



Immunizing the Immunocompromised

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Crowne Plaza Galleria Manila, 21 February 2013

WHO World Health Statistics 2012

2. Cause-specific mortality and morbidity

Member State	Age-standardized mortality rates by cause* (per 100 000 population)			Number of deaths among children aged <5 years* (000s)		Mortality Distribution of causes of death among children aged <5 years* (%)											
	Communicable	Non-communicable	Injuries	2000	2010	HIV/AIDS		Diarrhoea		Measles		Malaria		Pneumonia		Prematurity	
						2000	2010	2000	2010	2000	2010	2000	2010	2000	2010		
Ranges of country values																	
Minimum	11	273	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Median	105	637	58	4	3	0	0	6	4	0	0	0	0	12	11	18	19
Maximum	1552	1289	347	2294	1696	48	28	80	16	22	11	29	27	35	29	50	45
WHO region																	
African Region	798	779	107	3836	3508	6	4	13	11	8	1	16	15	16	17	11	12
Region of the Americas	72	455	63	430	284	1	1	8	4	0	0	0	0	13	9	20	19
South-East Asia Region	334	676	101	3042	2127	0	0	13	11	4	3	0	1	22	22	19	21
European Region	51	532	63	230	155	0	1	5	4	0	0	0	0	16	12	20	21
Eastern Mediterranean Region	254	706	91	1149	1070	0	0	13	11	4	1	1	1	21	20	17	19
Western Pacific Region	74	534	64	889	467	0	0	6	4	1	1	0	0	23	16	15	17
Income group																	
Low income	636	757	124	3065	2658	4	3	14	12	5	1	11	11	19	18	12	14
Lower middle income	233	658	82	5104	4180	2	2	13	11	6	2	6	6	20	19	16	18
Upper middle income	125	608	81	1315	691	3	3	6	4	0	1	0	0	19	14	17	19
High income	31	380	41	98	85	0	0	1	1	0	0	1	1	5	4	25	23
Global	230	573	78	9581	7614	3	2	12	10	5	1	7	7	19	18	15	17



Ten (10) Leading Causes of Child Mortality

No. & Rate / 100,000 population

Ten (10) Leading Causes of Child Mortality
By Age-Group (1-4, 5-9, 10-14) & Sex
No. & Rate/100,000 population
Philippines, 2006

Cause	1-4 Years			
	Male	Female	Both Sexes	Rate*
1. Pneumonia	1,046	930	1,976	23.18
2. Accidents	752	514	1,266	14.85
3. Diarrheas and gastroenteritis of presumed infectious origin	592	446	1,038	12.18
4. Congenital anomalies	379	364	743	8.72
5. Ill-defined and unknown causes of mortality	324	260	584	6.85
6. Other diseases of the nervous system	236	179	415	4.87
7. Chronic lower respiratory diseases	185	226	411	4.82
8. Malignant neoplasms	223	175	398	4.67
9. Septicemia	200	164	364	4.27
10. Meningitis	166	143	309	3.63



Ten (10) Leading Causes of Child Mortality

No. & Rate / 100,000 population

Cause	5-9 Years			
	Male	Female	Both Sexes	Rate*
1. Accidents	967	574	1,541	15.37
2. Pneumonia	287	244	531	5.30
3. Malignant Neoplasms	218	141	359	3.58
4. Dengue fever and dengue hemmorrhagic fever	153	196	349	3.48
5. Congenital anomalies	159	148	307	3.06
6. Other diseases of the nervous system	156	143	299	2.98
7. Ill-defined and unknown causes of mortality	163	107	270	2.69
8. Diarrheas and gastroenteritis of presumed infectious origin	141	97	238	2.37
9. Nephritis, nephrotic syndrome and nephrosis	87	81	168	1.68
10. Meningitis	92	67	159	1.59

Last Update: October 3, 2011

Objectives

- To present the current recommendations and evidence in the immunization of immunocompromised pediatric patients
- To discuss the risks, benefits, and timing of vaccination in the setting of immunosuppression
- To highlight the management considerations and prospective immunization strategies for particular special risk groups



