



The Pediatric Infectious Disease Journal Newsletter

June 1992

VOL. 18, NO. 6

by John D. Nelson, M.D. and George H. McCracken, Jr., M.D.

vaccine as discussed in the February 1992 issue of the Newsletter.

THE PERILOUS PNEUMOCOCCUS We have great concern for the increasing prevalence of relatively or absolutely penicillin-resistant pneumococci coupled with the increased relative frequency of pneumococcal diseases as a result of universal *Haemophilus* vaccination. For example, we recently managed a 9 month old infant with pneumococcal meningitis who failed to respond adequately to ceftriaxone therapy. After 6 days of treatment he still had a positive CSF culture. He promptly responded to vancomycin therapy. The organism had the following minimum bactericidal concentrations (MBC), expressed in $\mu\text{g/ml}$: penicillin, 4; chloramphenicol, 8; ceftriaxone, 8; and vancomycin, 0.25. This case is similar to the case by Bradley and Connor published in our journal (*Pediatr Infect Dis J* 1991;10:871) and to a report by Sloas et al that will appear in the August issue. Additionally, we managed recently a 3 year old boy with pneumococcal endocarditis caused by a relatively penicillin resistant strain (MIC, 0.25 $\mu\text{g/ml}$). He responded satisfactorily to very high dose penicillin (500,000 units/kg daily) given intravenously for 6 weeks and the C-reactive protein and sedimentation rate returned to normal values. However, the serum bactericidal titer against the organism was only 1:8. Two weeks after stopping therapy the affected pulmonary valve was removed and the valve containing the vegetation appeared unremarkable to the surgeon. This was not the case histologically where acute inflammation and Gram positive cocci were observed. We need new agents that are active against these strains, especially when they cause infection of difficult to treat sites like the meninges or heart valves.

NPIDS SURVEY At our recent 1992 National Pediatric Infectious Disease Seminar in Washington, DC we again asked the almost 600 registrants to answer some questions regarding their prescribing habits. Of the 482

respondents the majority were pediatricians (75%), the remaining being infectious disease fellows (8%), residents (5%) family practitioners (4%) and pediatric nurse practitioners or physician assistants (4%). As to which antibiotic was their first line drug for acute otitis media, 91% said amoxicillin (87% in 1991). If that treatment fails, their usual backup drug for acute otitis media was Bactrim/Septra (29%), Augmentin (29%), Ceclor (22%) and Pediazole (17%). These results are similar to those last year except that Pediazole fell from 26% and Augmentin increased from 18%. For treatment of acute sinusitis, amoxicillin (58%) and Augmentin (26%) were the winners with Ceclor (8%) and Bactrim/Septra (6%) lagging behind.

We asked several questions regarding management of streptococcal pharyngitis. For diagnosis 45% of responders use the culture exclusively, 40% a rapid test with culture backup for a negative test, 8% a rapid test and culture for all and 7% the rapid test exclusively. The latter two options are inappropriate since a culture is not needed when the rapid test is positive (there are very few false positives) and the diagnosis will be missed too often if the rapid test is used exclusively (there can be from 10-35% false negative results). Regarding management of the child who has a clinical and bacteriological relapse of strep throat after penicillin therapy, 50% preferred a cephalosporin and 38% penicillin for retreatment. Rifampin and Bicillin or clindamycin was the choice of 6% each. We were surprised that 13% of responders routinely obtain a throat culture after a successful course of antibiotics for strep throat. (It is usually not advisable.)

For the choice of *Haemophilus influenzae* type b vaccine, 70% use HibTITER, 16% ProHIBit and 14% PedvaxHIB. Twenty-eight percent of physicians routinely start hepatitis B immunization in all newborns. We asked the registrants what they prescribed for acute bronchitis and were modestly surprised that 52% use an antibiotic whereas 48% administer symptomatic therapy.

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1 May 1993.

Ref No: 93.1406

Dear Mr Birch,

This is a follow-up letter regarding the Haemophilus vaccine, because the most recent issue of the Lancet has confirmed suspicions that while this vaccine may assist in eradicating Hib, the vaccine will essentially leave a microbial "hole" which appears to be being filled with other organisms.

This has happened in the past as detailed in a joint letter to the Infectious Diseases Journal amongst the enclosed documentation.

I believe that the subject of this letter could perhaps have more importance than my previous letter, because the real question that parents will want the answer to, is this:

Will this vaccine solve the problem of my children catching Haemophilus? In other words, will it work? The answer to this one is according to Heikki Peltola, No, not entirely, (See latest Lancet) because a vaccine cannot be given to prevent the non-capsular haemophilus type B, or the non-serotypable haemophilus strains, which appear to be becoming more prevalent with the use of the Haemophilus B vaccine.

