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THE 2003 ANTIMICROBIAL RESISTANCE SURVEILLANCE DATA

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For 2003, resistance data for 24,112 isolates were reported and analyzed. There were 28% less isolates from the number reported in 2002. This was mainly due to the decrease in the number of bacterial isolates reported for 2003 from twelve sentinel sites, namely the Philippine General Hospital (PGH). Research Institute for Tropical Medicine (RITM), Baguio General Hospital and Medical Center (BGH), Eastern Visayas Regional Medical Center (EVR), Cotabato Regional Hospital and Medical Center (CMC), and Bicol Regional Teaching and Training Hospital (BRT), Lung Center of the Philippines (LCP), Vicente Sotto Memorial Medical Center (VSM), Zamboanga Medical Center (ZMC), Corazon Locsin Memorial Medical Center (MMH), Davao Medical Center (DMC), and Celestino Gallares Memorial Hospital (GMH), Rizal Medical Center (RMC), National Kidney and Transplant Institute (NKI), San Lazaro Hospital (SLH), Nicanor Reyes Memorial Hospital and Medical Center (FEU), and Santo Tomas University (STU) had more isolates in 2003. The major contributor of antibiotic susceptibility data were the PGH - 5,191 (22%), NKI - 4,412 (18%), DMC - 2,549 (11%), STU 2,019 (9%), and SLH- 1,213 (5%). The rest of the participating hospital contributed less than 5% of all isolates.

The most common specimen source were urine 25%, Blood - 22%, respiratory - 20%, and wounds - 16% , There were 340 genital tract specimens reported, compared to 465 in 2002. The distribution of pathogens reported were as follows: *E. coli* - 17% , *Klebsiella* 12%, *Pseudomonas aeruginosa* 11%, *Enterobacter* - 10%, *Staphylococcus aureus* - 7%, *Acinetobacter* - 6%, coagulase negative *Staphylococci* - 6% and others. There were only 75 isolates of *Moraxella catarrhalis* and 163 isolates of *Neisseria gonorrhea*.

Enteric pathogens

Resistance rates of all *Salmonella typhi* isolates to ampicillin, chloramphenicol and cotrimoxazole remained low at 0%, 1% and 0.3% respectively as compared to 2%, 0% and 3% in 2002. The chloramphenicol and cotrimoxazole-resistance *S. typhi* came mainly from SLH, which reported 2 and 1 respectively of such isolates. None of the isolates were referred to RITM for confirmation. There were two (2) ceftriaxone resistant *S. typhi* reported by SLH but no ciprofloxacin resistance isolate reported for 2003.

All the ARSP sentinel sites reported *S. typhi* isolates except LCP, NKI and VSM, The resistance rate of *S. typhi* gathered from regional hospital show that the organism remains to be sensitive to chloramphenicol, cotrimoxazole and ampicillin, where no resistance was observed to the 3 antibiotics except for ZMC where chloramphenicol resistance was 8%.

As has been previously observed, nonptyphoidal *Salmonella* showed higher resistance rates to chloramphenicol 22%, ampicillin 47%, cotrimoxazole 31% and ciprofloxacin 8% compared to rates for *S. typhi*. These rates were higher than those of 2002 especially for ampicillin where the resistance rate increased to 47% from 24% in 2002 and contrimoxazole from 14% to 31%. The rates also increased for chloramphenicol from 16% to 22% and ciprofloxacin from 4% to 8%. The continued presence of ciprofloxacin resistance is of particular concern.

For 2003, every sentinel site was requested to refer all *Salmonella* isolates to the Antimicrobial Resistance Surveillance Reference Laboratory (ARSRL) for identification, antibiotic susceptibility testing and serotyping in view of ARSP's participation in the WHO Global *Salmonella* Surveillance Program. The most common nontyphoidal *Salmonella* serotypes identified were *Salmonella* ser Welteverden (5 isolates), *Salmonella* ser Enteritidis (3 isolates), *Salmonella* ser Typhimurium (2 isolates) and *Salmonella* Heidelberg (2 isolates). *Salmonella* serotype Weltevreden isolates all came from the eastern portion of Metro Manila (i.e Pasig).