Immunosuppression

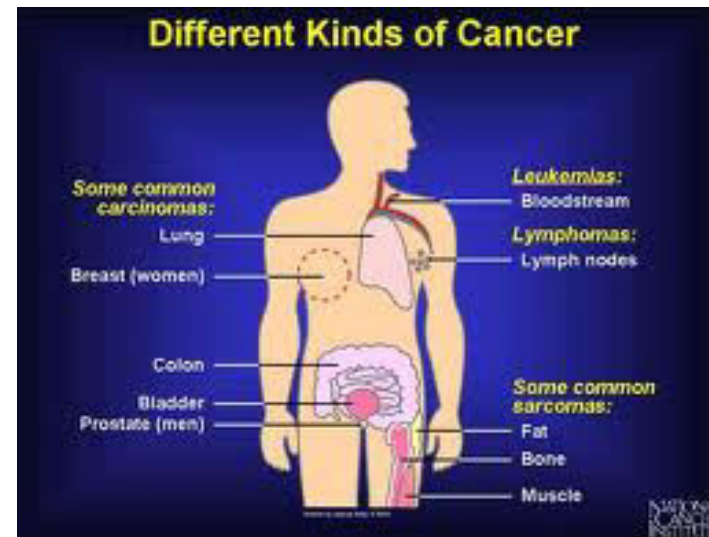
■ Disease

- Primary immunodeficiency
- Secondary immunodeficiency
 - Leukemia or Lymphoma
 - Generalized malignancy

■ Chemotherapy

- Alkylating agents
- Antimetabolites
- Radiation

■ Corticosteroids



Challenges of Vaccinating Immunocompromised Children

- Safety issues
- Immunogenicity
- Decreased vaccine efficacy
- Changing immune status
- Heterogeneous patient groups with variable immune deficits
- Increasing use of potent immunosuppressive regimens
- Preimmunosuppression immunization
- Vaccination of contacts to reduce exposure of the immunocompromised child
- Compliance

Nield LS, Troish MJ, Kamat D. Vaccinating the immunocompromised child. *Consultants for Pediatricians*.2009;8(Suppl):S7-S14



A scroll with a light brown, parchment-like texture, unrolled to reveal text. The scroll is held by four wooden rollers, two on the left and two on the right, each with a decorative knob. The text is centered on the scroll in a black, serif font.

The 10
Commandments for
Immunizing the
Immunocompromised

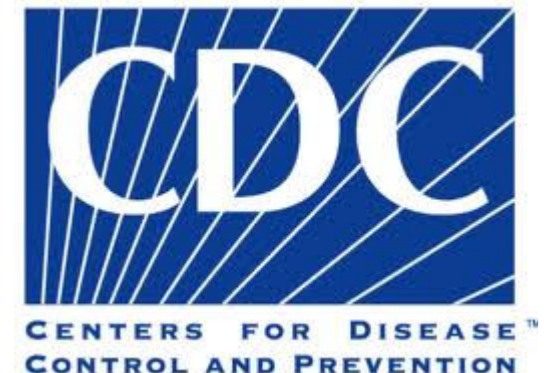
The Ten Commandments of Immunizing the Immunocompromised



- Live vaccines can cause severe or fatal reactions in immunocompromised patients due to uncontrolled replication of the vaccine virus.
- Live vaccines can be given to children with isolated immunoglobulin A deficiency.
- Attenuated live-virus vaccine can be given to children with complement deficiencies and disorders of phagocyte function.

Severely Immunocompromised Patients

- Active leukemia, lymphoma, generalized malignancy, aplastic anemia, graft-versus-host disease, or congenital immunodeficiency
- HIV-infected persons with CD4 cell counts $< 200/\text{mm}^3$, history of AIDS-defining illness, or clinical manifestations of symptomatic HIV
- Recent radiation therapy
- Solid-organ or bone marrow transplants, within 2 years of transplantation
- Transplant recipients still taking immunosuppressive drugs



Severely Immunocompromised Patients

- High-dose corticosteroids
- Alkylating agents (such as cyclophosphamide)
- Antimetabolites (such as azathioprine, 6-mercaptopurine)
- Transplant-related immunosuppressive drugs (such as cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil, and mitoxantrone)
- Cancer chemotherapeutic agents (excluding tamoxifen but including low-dose methotrexate weekly regimens)
- TNF blockers (such as etanercept, rituximab, adalimumab, and infliximab)



