Off lable recommendations

The art of medicine

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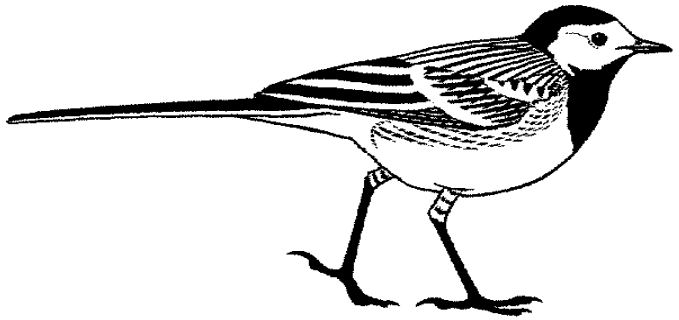
Reiseklinikken®



Evidence-based medicine:

For patients «of a certain category»,
a certain treatment is indicated

The art of medicine:

Evidence-based decisions of what is

the best for your patient

IF WE ONLY HAD TO FOLLOW RULES, WE COULD HAVE BEEN REPLACED BY MACHINES

Dilemma:

You do what you mean is the best for the patient,

but when breaking a rule, you are liable to legal persecution.

Situation 1.
A Vietnamese family, will go to a rural area in Viet Nam for six weeks, and they cannot afford the vero cell based japanese B encephalitis vaccine

- You have some doses of expired JE vaccine, which otherwise would be thrown away
- Would you give them free to this family?

What happens at the expiry date?

- The only thing that expires is the manufacturer's responsiblity
- The effect will not stop at the day of expiry
- The vaccine will certainly not turn into poison

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But:

- You have not longer covered your back

Situation 2.
A woman from Mali will visit her family in Mali with a two months old baby for four weeks in the dry season.

The age limit of the conjugated meningococcus ACWY vaccine is 12 months

- Would you give the vaccine to this baby?
- Would it make a difference if it was your own grandchild?

There is ample documentation:

For the meningoccus A and C conjugated vaccine is since long time documented as safe and effective in infants:

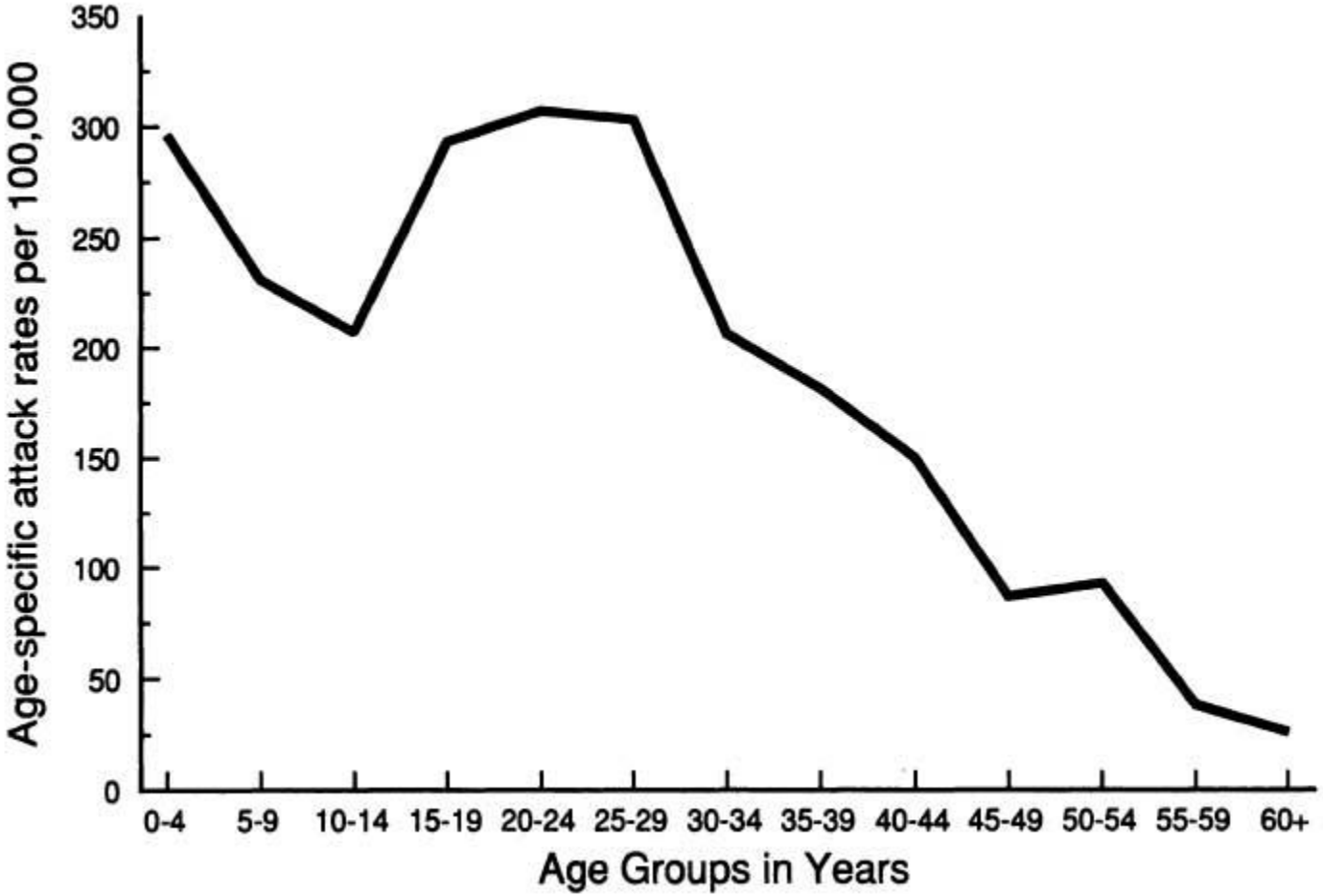
- Conjugate Meningococcal Serogroup A and C Vaccine: Reactogenicity and Immunogenicity in United Kingdom Infants. J Infect Dis. (1996) 174 (6): 1360-1363.doi: 10.1093/infdis/174.6.1360
- Peter Richmond, Ray Borrow, Elizabeth Miller, Sarah Clark, Francesca Sadler, Andrew Fox, Norman Begg, Rhonwen Morris, and Keith Cartwright. Meningococcal Serogroup C Conjugate Vaccine Is Immunogenic in Infancy and Primes for Memory. J Infect Dis. (1999) 179 (6): 1569-1572 doi:10.1086/314753
- MacLennan JM, Shackley F, Heath PT, et al. Safety, Immunogenicity, and Induction of Immunologic Memory by a Serogroup C Meningococcal Conjugate Vaccine in Infants: A Randomized Controlled Trial. JAMA. 2000;283(21):2795-2801. doi:10.1001/jama.283.21.2795.

Also the ACWY conjugated vaccine is tested and found safe and effective in infants:

- Perrett, Kirsten P.; Snape, Matthew D.; Ford, Karen J.; John, Tessa M. RN; Yu, Ly-Mee M.; Langley, Joanne M.; McNeil, Shelly; Dull, Peter M.; Ceddia, Francesca; Anemona, Alessandra D.; Halperin, Scott A.; Dobson, Simon; Pollard, Andrew J. Immunogenicity and Immune Memory of a Nonadjuvanted Quadrivalent Meningococcal Glycoconjugate Vaccine in Infants. Pediatric Infectious Disease Journal: March 2009 - Volume 28 - Issue 3 - pp 186-193. doi: 10.1097/INF.0b013e31818e037d
- Klein, Nicola P. MD,; Reisinger, Keith S.; Johnston, William; Odrljin, Tatjana; Gill, Christopher J.; Bedell, Lisa; Dull, Peter. Safety and Immunogenicity of a Novel Quadrivalent Meningococcal CRM-conjugate Vaccine Given Concomitantly With Routine Vaccinations in Infants. Pediatric Infectious Disease Journal: January 2012 - Volume 31 - Issue 1 - p 64–71 doi: 10.1097/INF.0b013e31823dce5c

Age distribution of a meningococcal outbreak in Nairobi

Pinner, R.W. et al., 1992. Epidemic Meningococcal Disease in Nairobi, Kenya, 1989. The Journal of Infectious Diseases. 166(2):359-364.



According to the product information sheeth we may not give the vaccine before 12 months age, but according to the evidence, it will protect the children in their most vulnerable age.

