TAIWAN (1)

Appropriate & discuss - 1996 - Year of Vaccines - U.N. Geneva DEC 1995

Vaccines - single most cost-effective simplest of all med. proc.

1993 World Bank Report

c ORT - accounts for saving of ≥ 3-4 $\times 10^6$ children annually

TAIWAN's role c Hepatitis Bp - epidem. / vacc testing / 1st nat. prog.

This A.M. -

- Briefly - Hx. immun. prog. over past 20 years.
- Where we are today - a situation radically changed from 5 or 10 yrs. ago
- Potential for the future - very bright
  - very complicated.

9667.41

I Hx: Smallpox erad. -

- What can be accomp. c Low bitto. -

Personnel -

Org. -

Qual. control - vaccines -

- progs.

1969 - 1st mtg. on exp. prog. - why < disease prev. / bitto vac. being delivered

1974 - WHA resolution

1977 - Prog. started. DPT/polio/measles/BCG. (List yellow fever/Hep B)

Progressed slowly - c help from UNICEF / bitto help from most donors.

~~1980 UNICEF~~ - WHO "Health for All" (1° care but Low)

1983 UNICEF - Childhood initiative - immun. the central pillar

Rotary - $ 100 $\times 10^6$

Target - 80% vac. levels by 1990.

1988 - Status of vac. / dev. / production - Why 1988?

Not one of the vaccines fully satisfactory.

No research being done in any of them - WHO attitude. until 1985.

New vaccines –

Hep B – Salute & Taiwan for pioneering efforts.

Mumps – forget it

Rubella – O.K.

Research ↑ (recently) because of NIH funding – began 1983 – now reaching $200 × 10^6$/yr. (later – not necessarily)

↑ Interest by ~~some~~ priv. companies in vac. production ~~but not much~~

Primarily – Pasteur – Merrieux
– Connaught
– SKB
– Sklavo

} 200 – 500 × 10^6 doses/yr.

not U.S. companies. (1/10 the orgs of Europ. companies)

Production – being conducted in a number of countries –

Primarily DPT / BCG / repackaging of ~~OPV~~ OPV. ~50 × 10^6

Few countries ē GMP standards

Few " ē adequate regulatory authority.

What was WHO doing? NOTHING.

II Today – last 5 – 10 years – ↑ exploration of interest in research
– ↑ strengthening standards GMP
– emphasis on stricter regulatory

Routine (6)	Other vacs.	On the horizon – (>100 in phase I/II/III)
	Hi to Jap ~~Hib~~	Mega Shig.
Hepatitis B	Rubella	Strep. B
~~Typhoid~~	Varicella	Rotaviruses
(aP)	Hep A.	RSV
	Typhoid	Vzv. sig.
	Cholera	~~HIV~~
	Str. Pneu.	~~Gonococcus~~
	Rabies.	CANCER – HIV

250 000 000
250 000

How do we administer them — what much used only U.S./Europe coming + expensive

2	4	6	12–18
Hib.	Hib	Hib	Measles (MMR)
DPT	DPT	DPT	DPT
HepB.	HepB	HepB.	

★ Complications of DTaP — more complicated/expensive to produce/is it better.

How many injections and when — ~~[illegible]~~

~~[illegible]~~

DTaP – Hib.

DTaP – Hib – HepB

HepB – Hib –

~~[illegible]~~

MMR – ~~[illegible]~~ / How many want mumps?

IPV controversy –

OPV causes VAPP –

How many cases – U.S. – 8 per year. –

4 vaccines / 4 contacts

What is present – 1988 U.S. policy IPV ×2 + OPV ×2

Why OPV.

Prevent ~~2~~ 3 cases. ← at most – 5 000 000 new vaccines each year.

Not much effect for huge expense and disruption of vaccine schedules (2 more inj.) but acceptable (barely) if contained.

Predict: You will hear plenty from P-M-C.

and IPV will become part of schedule for many countries

★ WHO Review of ~~[illegible]~~ articles Regulation

~~GMP stands~~ 70% in countries ∴ inadequate regulatory auth.

∴ ↑ emphasis on GMP

~~∴ ↑ emphasis on~~

∴ ↑ emphasis on tower labs. & tight QC regulatory controls.
Scale of ~~production~~ infrastructure in vaccine prod - very important.
- Building
- Equipment
- Testing.

∴ Discourage labs. in countries & populations $< 100 \times 10^6$.

Note - ↑ interest in large volume vac. producers in supplying many countries
costs partly supported by sales & developed countries.
costs lower than most small scale producers.

★ IPR - !! - proprietary restrictions. - how does this fit in

Summary: Vaccine production prospects - very different than 5 & 10 yrs ago.

!!! but: let us look @ the future and ~~stop~~ @ present seems prohibitive, imagine what the next 10 years will bring.

SURVEILLANCE

Reminder: Vaccines - most cost effective. Want & use !!

~~Rapidly~~ ~~capacity~~ ~~expanding~~
~~New Vaccines~~: ~~expanded~~ understanding of microorganisms, immune process, and approaches & presenting antigens & the immune system.