The Ten Commandments of Immunizing the Immunocompromised



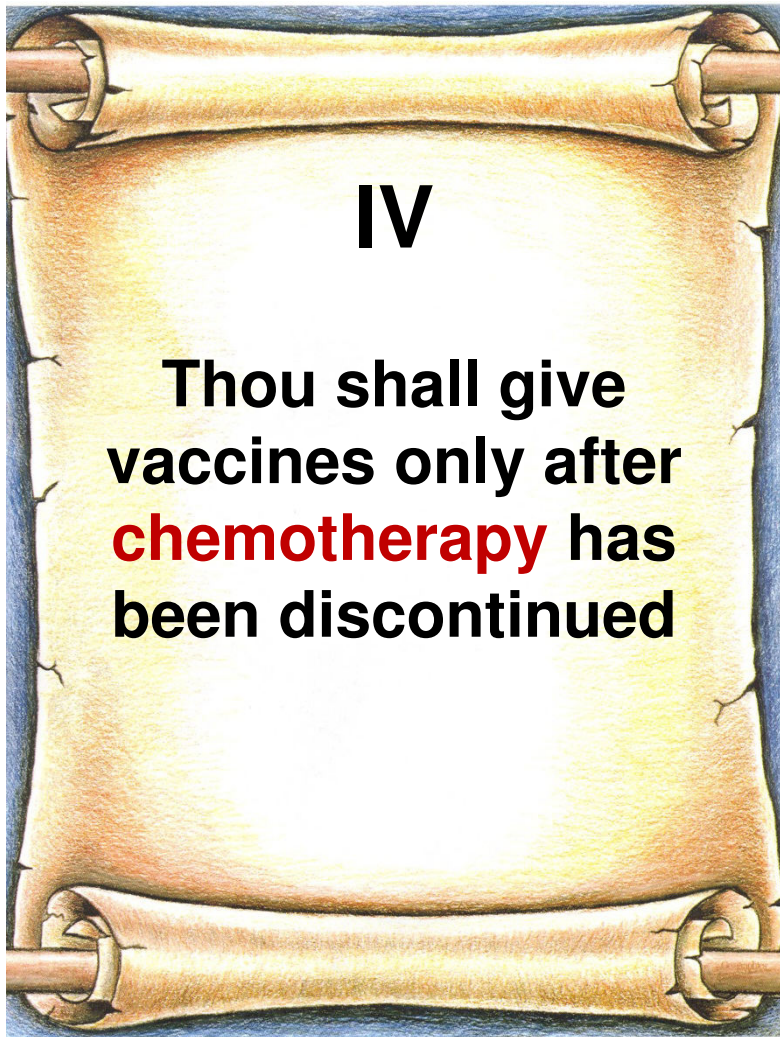
- Immune responses to inactivated vaccines may be inadequate.
- All children 6 months of age or older and adolescents with primary or secondary immunodeficiencies should receive an annual age-appropriate inactivated influenza vaccine

The Ten Commandments of Immunizing the Immunocompromised



- The following live vaccines may be given:
 - MMR
 - Varicella
 - Rotavirus
 - LAIV
- Immunocompetent siblings and other household contacts should **not** receive OPV

The Ten Commandments of Immunizing the Immunocompromised



- Inactivated or recombinant vaccines may be administered **3 months after** the end of chemotherapy
- Live vaccines are deferred until **6 months after** chemotherapy

