Taking a 'PASS' on Alternative Immunization Schedules

Stan L. Block, MD, FAAP

You don't have to look far in the press these days to find pediatricians venting their frustrations as a result of their interactions with vaccine-hesitant parents. Two leading pediatric publications cogently point out the issues pediatricians and others confront daily with families who choose alternative vaccine schedules.

> "Their decision about vaccines is based on an emotional response to the perceived risk of harm from vaccines, weighed against the intangible risk of disease they have never seen." David A. Horowitz, MD, Cary, NC[1]

> "One of my mentors taught me long ago that vaccine refusal is often only the first step in a one-sided parent-physician relationship, where our experience, training and expertise are disregarded." Bradley J. Dyer, MD, FAAP, Exton, PA[2]

Yes, many of us are frustrated in the trenches of pediatric medicine regarding parental demands for alternative infant-immunization approaches. In a 2011 statement from the American Academy of Pediatrics, Gilmour and colleagues[3] wrote that, "parents who are unwilling to consent to vaccination may be willing to consent to accept a compromise (eg, vaccinations with a single component of a multivalent vaccine, staggered doses, adjusted scheduling). Although some physicians find this contentious because it is not in keeping with current guidelines, others argue that some vaccination is preferable to none."

In fact, between 2006 and 2009 the rate of shot limiters increased from 2.5% to 9.5%.[4] In 2012, 24% of pediatricians reported that greater than 10% of parents made a request to "spread out vaccines." Seventy-seven percent of pediatricians agreed to spread out vaccines, and 28% required extra provider visits for these types of visits.[5] We need help!

For we staunch vaccine advocates, is there any palpable hope of compromise with these followers of the alternative-vaccine schedule, mostly perpetuated by the books of Robert W. Sears, MD, FAAP? Looking into his first edition of *The Vaccine Book: Making the Right Decision for Your Child*,[6] – no way! We do not have to accept many of his earlier controversial contentions, which are often opposed by the Centers for Disease Control and Prevention and the American Academy of Pediatrics. But in his second edition of same title,[7] he has compromised his highly controversial pediatric stance enough, that, I think we can acceptably work within many of his book's parameters. His adolescent platform is another story**!**

CASE: 'THE ANXIOUS FAMILY'

Today you are seeing for the first time this 5-day-old full-term healthy infant girl who was born by spontaneous vaginal delivery to a 27-year-old healthy G2P2 mother. You are excited that the mother has picked your practice for her daughter's pediatric care. As you review her history, you uncover that the child has not received the hepatitis B vaccine at birth. You inquire whether there is any particular reason for not vaccinating her infant.

The mother calmly explains to you that she has read up on the hazards of the infant hepatitis B vaccine, and has declined any hepatitis B vaccination based on the guidelines proposed

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by Dr. Sears, one of the nation's leading proponents on alternative vaccine schedules. She says that, as he explains in the second edition of his book, infants are getting too many shots at one time which may overload their immune systems, and that many injectable vaccines contain too much aluminum, a "known toxin" when injected in large amounts in certain susceptible populations.

'DANGERS' OF NEWBORN HEPATITIS B VACCINE?

In his book, Sears unequivocally and vocally states that hepatitis B vaccine is actually unnecessary until teen years, but feels it should still be given to preschoolers.[7] You can actually almost accept this assertion that when the hepatitis B vaccination is not received at birth, and parents have no risk factors along with a maternal negative hepatitis B screen, hepatitis B infection would be almost unheard of until teen years. Almost.

Dennis Murray MD, pediatric infectious disease specialist, of Medical College of Georgia, [in personal communication] warns that he has seen cases of postnatally acquired hepatitis B in young children — which at this age is associated with a nearly 50% chance of chronic active hepatitis B often with later cirrhosis or liver cancer. Sears also worries that hepatitis B vaccine at birth may precipitate some cases of fever, irritability and poor feeding, which in turn may trigger a hospitalization for a newborn septic workup. He cites a 1999 in-patient retrospective study which showed a twofold increase in newborn hospitalizations by 5 days of life after implementation of a birth HBV dose.[8] Statistical fluke? Or, cause and effect? My guess is the former.