I want to quote my mother:

«WHEN THE LAW IS WRONG, YOU MAY BREAK IT»

Situation 3

A girl has returned from Thailand, where she ten days ago has played with a puppy that died five days later. It is confirmed that the puppy died from rabies. There were no bites, and no licks in any wounds.

- She does not qualify for getting PEP paid by the state or by the insurance, and the treatment according to the protocol would cost 1000-2000€ for the RIG plus 300€ for five doses of rabies vaccine
- Would you give her a «half hearted» PEP with only vaccine?

WHO: PEP according to types of contact with the «rabid animal»:

- category I – touching or feeding animals, licks on the skin: No prophylaxis
- category II - nibbling of uncovered skin, minor scratches or abrasions without bleeding, licks on broken skin: Immediate vaccination days 0, 3, 7, 14 and 30.
- category III – single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks; exposure to bat bites or scratches: Immediate vaccination days 0, 3, 7, 14 and 30, and rabies immunoglobuline

Concerning these so-called «rabid animals»:

Treatment may be discontinued if the animal involved (dog or cat) remains healthy throughout an observation period of 10 days; or if the animal is killed humanely and found to be negative for rabies by laboratory examination.
http://www.who.int/rabies/human/postexp/en/

In «our» case it is a confirmed rabid animal

One week after start of vaccination she will have detectable antibodies, and after two weeks she will have protecting immunity against rabies.

- I. e.: If she is well after 2-3 weeks there is no more need to worry.
- Rabies may have an incubation period of several years
- The average incubation time of rabies in humans is between 1 and 2 months.

How much money do we need to give an acceptable protection?

- Conventional PEP vaccination: 0, 3, 7, 14 and 28 days: 300€

Mulitple site intradermal, one dose vaccine, cost 60€:

- Karl G Nicholson, Howard Prestage, PeterJ Cole, George S Turner, Sally P Bauer. MULTISITE INTRADERMAL ANTIRABIES VACCINATION: Immune Responses in Man and Protection of Rabbits Against Death from Street Virus by Postexposure Administration of Human Diploid-Cell-Strain Rabies Vaccine. The Lancet Volume 318, Issue 8252, 24 October 1981, Pages 915–918.

Question

What would you give to this patient?

1. Full PEP, i.e., rabies immunglobulin and five doses of rabies vaccine
2. Five doses of rabies vaccine
3. Three doses of rabies vaccine
4. On dose intracutaneously administered on four different sites
5. No prophylaxis

Situation 3B.
A man has got a penetrating dog bite in southern Spain one week ago, and he has no way to find out if the dog is vaccinated, or if it is still healthy

Rabies is reportedly not a problem in Southern Spain, and he will not be given a full PEP.

May be we could just recommend him to take an ordinary three dose rabies vaccination,

day 0, 7 and 28?

Situation 4

A woman, 20 year, is going to India to participate for three weeks in a project for rescuing homeless dogs

- She leaves in five days and has no previous rabies vaccine

Is one dose of rabies vaccine far better than no dose?

Definitely yes!

Situation 5.
Somebody wants to go to Mexico for two weeks

- There is a high risk of contracting travellers' diarrhea caused by LT ETEC in Mexico

Flores J, DuPont HL, Jiang ZD, Belkind-Gerson J, Mohamed JA, Carlin LG, Padda RS, Paredes M, Martinez-Sandoval JF, Villa NA, Okhuysen PC.. Enterotoxigenic Escherichia coli heat-labile toxin seroconversion in US travelers to Mexico. J Travel Med. 2008 May-Jun;15(3):156-61.

- A cholera B subunit vaccine which is crossreacting with LT ETEC is available, and possibly effective against LT ETEC diarrhea
- The vaccine is in most countries not registered as a vaccine against travellers'diarrhea

A simple calculation for a two weeks trip to Mexico

- The risk of contracting TD is about 1/3
- Mean duration of TD is 3 days
- About ½ of TD would be caused by LT ETEC
- Price of two doses cholera vaccine: 60€

Price per day not destroyed by TD 120€

Questions

Is travellers diarrhea an indication of cholera vaccine?

- In Mexico, Morocco, Egypt and India?

1. Yes
2. No

- In Africa south of Sahara?