One (1) isolate referred with serotype Schwarzengrand from a patient at STU hospital was associated with ciprofloxacin resistance although there were 13 ciprofloxacin resistant isolates of nontyphoidal *Salmonella* from 6 sentinel sites namely: 2 from EVR, 2 from MMH, 4 from NKI, 2 from RMC, 1 from STU and 2 from VSM.

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The resistance rate of *Shigella* to the drug of choice cotrimoxazole was 78% which was significantly higher than the figure of 72% in 2002 whereas that for nalidixic acid, the alternative drug, was 0%. The first isolate of *Shigella* resistant to ciprofloxacin was also reported. Among the regional sentinel sites, data on *Shigella* only came from BRT, which consisted of 1 isolate. The isolate from BRT was cotrimoxazole resistant.

Resistance rates of *Vibrio cholera* 01 to tetracycline, chloramphenicol and contrimoxazole were 0.6%, 0.3% and 1.4%, respectively which were almost the same as those 2002 figures except for contrimoxazole where there was a marked decrease from a figure of 36% in 2002. There was hardly any tetracycline resistance reported among the cholera isolates in Metro Manila and all regional sentinel sites. There were only 2 tetracycline resistant *V. cholerae,* namely: an outbreak (OBK) isolate - 1 and PGH - 1. None of he tetracycline resistant isolates were referred to the ARSRL for conformation. The outbreak isolate originated from a patient in Manila Health Department (MHD) where there was an outbreak in November 2003.

ARI pathogens

Among the respiratory and invasive isolates of *Streptococcus pneumoniae* 9%, 9% and 3% were resistant to penicillin (as determined by screening with 1ug oxacillin disk), cotrimoxazole and chloramphenicol respectively. The extent of resistance to all three drugs was slightly higher than those of 2002 where it was 6% for penicillin, but the same for cotrimoxazole and chloramphenicol. Majority of penicillin resistant isolates were reported by NKI, 7 isolates and PGH 4. None of the 23 penicillin resistant isolates were referred for confirmation. The number of isolates tested from most sentinel sites were too small to be able to draw conclusions on the individual resistance patterns by sentinel site.

Among the 112 isolates of *Haemophilus influenzae* -18%, 18% and 13% of the isolates were resistant to cotrimoxazole, ampicillin and chloramphenicol respectively. These were higher for all 3 antibiotics whose resistance rates were 11%, 5% respectively in 2002. Most of the resistant isolates came from GMH.

Staphylococci* and other Gram positive *cocci

Eighty two per cent (82%) of *Staphylococcus aureus* isolates remained sensitive to oxacillin except 304 isolates which came from the following hospitals: PGH (107), RMC (62), VSM (22), GMH (17), EVR (15), BRT (14), ZMC (13), SLH (10), BGH (9), MMH (8), CMC (7), DMC (6), NKI (6), LCP (4), FEU(3), RITM (3), and STU (1). Results of MICs done by ARSRL-RTM on 136 oxacillin-resistant isolates showed that 94 (69%) were truly methicillin-resistant (MRSA).

In Metro Manila, overall MRSA rate was 18%. Among the regional sites, the following had the highest MRSA rates: BRT (33%), ZMC (50%), EVR (29%), VSM (27%) and GMH (23%). BRT and ZMC also had one of the highest rates of MRSA in 2002, which were 54% and 43% respectively.

In contrast, 51% of *Staphylococcus epidermidis* isolates were resistant to oxacillin, which was higher than the 47% reported in 2002. Vancomycin resistance was at 0.3%, which was unconfirmed and consisted of 3 isolates, all from NKI.

Gram negative *bacilli*

For *Pseudomonas aeroginosa*, resistance to ceftazidime was 16%, to ciprofloxacin 27%, to amikacin 16%, to imipenem 15% and to cefepime 12% which were slightly higher than 14%, 28%, 12%, 14% and 9% reported for these five antibiotics in the previous year. The rise in antibiotic resistance rates was most notable with amikacin, ceftazidime and cefepime. Among aminoglycosides, resistance to amikacin was lowest at 16% in comparison to rates for gentamicin, tobramycin and netilmycin which ranged from 22-30%. Metro Manila had resistance rates that were generally higher compared to other regions except for BRT where ceftazidime resistance was 21%.