New Vaccines - last WHO report - > 100 new vaccines stage 1 +

~~Conj~~
Attenuated, inactivated, subunit, conjugates, recombinants.

Adjuvants: old Al OH conjugate → microcapsules
novel ones (tric/ulose)
other strategies.

Microcapsules by month

Recombinant vectors such as vaccinia:

Large virus; possible express in flu / measles / hep / rabies + ? how many others.
but also used BCG, polio, salmonella, adenovirus and others.

Bottom line:

So many potential antigens & so many potential avenues of research, becoming ever more difficult to set research agenda ~~[illegible]~~

To compete in this arena

to be in the forefront of research at least in the main cutting edges
to be able to meet the new GMP and regulatory requirements
~~& be able to produce this~~
& be prepared to produce at all large volumes.
necessary

Underwritten upon the meet such requirements — you will have a terrible selling the product!

Conclusion

A bright, new, challenging field of medicine — probably ~~perhaps~~ to most important advances / potential saving of lives

~~but~~ & complex / will require very significant investment of managerial
manpower
resources

Need now to work collectively & identify combinations of vaccine which make the most sense

, Taiwan could play important role in res. testing.

Develop regulatory authority — to test and approve products offered.
(WHO/CDC role limited)

NEW TECHNOLOGIES

1) Vaccine Combinations

Immediate possibilities - inactivated vaccines

DTaP
Hib
Hepatitis B (HB)
Inactivated polio vaccine (IPV)

Immediate possibilities - live vaccines

Measles
Mumps
Rubella
Varicella

Might hepatitis A and Str. pneumoniae be added?

Combinations now being tested

DTaP Hib	**DTaP - HB**
DTaP IPV	**DTaP - Hib - HB**
Hib - HB	**DTaP - Hib - HB - IPV**

Problems:
1) **Confirmation of schedules**
2) **Potency and stability of ingredients**
3) **Clinical efficacy**
4) **Propriety ownership of strains**

"PACKAGES" OF VACCINES

Pregnant women (IgG transplacental transport)

- **Group B streptococci**
- **Respiratory syncytial virus**
- **Rotavirus**

Pre-teen children (10-12 years)

- **Booster doses - DTaP, Measles**
- **STD vaccines**

Seniors

- **Influenza**
- **Streptococcus pneumoniae**

NEW TECHNOLOGIES

2) New formulation strategies

Encapsulation of antigens in biodegradable polymers

Perinatal inoculation

Oral administration

Novel adjuvants

Liposomes

Squalene emulsions

NEW TECHNOLOGIES

3) New vector systems

Bacteria (intracellular replication)

- **Salmonella typhimurium**
- **Mycobacterium tuberculosis**

Viruses

- **Vaccinia**
- **Canary Pox**
- **Poliomyelitis**
- **Adenovirus**
- **Herpes simplex**

"Vaccine research, development and production is no longer a cottage industry"

1. **Rapid progress on many fronts**
    - **Improved old vaccines**
    - **Many candidate new vaccines**
    - **Combination vaccines**

2. **Proprietary rights - critical for vaccine development**

3. **More stringent requirements**
    - **Good manufacturing practice**
    - **Potency, stability, purity of vaccine**

4. **Economies of scale in production**
    - **Physical plant**
    - **Equipment**
    - **Vaccine testing**

VACCINES - TODAY AND TOMORROW

EPI VACCINES

Diphtheria

Pertussis

Tetanus

Measles

Polio

Hepatitis B*

BCG*

Yellow Fever*

*** Not routine in all countries**

VACCINES - TODAY AND TOMORROW

EPI VACCINES	NOW LICENSED FOR GENERAL USE
Diphtheria	Rubella
Pertussis	Mumps
Tetanus	Varicella
Measles	Hepatitis A
Polio	Hem. influenza B
Hepatitis B*	Typhoid
BCG*	Cholera
Yellow Fever*	Str. pneumoniae
	Influenza
	Japanese encephalitis
	Rabies

* Not routine in all countries

VACCINES - TODAY AND TOMORROW

EPI VACCINES	NOW LICENSED FOR GENERAL USE	IN CLINICAL TRIALS
Diphtheria	Rubella	Meningococcus A, C
Pertussis	Mumps	Parainfluenza
Tetanus	Varicella	Resp. Syncytial Virus
Measles	Hepatitis A	Herpes simplex Type 2
Polio	Hem. influenza B	Cytomegalovirus
Hepatitis B*	Typhoid	Enterotoxigenic E. Coli
BCG*	Cholera	Rotavirus
Yellow Fever*	Str. pneumoniae	Lyme disease
	Influenza	Dengue
	Japanese encephalitis	Coccidioidomycosis
	Rabies	Epstein-Barr virus
		Streptococcus A
		Leishmania
		Leprosy
		Neissonia
		Malaria
		Shigella
		Venezuelan encephalitis

* Not routine in all countries