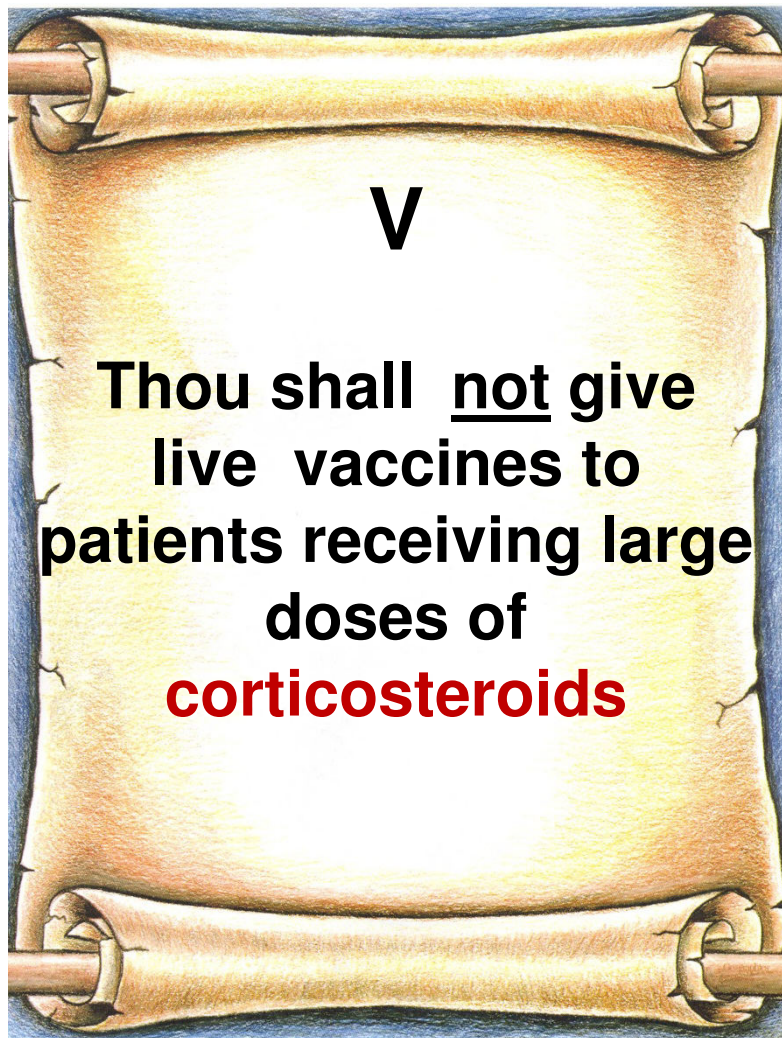
Suggested vaccination schedule for children with cancer

Vaccine	Patients who have not started or not completed the vaccination schedule at the time of cancer diagnosis	Patients who have completed the vaccination schedule at the time of cancer diagnosis
<i>Live attenuated vaccine</i>		
MMR	Two doses separated by at least 3 months in patients who have not received any dose and have been off-therapy for 6 months	Booster dose in patients who have been off-therapy for 6 months
VZV vaccine	Two doses separated by 3 months in patients in continuous remission for at least 1 year, with a lymphocyte count of $>700/\mu\text{L}$ and a platelet count of $>100,000/\mu\text{L}$; if still being treated in an epidemic period, they should stop drug administration 1 week before and for 1 week after vaccination	Booster dose in patients in continuous remission for at least 1 year, with a lymphocyte count of $>700/\mu\text{L}$ and a platelet count $>100 \times 10^3/\mu\text{L}$; if still being treated in an epidemic period, they should stop drug administration 1 week before and for 1 week after vaccination
<i>Inactivated or recombinant vaccine</i>		
DT	Administration of the primary schedule in patients off-therapy for 3 months	Booster dose in patients off-therapy for 3 months
Pertussis	Administration of the primary schedule in patients off-therapy for 3 months	Not known whether a booster is required
Inactivated poliovirus	Administration of the primary schedule in patients off-therapy for 3 months	Booster dose in patients off-therapy for 3 months
Hib	Administration of the primary schedule in patients off-therapy for 3 months	Booster dose in patients off-therapy for 3 months
Pneumococcal vaccines	Administration of the primary schedule in patients off-therapy for 3 months	Booster dose in patients off-therapy for 3 months, but more studies are required
Meningococcal vaccines	Administration of the primary schedule in patients off-therapy for 3 months	Booster dose in patients off-therapy for 3 months, but more studies are required
Inactivated influenza	Two doses if ever vaccinated or aged <9 years; otherwise, 1 dose regardless of chemotherapy	Booster dose regardless of chemotherapy
Hepatitis A	Two doses separated by at least 6 months regardless of chemotherapy in presence of epidemiologic risk	Booster dose regardless of chemotherapy in the presence of epidemiologic risk
Hepatitis B	Doses at $t = 0, 1$ month, 2–6 months, 12 months regardless of chemotherapy in the presence of epidemiologic risk	Two booster doses separated by 3 months regardless of chemotherapy in the presence of epidemiologic risk

Abbreviations: DT, diphtheria and tetanus; Hib, *Haemophilus influenzae* type b; MMR, measles, mumps, and rubella; VZV, varicella zoster virus.