For *Acinetobacter*, lesser resistance was noted for imipenem (9%), amikacin (24%), piperacillin/ tazobactam (15%), ciprofloxacin (24%) ceftazidime (18%) and cefepime 914%) compared to 2002 data. There was an increased in cefepime resistance from 10% in 2002 to 14% in 2003.

Many of the *Enterobacteriaceae* showed high resistance rates to several antibiotics teste. Sixty five per cent (65%) and 76% of *E. coli* isolates were resistant to cotrimoxazole and ampicillin, which was almost the same as those of 2002. It remained to be relatively susceptible to third and fourth generation cephalosporins but exhibited high resistance rates to second generation cephalosporins (i.e. cefuroxime at 20% and beta lactam-beta lactamase inhibitors (i.e. ampicillin sulbactam at 22%).

Comparing data for E. coli among regions, very high resistance rates existed against cotrimoxazole (range: 34% to 68%), cephalothin (range: 30% to 70%), but were variable for co-amoxiclav (range: 14% at GMH to 58% at BRT). Other sentinel sites with high resistance rates to co-amoxiclav were ZMC (43%), VSM (40%), DMC (33%) and Metro Manila (25%). Against ceftriaxone, low resistance were generally observed (range: 0 to 6%) which were almost the same as data in 2002.

Comparing resistance rates of urinary *E. coli* from outpatients versus inpatients, there was no significant difference in rates for most antibiotics with a trend towards higher resistance rates for outpatient isolates. In isolates obtained from outpatients, least resistance was observed against cefuroxime axetil among oral antibiotics. There was a marked decrease in resistance to ampicillin from 79% in 2002 to 26% in 2003 and 40% in 2002 to 26% in 2003.

Klebsiella had high resistance rates (26%) against the gentamicin but low for amikacin where the resistance rate was 14%. High resistance rates were likewise exhibited against first generation cephalosporins like cephalothin (44% same rate for 2002) and second generation cephalosporins like cefuroxime (33%) and beta lactam-beta lactamase inhibitors like ampicillin-sulbactam at 32%. There was a higher resistance rate in 2003 against ceftriaxone and cefepime at 14% and 4% respectively but lower for ampicillin-salbactam (from 38% in 2002 to 32% in 2003). For data on other *Enterobacteriaceae*, please see accompanying table. The presence of extended spectrum beta lactamses had been confirmed from bacterial isolates of *E. coli* and *Klebsiella* referred by 8 sentinel sites to the ARSRL.

Neisseria gonorrheae

Resistance to penicillin was 78%, ciprofloxacin 58%, ofloxacin 60% and tetracycline 40%, which were generally similar to the rates reported in 2002 especially for ciprofloxacin, ofloxacin and tetracycline whose rates were 55%, 54% and 48% respectively in 2002. There was no resistance to spectinomycin. There were only 3 reported ceftriaxone resistant *N. gonorrhea* from the following hospitals: RTH - 1, NKI - 1, BRT - 1; but no cefixime resistant *gonococci*. None of these isolates were confirmed at the ARSRI.

