The Place of IPV in Polio Vaccination of Developing Countries

Better Late than Never or Better Never than Late ???

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Key Issues with IPV

- Immunogenicity on EPI Schedule
- Influence on virus excretion and transmission
- Individual vs. collective protection
- Utility in eradication
- Supply
- Cost

PAHO-CDC Cuba study results

	% seroconversion		
	Type 1	**Type 2**	**Type 3**
DTP-IPV//Hib 2, 4 months	**94%** (68/72)	**89%** (64/72)	**96%** (69/72)
DTP-IPV//Hib 6, 10, 14 weeks	**98%** (49/50)	**83%** (44/53)	**98%** (52/53)
DTP//Hib 6, 10, 14 weeks	**4%** (2/55)	**2%** (1/55)	**5%** (3/55)

Efficacy of e-IPV

Senegal	**(1987)2 doses 89% (62-97%**
India	**(1990) 3 doses > 90%**
Canada	**(1959) 3 doses 96%**

Influence on Virus Excretion

Viral Shedding in Stool of Any Type After OPV Administration to IPV Vaccinees, OPV Vaccinees or Unvaccinated Infants

(Lassri et al, JID, 2006)

	1 Week Post OPV		3 Weeks Post OPV			
Prior Vaccination	*N*	% PCR Pos.	*N*	% PCR Pos.	Median Copy No.*	Median Copy No. #
None	48	92 (80-96)	48	81 (67-91)	655	1143
OPV x 2	41	22 (0-26)	42	5 (1-16)	NA	NA
IPV x 2	42	76 (61-88)	38	37 (22-54)	143	174

Individual vs.

Collective Protection

IPV/eIPV field study, 1980-83. Half block on DPT, half on DPTP

	DPT	DPTP
No. of children	3104	3220
Child-years of study	6612	6911
Children with polio	17	0
Vaccine efficacy %	–	100

John TJ. Rev. Med Virol. 1993 3:149-160

This study examines the possibility of polio vaccine virus circulating within the United States (highly IPV-immunized) population that borders Mexico (OPV-immunized). A total of 653 stool samples from children and 20 sewage samples collected on the US side of the border were tested for the presence of poliovirus. All samples were found to be negative. These results suggest that the risk of circulating vaccine-derived poliovirus is low in fully immunized IPV-using populations in developed countries that border OPV-using populations.

Gary HE,e t al. Epidemiol Immun 2007(ahead of print).

Utility in Eradication:

The Indian Case

Virology of AFP Cases in India, 2006-July 2007 in which Poliovirus was Isolated

	T1	T2	T3	Mix	Total
Wild Virus	659	0	109	0	768
Vaccine Virus	1366	266	467	402	2501

Source: www.npspindia.org

Chronology of Proposed Use of IPV in Uttar Pradesh

April 2006	Talks between Sanofi Pasteur and WHO about a trial in U.P.
May 2006	Sanofi Pasteur confirms offer of 1.3 million doses of IPV
May – December 2006	No response from Indian government
December 2006	Sanofi Pasteur visits Government of India to reiterate offer
Oct. 2007	IPV doses expire and are to be destroyed.

Supply

Manufacturers in IPV (bulk)

Manufacturer	Where Made	Cell Substrate
Sanofi Pasteur*	France, Canada	Vero, MRC-5
Novartis	Italy	Vero
GlaxoSmithKline*	Belgium	Vero
National Biological Laboratory (S.B.L.)	Sweden	Vero
NVI	The Netherlands	Vero
Statens Serum Institut (SSI)	Denmark	Vero

*Licensed in U.S.

Supply Situation for IPV

- Current supply capacity: 100 million doses
- Very significant investment is currently being made to increase capacity close to 200 million doses.
- Additional investment will be needed to further increase to overall capacity up to 300 million doses.
- No company will invest without an expectation of use.

(i) reduction to an absolute minimum of the number of facilities storing, handling and/or amplifying polioviruses;
(ii) restriction of these facilities to countries with routine childhood IPV immunization activities that maintain coverage sufficient to prevent polio transmission;
(iii) implementation of high-level biocontainment;
(iv) substitution of wild-type polioviruses with Sabin viruses in all processes and procedures: and
(v) maintenance of polio immunity among all laboratory workers, all production operators and the general population.

= No developing country manufactures

WHO, Wkly Epidem. Record 81:137-38, 2006

Cost

Break-even IPV prices in South Africa

Polio vaccine alternative	Break-even IPV price per dose:
2 doses IPV in a 10 dose vial	0.41
3 doses in a single dose vial	0.39
3 doses IPV in 10 dose vial	0.24
3 doses IPV-DTPa-Hib	4.11
3 doses IPV-DTPa-Hib-hepB	4.68
4 doses IPV in single dose vial	.26
4 doses IPV in 10 dose vial	.16

Griffiths UK, et al. Vaccine 24:5670-5678, 2006

Options for Pre-Eradication Use of IPV with OPV

IPVx2 – 6, 10 wks or 10, 14 wks.

IPVx2 – 6 wks, 9 mos.

IPVx3 – 6, 10 wks, 9 mos.

IPVx3 – During campaigns

Options for Post-Eradication Use of IPV

- **Universal childhood vaccination to prevent natural or malicious return of wild virus**
- **Focused vaccination in high-risk countries**
- **Response to outbreaks**

The Possible Use of Super-concentrated IPV to Contain Post-eradication Epidemics

- Evidence that antibody response is directly proportional to D antigen concentration
- Current vaccine composition is 40-8-32
- Evidence that excretion is inversely related to concentration of serum antibody, probably because of diffusion of IgG into the intestine

Super Concentrated IPV for Post-Eradication

	Conc. (D units)
Existing	40/8/32
Feasible	200/40/160
Theoretical	400/80/320

Issues: **Stability, Formol, Protein**

Conclusions

IPV could be useful both for eradication of paralysis due to wild or vaccine-derived polioviruses and for dealing with outbreaks after presumed eradication.

However, IPV will never be available in sufficient quantity unless authorities ask manufacturers to make it, and persistent vacillation continues to prejudice its utility.