Data from Esposito S. et al. Vaccinations in children with cancer. *Vaccine* 2010;28(19):3278–84.

The Ten Commandments of Immunizing the Immunocompromised



- $\geq 2\text{mg/kg}$ per day of prednisone or equivalent
 $\geq 20\text{mg/day}$ for children who weigh $>10\text{ kg}$
Given for 14 days or longer
- Live vaccines can be given only after corticosteroid therapy has been **discontinued for at least 1 month.**

The Ten Commandments of Immunizing the Immunocompromised



- Cytokine inhibitors
- TNF α inhibitors are the prototype agents
(adalimumab, certolizumab, etanercept, golimumab, infliximab)
- Live vaccines can be given only after therapy has been **discontinued for at least 1 month.**
- Administer all live vaccines a minimum of **1 month before** initiation of therapy.

The Ten Commandments of Immunizing the Immunocompromised



VII

**Thou shall revaccinate
hematopoietic cell
transplant (HCT)
recipients**

- Antibody titers to vaccine preventable diseases decline during the 1-4 years after HCT.
- HCT recipients should be routinely revaccinated after HCT, regardless of the source of the transplanted cells.
- Transplant recipients should receive all recommended immunizations, preferably prior to transplantation.

Revaccination of HCT recipients

Inactivated vaccines

- Revaccination with inactivated vaccines should begin **6 months after HCT**.

Live attenuated vaccines

- MMR and varicella vaccines should be administered **24 months after transplantation** if the HCT recipient is presumed to be immunocompetent.

Vaccination Schedule After Allogeneic Hematopoietic Stem Cell Transplant for Children and Adolescents

Vaccine	Timing of Immunization Post-HSCT						
	4-6 mo	6 mo	7 mo	8 mo	18 mo	24 mo	26 mo
Indicated Vaccines							
TIV	Yes ^a						
DTaP		Yes	Yes	Yes	Yes		
IPV		Yes	Yes	Yes	Yes		
HBV		Yes	Yes	Yes	Yes		
Hib		Yes	Yes	Yes	Yes		
PCV		Yes	Yes	Yes	Yes		
MMR						Yes	Yes
Optional Vaccines^b							
VZV ^c						≥24 mo	
HAV ^d							
HPV ^d							
MCV							

^a Children aged <9 years of age should receive 2 doses of TIV annually.

^b Limited or no data are available on safety and efficacy.

^c Administer only to immunocompetent patients.

^d Follow ACIP/AAP Red Book general recommendation.

Ljungman P, Cordonnier C, Einsele H, et al; Center for International Blood and Marrow Transplant Research; National Marrow Donor Program; European Blood and Marrow Transplant Group; American Society of Blood and Marrow Transplantation; Canadian Blood and Marrow Transplant Group; Infectious Disease Society of America; Society for Healthcare Epidemiology of America; Association of Medical Microbiology and Infectious Diseases Canada; Centers for Disease Control and Prevention. Vaccination of hematopoietic cell transplant recipients. *Bone Marrow Transplant*. 2009 Oct;44(8):521-526.

Hilgendorf I, Freund M, Jilg W, et al. Vaccination of allogeneic haematopoietic stem cell transplant recipients: report from the international consensus conference on clinical practice in chronic GVHD. *Vaccine*. 2011 Apr 5;29(16):2825-2833. Epub 2011 Feb 20.