RECOMMENDATION

1. Based on the above-mentioned antimicrobial resistance surveillance data:
   a. Empiric for suspected typhoid fever could still consist of either chloramphenicol or cotrimoxazole or amoxicillin/ampicillin.
   b. The fluoroquinolones and 3rd generation cephalosporins are better treatment options for non typhoid *Salmonella*. However, physicians should aware of the existence of flouroquinolone resistant non typhoidal *Salmonella* in a small proportion of isolates.
   c. Nalidixine acid should be considered as the drug of choice for treatment of suspected *Shigellosis*. However, as for non typhoidal *Salmonella*, physicians should be aware of emerging resistance of *Shigella* to the fluoroquinolones. Tetracycline remains to be an effective antimicrobial for cholera.
   d. Infections secondary to *Streptococcus pneumoniae* can be covered with penicillin or chloramphenicol or cotrimoxazole. Since the resistance rate of *S. pneumoniae* to penicillin significantly increased (from 6% in 2002 to 9% in 2003), there was a need to closely monitor the changing trends of resistance among *pneumococci*, being one of the most important etiologic agents of respiratory and CNS infections in all age groups. Furthermore, there was a need for sentinel sites to refer all their isolates of *S. pneomoniae* to ARSRL for MIC testing. It is unfortunate that for 2003, no sentinel site referred their penicillin resistant *S. pneumoniae* (PRSP) for confirmation although this is part of the ARSP standard operating procedures. PRSP renders penicillin useless for the treatment of INVASIVE *PNEUMOCOCCI* DISEASES such as meningitis and requires use of more expensive antibiotics such as 3rd generation cephalosporins to achieve care for these types of infection.
   e. The increased resistance rates of *Hemophilus influenzae* to the conventional 1st line antibiotics ampicillin, chloramphenicol and cotrimoxazole is an important cause for concern. Ampicillin resistance in *H. influenzae* is usually mediated by beta lactamase enzymes and would therefore respond to beta lactam-beta lactamase inhibitor combinations, extended spectrum oral cephalosporins and the newer macrolides.

Laboratories should therefore screen all isolates of *H. influenzae* for beta lactamases as part of its antimicrobial susceptibility test procedure. Beta lactamase negative ampicillin resistant (BLNAR) *H. influenzae* exist and selection of antibiotics for treatment of these strains should be based on results of antimicrobial susceptibility tests (ASTs).

In summary, empiric treatment of ampicillin resistant noninvasive infections secondary to *H. influenzae* can consist of a beta-lactamase resistant agent, an extended spectrum oral cephalosporin, or a newer macrolide. For invasive infectious possibly caused by *H. influenzae* type B or strains other than type B. cefotaxime or ceftriaxone or ampicillin in combination with chloramphenicol can be used. For all isolates of *H. influenzae* if antibiotic sensitivity tests show that the isolate is sensitive to the three first line drugs, then antibiotics can be shifted to these drugs.

f. Hospitals should base their treatment recommendations for *staphylococci* and the *Enterobacteriaceae* on their institution's prevailing resistance patterns as these patterns have been found to be variable from hospital to hospital. The continued rise in MRSA rates and cases of infection secondary to HSBI may indicate very inadequate implementation of infection control procedures in some hospitals, which the Department of Health (DOH) should look into.

g. Cefixime and ceftriaxone should remain as empiric of choice for gonococcal infections.

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ORGANISMS	PERCENT RESISTANCE					
	Ampicillin	Chloram-phenicol	Ciprofloxacin	Cotrimoxazole	Tetracycline	Nalidixic Acid
A. Enteric pathogens						
1. *Salmonella typhi*	0	1		0		
2. Nontyphoidal *salmonella*	47	22	8	31		
3. *Shigella*	50	43	12	78		0
4. *Vibrio cholera*		0		1	0	

	Ampi-cillin	Cefuro-xime	Chloram-phenicol	Cipro floxacin	Co-amoxiclav	Cotri-moxazole	Erythro-mycin	Peni-cillin	Ampicillin sulbactan
B. ARI Pathogens									
1. *Streptococcus pneumoniae*			3			9		9	
2. *Haemophilus influenzae*	13		13			18			
3. *Moraxella catarrhalis*	10	11	9	14	6	43	21		6