1. Yes
2. No

- In South East Asia?

1. Yes
2. No

Situation 6.
A 15 years old boy, 180 cm 80 kg, needs hepatitis A vaccine

- According to the product sheeth he should get the pediatric dose
- The documentation of the vaccine is based on age, not weight
- The price of a pediatric and adult dose is the same

Should we follow the product sheeth, or common sense?

Situation 7

Five months stay in Addis Abeba

- He may be in potential malaria endemic areas in some (half?) of the week-ends.

Should he take Mefloquine or Atovaqvone-proguanil (AP) during the whole perod?

AP should, according to the product sheeth, be taken one week after leaving the malaria area.

Would it be defendable to take AP only from Friday-Monday those week-ends?

Atovaquone-proguanil works on *Plasmodium falciparum* sporozoits

- Theoretically one could stop AP when leaving the malaria-endemic area
- Deye et al. showed protection in 6/6 volunteers who got one dose AP one day prior to challenge with *P. falciparum*

Gregory A. Deye, R. Scott Miller, Lori Miller, Carola J. Salas, Donna Tosh, Louis Macareo, Bryan L. Smith, Susan Fracisco, Emily G. Clemens, Jittawadee Murphy, Jason C. Sousa1, J. Stephen Dumler, and Alan J. Magill. Prolonged Protection Provided by a Single Dose of Atovaquone-Proguanil for the Chemoprophylaxis of Plasmodium falciparum Malaria in a Human Challenge Model. Clin Infect Dis. (2012) 54 (2): 232-239.

Situation 7, continued

Five months stay in Addis Abeba

- He may be in potential malaria endemic areas in some (half?) of the week-ends.

This is a moderate risk situation that could perhaps be turned to a very small risk situation with a «halfhearted» prophylaxis, by taking AP just the days he is in a potentially endemic area.

Questions

What would you recommend this traveller?

1. Mosquito-bite prophylaxis only
2. Atovaquone-proguanil for 5 months
3. Mefloquine for 6 months
4. Atovaquone-proguanil only during travel outside Addis Abeba an one day after

Situation 8

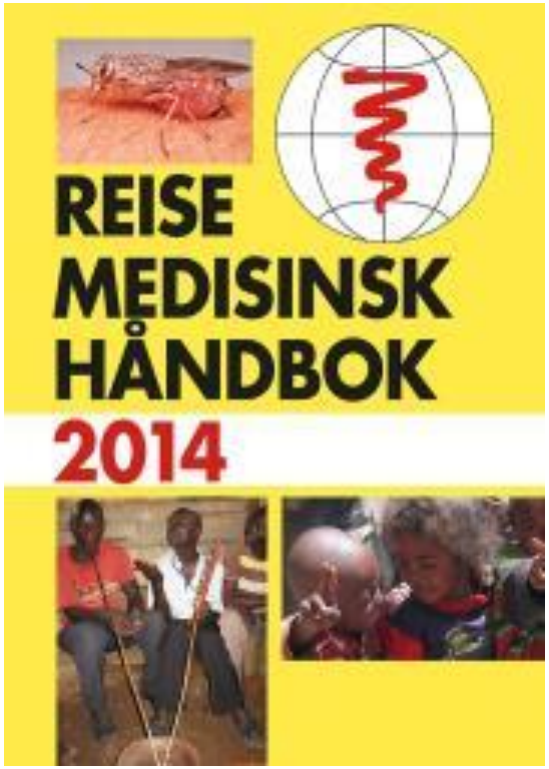
A 40 year old Norwegian, married with a Phillippinean woman, will visit her family in a tiny town in Luzon. They will stay in only one place, apart from a trip to Manila. Her family claims that there is no malaria in the community.

As this is a VFR family, CDC/WHO would recommend drug prophylaxis

Should we follow CDC/WHO or the local advice?

The Norwegian version of Rejsemedicinsk håndbok, by Mads Buhl

- «De anbefalinger som er gitt i denne håndboken er *så vidt mulig* i overensstemmelse med anbefalingene fra Folkehelseinstitittet»
- «The recommendations given in this book are *when possible* according to the recommendations given by the (Norwegian) National Institute of Public Health»



I.e., sometimes it is not possible to follow the official recommendations