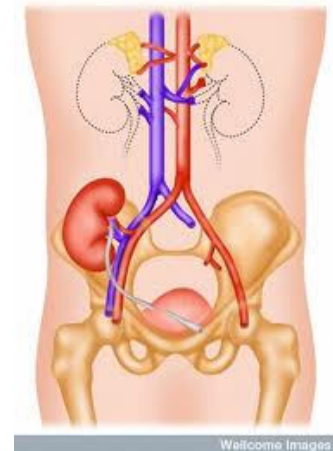
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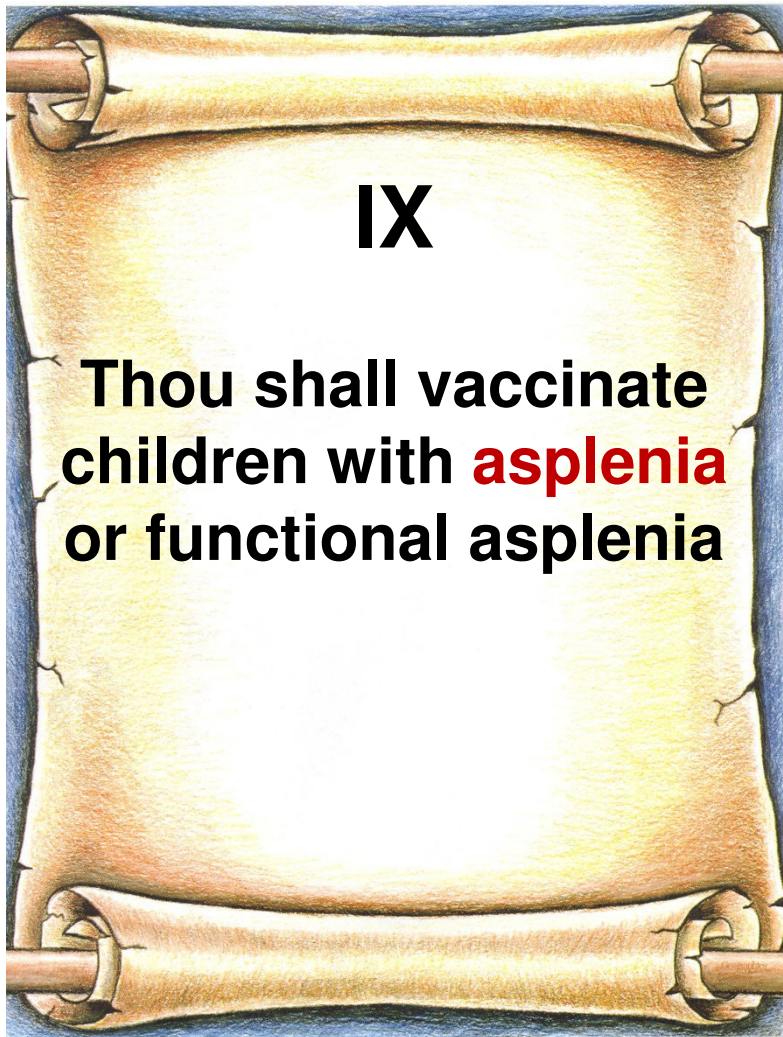
- Children and adolescents being considered for solid organ transplantation should receive immunizations recommended for their age at **least 2 weeks before** the transplantation is performed.
- Live-virus vaccines should be given at least 1 month before transplantation.

Vaccination of Solid Organ Transplant Recipients after transplantation

- After solid organ transplantation, DtaP, Hib, Hepatitis B, Hepatitis A, inactivated influenza, and pneumococcal and meningococcal conjugate and polysaccharide vaccines can be administered.
- Most experts recommend **at least 6 months after** transplantation, when immune suppression is less intense, for resumption of immunization schedules.
- There are no general recommendations on the use of live virus vaccines in this population.



The Ten Commandments of Immunizing the Immunocompromised



- When surgical splenectomy is planned, immunization status for Hib, pneumococcus, and meningococcus should be ascertained, and needed vaccines should be administered **at least 2 weeks before surgery**, if possible.
- If splenectomy is emergent, administration of indicated vaccines is **recommended 2 weeks after surgery**.

The Ten Commandments of Immunizing the Immunocompromised



- The risk of adverse events in these children following immunization is low.

Basic Principles of Vaccinating Immunocompromised Children

- Determine immune status
- Carefully assess risks versus benefits
- Understand that inactivated vaccines are generally safe and play an important role and that live vaccines are generally contraindicated, except in select circumstances
- Vaccinate contacts and healthcare workers
- Follow current vaccine recommendations
- Administer vaccines before immunosuppression when possible
- Consider antibody testing to evaluate vaccine response

Pickering LK, Baker CJ, Freed GL, et al; Infectious Disease Society of America. Immunization programs for infants, children, adolescents, and adults: clinical practice guidelines by the Infectious Disease Society of America. Clin Infect. Dis. 2009 Sep 15;49(6):817-840. Erratum in Clin. Infect. Dis. 2009 Nov 1;49(9):1465.



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Thank
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Kiitos

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