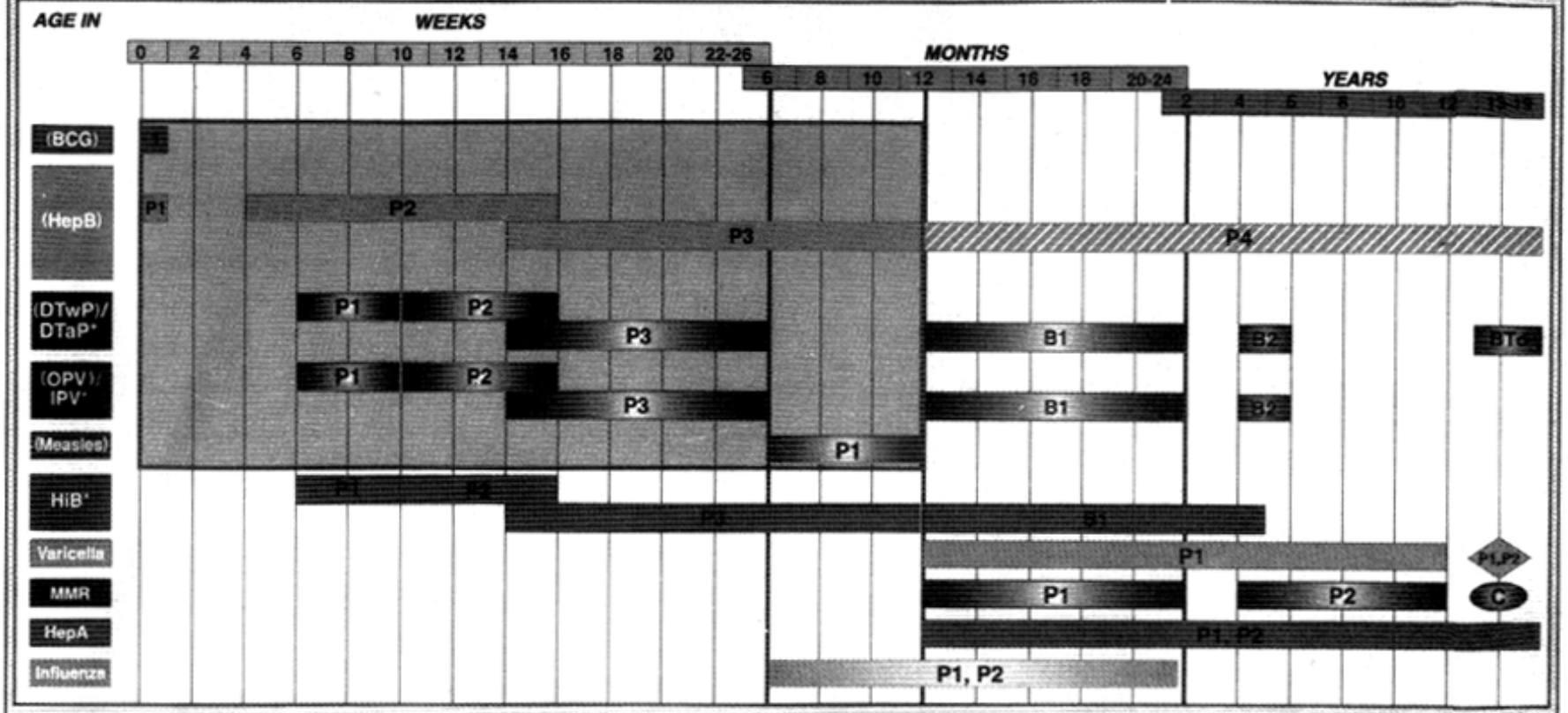
	Ampicillin	Benzyl penicillin	Ciprofloxacin	Cotrimo-xazole	Erythro-mycin	Oxacillin	Vancomycin
C. *Staphylococci* and *Enterococci*							
1. *Staphylococcus aureus*		96	7	8	11	18	0
2. *Staphylococcus epidermidis*		91		50	58	51	0
3. *Enterococcus faecalis*	5					4	

ORGANISMS	PERCENT RESISTANCE										
	Amikacin	Ampicillin	Ampicillin	Cefu-	Cipro-	Ceftria-	Cepha-	Genta-	Cotrimo-	Cefe-	Impe-
D. Enterobacteriaceae											
1. *E. coli*	6	76	22	20	30	5	47	21	63	2	
2. *Klebsiella*	4		32	33	27	14	44	26		4	0
3. *Enterobacter*	4				19	16	73	26			0

	Amikacin	Cefepime	Cefuroxime	Cipro floxacin	Genta-micin	Imperem	Netilmicin	Piper-Tazo	Tobramycin
E. Gram negative non fermenrative *bacilli*									
1. *Pseudomonas aeroginosa*	16	12	16	27	30	15	22	19	26
2. *Acinobacter*	24	14	18	24	30	9	23	15	24