Other than with maternal fever, chorioamnionitis or flu, I have never seen this early-life adverse event personally in our practice over the last 2 decades while dealing with a cohort of over 12,000 births. In addition, Niu and colleagues[9] reported that the VAERS data from 1991 to 1994 after 12 million doses of birth dose HBV vaccine revealed only 13 potential cases of newborn fever and hospitalization. Admittedly VAERS is underreported, but this tiny number is most reassuring.[9]

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VAERS data from 1991 to 1994 after 12 million doses of birth dose HBV vaccine revealed only 13 potential cases of newborn fever and hospitalization.

Not without some risk, this immediate HBV newborn decision to decline, however, is now irretrievable for this newborn. So you move on to see how many other immunization compromises may be needed to appease this family.

Immediately you have become skeptical, wary, and somewhat defensive about how you should optimally approach the issue of the remainder of routine vaccines for this family's infant. Having recently dealt with many families with similar "belief systems," you recollect that the markedly delayed and separate vaccine antigen tactics proposed in the first edition of Dr. Sears' book had driven an insurmountable wedge between your staunchly pro-CDC and -ACIP "timely" schedule, and the parents' "pick 'em" and "choose 'em" terribly delayed schedules. Have you reached an impasse? Or can you blithely accept a willy-nilly unorthodox and untested approach to the vaccine schedule from a set of parents who really do not fully comprehend all the rigorous testing that goes into vaccine development, safety, and schedules? They also have no actual idea about the devastation that these vaccines prevent. By contrast, you have seen it many times.

In the interest of connecting with your patient, you decide to take a dip into this murky literary pond. During your reading of Sears' book, you learn quickly that Dr. Sears claims to be" pro-vaccine" as he clearly alleges several times. Most of his discussions about infant vaccine side effects and efficacy are actually fairly well researched. Most of his warnings about side effects are no more "scary" than reading the actual CDC Vaccine Information Sheet (VIS), which each parent is supposed to read anyway. He clearly explains the rationales and benefits of each vaccine as well. This is not true about his ideas for older children. To sum up his approach, in order to gain cooperation from vaccine-doubters, "We need to offer schedules that acknowledge their concerns but don't compromise disease protection."[7]

He also tries to maintain some balance between the vaccine clinical trial data and the post marketing vaccine-negative publications. He does warn the reader about potential self interests of both respective groups, although I cannot fathom how a group like the well-respected and blatantly impartial FDA or the CDC can be portrayed as having any self interest here. For instance, if the FDA uncovers any irregularities in vaccine manufacturing processes, any major negative "scientific" clinical trial data about a new vaccine, or any off-label advertising of a vaccine, they will shut down vaccine manufacturing, prevent vaccine licensure, or fine the accused company, respectively. This would occur no matter how vital and life-saving the vaccine usually is — think HIB vaccine shortages.

Sears acknowledges that many of the negative vaccine articles were non scientific, and he notes that many of these negative authors were involved with their own competing "complementary" unapproved products.

THE NEAR IMPOSSIBILITY OF BIAS IN CURRENT CLINICAL TRIALS

Dr. Sears, however, does not seem to understand fully about the true "science" behind the clinical trial process of double-blinding, randomization, and comparator or placebo-controlled vaccine trials. All clinical trials and protocols for vaccine approval must be conducted strictly within the most stringent FDA guidelines. With all current investigative trials during the last 15 years or so conducted in this fashion, there just is no way to bias or taint the data — you, the investigator never see the data until it is totally locked into the main computer and then later analyzed by the coldly calculating computer. You are just recording patient diaries and physical examinations and adverse events into case books — totally blinded to the treatment arm.