On top of that, parents may not think to ask another perhaps more important question:

Will Haemophilus be replaced with something which is:

- a) just as bad, and
- b) potentially untreatable?

Most parents would not know to ask that question, because it would not occur to them that this could happen.

The answer to this question could well be as follows:

Journal of Paediatric Infectious Disease: June 1992:

"The Perilous Pneumococcus. We have great concern for the increasing prevalence of relatively or absolutely penicillin-resistant pneumococci coupled with the increased relative frequency of pneumococcal diseases as a result of Universal Haemophilus vaccination."

"We need new agents that are active against these strains, especially when they cause infection of difficult to treat sites like the meninges or heart valves."

Journal of Paediatric Infectious Disease: October 1992:

"Drs Leggiadro and colleagues show a substantial REDUCTION in cases of invasive Haemophilus disease admitted to LeBonheur Children's Hospital, Memphis from 1982 - 1991... Of concern was a two-fold increase in the rate of pneumococcal disease in 1991."

Lancet, 3rd April 1993 page 851: talking about Non-capsular Haemophilus influenzae not covered in the vaccines:

"Infections due to these H influenzae strains are, after the implementation of Hib vaccines, likely to persist and represent a substantial proportion of the serious infections cause by this species."

and talking about both non capsulated and non serotypable haemophilus, and other types of haemophilus they go on to say:

"Furthermore, the relative importance of such organisms may increase because of the general introduction of type B polysaccharide vaccines, which will greatly diminish invasive Hib disease but not systemic infection caused by non serotypable strains or H influenzae of other capsular type."

"...the proportion of H influenzae disease caused by these strains in the Oxford region would have increased from 6% to 36%."

And more definitively, in the same issue of Lancet, from Heikki Peltola in Finland, the country that the "Immunisation" Committee so likes quoting, comes this:

"So is the H influenzae problem being solved? Unfortunately no. The more the vaccines are used, the greater, proportionally, will be the role of the non-capsular H influenzae that are a major cause of acute otitis media, sinusitis, exacerbations of chronic bronchitis, and other mostly respiratory infections."

Furthermore, our unimmunised children probably already have immunity to haemophilus type B. If by introducing this vaccine in New Zealand, haemophilus is replaced by other, more untreatable types of meningitis, the medical profession will have unnecessarily increased the risk of both immunised AND unimmunised children catching these new diseases.

Since parents who do not immunise their children, do not want this vaccine, we deeply resent any change in circulating microbial flora being forced upon us by those who want to use this vaccine, because at present, the circulation of haemophilus type B keeps these other potentially more dangerous organisms in control.

This is how I would put the above medical situation in layman language. In shooting the white wolves (hib) to stop them eating the rabbits (babies), some black ones (other bugs) are moving in to fill the hole where the white ones (hib) left off.

This to me is an appalling solution, because the country would then CONTINUE to use this vaccine, (to the pharmaceutical company's profit) while creating the NEED to develop new drugs

and new vaccines (more profit for the pharmaceutical companies, and taxes from the people) to combat the problems created BY USING the Hib vaccine.

The only people pleased about this would surely be the companies that research these drugs and vaccines.

The use of this new vaccine may be seen as the ideal short term solution, but the long term cost to the country in Hib vaccine, treatment of the newer diseases etc would seem to me to be unacceptable in the light of the fact that if parents are taught what to look for, and if Hib is caught early, it is easily treatable - far more so than pneumococcus meningitis. Perhaps we need to be considering educative measures, rather than creating other more long-term problems.

M = PREVNAR

The "replacement scenario" is exactly what happened in America when Adenovirus vaccines were introduced to control type 3, 4 and 7. It did that, but the void was filled with other adenovirus types which did all the same things as 3, 4 and 7. However, in that incident, the U.S.A. withdrew the vaccine (except for the military) to allow the 3,4 and 7 to come back and balance the situation.

The most important question to me is:

"Will the New Zealand Health Department stand back, look at the new developments and decide to use caution and postpone the introduction of this vaccine?"

While I would like to think that they are big enough, and brave enough to say, "Hang on, lets relook this..." I feel that it is unlikely, because too much has been said, and there is so much professional vested interest involved.

Should this long-term scenario develop in New Zealand, as it is overseas, it is my opinion that that responsibility lies with you, as Minister of Health, because overseas, it did not occur to the medical authorities that it would happen. By drawing your attention to these facts, you now KNOW that it IS happening. On the other hand, it could well be that your medical advisors will consider that this is, yet again, me misinterpreting medical literature! An easy escape!

I will be ensuring that these above facts are well circulated, because so often political decisions are made for short term expediency. Then the long term disastrous effects are left for someone else to clean up - usually at the tax-payer's expense. Are you as Minister of Health prepared to accept the responsibility for these implications?

On receipt of your replies to this letter, and the last letter, I will make an appointment to see you in person.

Sincerely,