	Cefixime	Ceftriaxone	Ciproflo-xacin	Ofloxacin	Penicillin	Spectino-mycin	Tetracycline
F. *Neisseria gonorrheae*	0	0	58	60	78	0	40

Childhood Immunization Schedule 2005



Legend:

- P - primary dose
- B - booster dose
- C - catch up immunization
- BTd - booster tetanus diphtheria
- ( ) - Covered by EPI
- ★ - primary doses are at least 4 weeks apart
- ■ - Ideally given at birth. If given beyond 12 months do PPD. Give BCG if negative
- ■ - 1st dose should be given at birth. The Hepatitis B vaccine birth dose can be used as the first dose in a 3 dose primary series. Doses are at least 4 weeks apart.
- ■ - A fourth dose is needed for the following:
  - If the 3rd dose is given at age less than 6 months
  - If no Birth dose was given using the EPI schedule of 6, 10, 14 weeks
  - For preterm infants < 2k, because of poor immunogenicity of the vaccine for these infants, the initial dose should not be counted in a 3-dose immunization schedule to complete the series.
- ◆ - If started 13 years and above give 2 doses 4 weeks apart
- ■ - Doses are 6-12 months apart

Vaccines in the pink area are given in the expanded program of immunization (EPI) of the DOH. In the EPI, measles is given from 9 to 12 months as a single-dose schedule.

■ Influenza Vaccine:

A. Influenza vaccine is also recommended in:
1. Children with the following high-risk factors: chronic cardiovascular disease (eg. congenital heart disease, valvular heart disease), chronic lung disease (eg. asthma), chronic metabolic disorders, renal disorders and hemoglobinopathies.
2. Children receiving long-term aspirin treatment.

B. Timing of vaccination:
The flu vaccine is recommended to be given annually preferably from February to June.

C. Children (6 months - 8 years) receiving influenza vaccine for the first time needs 2 doses, at least 4 weeks apart.

Typhoid Vaccine:

A. Optional

B. Single dose IM as early as 2 years old

C. Revaccination every 3-5 years

Meningococcal vaccine is not recommended to be given routinely due to lack of local data.

N.B. Recommended by the Committee on Immunization, Pediatric Infectious Disease Society of the Philippines (PIDSP), the Philippine Foundation for Vaccination (PFV) and the Philippine Pediatric Society (PPS).

Routine Adult Immunization for Filipinos 2005

VACCINE NAME ROUTE	TARGET INDIVIDUALS	SCHEDULE	PRECAUTIONS/ CONTRAINDICATIONS
1. Tetanus- diphtheria toxoid Inactivated vaccine Intramuscular	Recommended for all susceptible adults particularly : • Pregnant women • Health care workers	3 doses 0,1,6-12 months Booster every 10 years	• Severe allergic reactions to vaccine component or following prior dose • Moderate to severe illnesses
2. Hepatitis B Inactivated vaccine Intramuscular	Recommended for all adults particularly: • Immigrants from areas of high HbsAg endemicity • Hemodialysis patients • IV drug users • Homosexual males • Household contacts of HBV carriers • Recipients of blood products • Health care workers with frequent blood contacts	3 doses 0,1,6 months Alternate: 4 doses 0, 1, 2, 12 months Booster is not routinely recommended	• Severe allergic reaction to a vaccine component or to a previous dose
3. Varicella Live attenuated vaccine Subcutaneous	Recommended for all adults particularly: • Persons >13 years of age without history of varicella infection or vaccination • All health care workers • Teachers of young children • Non-pregnant women of childbearing age • International travelers • Military Post-exposure prophylaxis • Given within 72 hrs. of exposure	<13 years- 1 dose ≥13 years - 2 doses 0, 1 month	• Severe allergic reaction to a vaccine component (gelatin or neomycin) or to a previous dose • Moderate or severe acute illness • Pregnancy • Immunosuppression • Recently received a blood product • Untreated active tuberculosis • Adolescents in aspirin therapy
4. MMR Live attenuated vaccine Subcutaneous	Recommended for all adults particularly: • All susceptible adolescents and adults without documented evidence of immunity to any one of the components (especially non- pregnant women of childbearing age)	2 doses 0, 1 month	• Severe allergic reaction to a vaccine component (gelatin or neomycin) or to a previous dose • Moderate or severe acute illness • Pregnancy • Immunosuppresion • Recently received a blood product • Thrombocytopenia /ITP

