~All Moscow isolates alike -~~

~~Moscow passage study - monkeypox - whitepox~~ ^{retention endogenous} ^{of the genome}
Last summer - thanks to Watkins & Smith - genetic analysis possible

All Moscow isolates similar

Netherlands isolates look like Asian strains & v. v.

Monkeypox virus differed at many dif. sites along the genome - mutation unlikely.

With epidem. info. & genetic analysis - now rest comfortably

But - reservoir of monkeypox still not known. Studies in progress.

To those who say in regard to any problem, "we have the tools, we know what to do, go out and do it - forget the research". I can only reply with feeling - if ever there was a situation in which these conditions prevailed, it was c. smallpox in 1966.

Absent continuing query - we would today be engaged in ^a ~~an~~ apparently never-ending struggle against this. The most devastating disease known to man.