5. Pneumococcal vaccine
Inactivated vaccine
Intramuscular
	Persons ≥60 years of age
	< 60 years of age with:
	
	• Chronic illness (cardio-pulmo, diabetes, alcoholism, cirrhosis, CSF leak)
	• Immunocompromised conditions:
	  • Lymphoma/ leukemia
	  • Chronic renal failure, nephritic syndrome, transplants, chemo/ radiation therapy)
	  • HIV/ AIDS
	  • Functional or anatomic asplenia
		Single dose
		
		Revaccination may be given after 5 years
			• Serious allergic reaction to vaccine component (thimerosal or phenol) or previous dose
			• Moderate or severe acute illness
			• Pregnancy (safety is unknown); if indicated give before pregnancy

6. Influenza vaccine
Inactivated vaccine
Intramuscular
	• Persons at increased risk for complications:
	  • Persons ≥50 years of age
	  • Adults with the following risk factors: chronic cardiovascular disease, chronic lung disease, chronic metabolic disease, chronic renal dysfunction, hemoglobinopathels,
	  • Immunosuppressed persons
	  • Residents of nursing homes and chronic care facilities,
	  • Pregnant women 2nd or 3rd trimester whitout flu shot in the last 12 months.
	
	• Persons who can transmit influenza to those at high risk:
	  • Health care workers and other personnel of out patient care settings, household contacts and caregivers.
	
	• Healthy persons providing essential and emergency community services, students and other persons in institutional settings and any person who desires to reduce likelihood of becoming ill with influenza including travellers.
		Given once every year
		
		preferably from February to June
			• Serious allergic reaction to a vaccine component or to previous dose
			• Moderate or severe acute illness
			• History of severe acute illness
			• Guillian-Barre Syndrome

Additional Vaccines for Health Care Workers and Trainees

VACCINE TYPE/ ROUTE	TARGET INDIVIDUALS	SCHEDULE	PRECAUTIONS/ CONTRAINDICATIONS
1. Typhoid a) Oral-enteric-coated capsule, live attenuated Ty2la b) Intramuscular-Vi capsular polysaccharide Ty 21	• Food handlers such as dietary personnel cooks, waiters, servers, dieticians, nutritionists • Microbiology lab technicians • Persons with intimate exposure to a documented S. Typhi carrier or patient	Oral-for primary and booster, 1 capsule each on day 0, day 2, day 4, 1 hr before a meal, with lukewarm or cold liquid drink Intramuscular-for primary and booster single 0.5ml IM dose on the deltoid Booster every 2-3 years	Oral: • Moderate or severe illness • With vomiting or diarrhea • After alcohol intake • Antibiotic intake • Immunocompromised Parenteral: • If with bleeding disorder • Previous anaphylactic reaction to vaccines or its components
Rabies a) HDCV-Human diploid cell vaccine* b) PVRV- purified vero cell rabies vaccine c) PDEV- purified duck embryo vaccine d) PCECV - Purified chick embryo vaccine Intramuscular/ Intradermal *Not available locally	• Health care workers in hospitals that treat dog bites and rabies cases • Rabies research diagnostics/lab workers • Veterinarian and vet students • Field workers	Primary-series of 3 injections on days 0, 7, 21 or 28 IM-on the deltoid PVRV - 0.5 ml. PCECV, HDCV, PDEV - 1.0 ml. ID-on the deltoid PVRV,PDEV,PCECV - 0.1 ml. Booster-single dose IM or ID every 2 years For post-exposure prophylaxis- refer to Standard guidelines	• Moderate or severe acute illness • Intake of corticosteroids, chemotherapeutic agents,antimalarials

N.B. Recommended by the ad hoc Committee on Immunization, Philippine Society for Microbiology & Infectious Diseases (PSMID), and Philippine Foundation for Vaccination. (PFV)