In addition, the company's own internal and external auditors constantly monitor the entire data set as it pours in from the office — also in a totally blinded fashion. And the (external) FDA itself audits a large portion of the trial data for fraud, irregularities, and good research compliance — audits that I have personally experienced and survived unscathed from multiple times over the course of my career.

Whether any discovered problems are due to intentional or human error — sanctions, fines, or data exclusion (meaning all that work for no pay at all) by the FDA additionally ensure that you do your job as a scientist correctly. Unlike Andrew Wakefield, MD of "MMR and autism" infamy,[10] you as an investigator are not even remotely thinking about veering from the protocol, inappropriate patient enrollment or data manipulation. In addition, the overall sample size of patients enrolled must be sufficient enough to show statistical significance or non-inferiority.

Dr. Sears and his followers coming into each of your offices also have trouble grasping the implications of the vaccine adverse event reporting system (VAERS) relative to true background rates and "noise" always simultaneously occurring with any reported vaccine adverse effects. Nearly a third of national VAERS reports originate from trial lawyers trying to drum up litigation.[11] When it comes to the adverse effects of vaccines, "temporal" or anecdotal associations more often do not ever translate into "causal" associations. For example, just because the child was riding in a car seat and dies from SIDS later that night, does not translate as the association: the car seat caused SIDS. The rate of naturally occurring "background noise" versus vaccine adverse effects must always be considered in good, accurate science.

TABLE 1.

Aluminum Content Within Specific Infant Vaccines Containing Aluminum

Vaccine	Aluminum content (mcg)
HIB (Pedvaxhib only)	225
PCV13	125
DTaP	170 to ≤ 625
Hepatitis B	250
Hepatitis A	250
Pentacel	330
Pediarix	≤ 850

Adapted from Sears[7]

THE UNPROVEN ALUMINUM TOXICITY CONTENTION

Aluminum adjuvants are critical to the high immunogenicity, durability, and reduced number of doses for many of our vaccines. Because the aluminum content of vaccine during each visit is such an important point of contention for Dr. Sears, let's examine the amounts in those aluminum containing vaccines (see Table 1) Aluminum toxicity has mostly been reported in two populations: premature infants and dialysis patients. The

TABLE 2.

The Block Almost Timely and Tenable Alternative to Sears Schedule (BATTASS)

Age	Alternative Age (months)	"Main" Vaccine	Concomitant Vaccines
4 weeks	1 month	Hepatitis B vaccine*	
6 weeks	2 months	Pentacel	RV5 or RV1
10 weeks	3 months	PVC13	
14 weeks	4 months	Pentacel	RV5 or RV1
18 weeks	5 months	PCV13	
22 weeks	6 months	Pentacel	RV5
26 weeks	7 month	PCV13	
9 months/ 10months		Injectable flu vaccine (preservative-free)†	Hepatitis B vaccine
12 months		MMR	PCV13
13 months		(Hepatitis A vaccine)‡	
15 months		Pentacel	Varicella

**Hepatitis B is administered at 1 month for those infants enrolling in day care, although no hepatitis B vaccine is supposed to be administered in the first 2 years to accommodate Dr. Sears' usual schedule.*

†The intranasal vaccine is only FDA approved after age 24 months, and definitely should NOT be given as early as age 9 months, as stated by Dr. Sears, due to increased risk of hospitalization under 12 months.[29]

‡First dose of Hepatitis A vaccine can be given as late as 24 months, and still "almost" be within the ACIP guidelines, unless an outbreak occurs.

toxicity is due to chronic large exposures and is characterized by dementia, memory loss, fatigue, depression, and learning impairments. However, Keith and colleagues calculated that the standard immunization doses of aluminum are eliminated within 1 to 3 days.[12]

Also, injection total doses of 850 mcg or 1,225 mcg of aluminum via vaccine(s), respectively, did not cause any changes to normal plasma concentrations in either adults or premature infants.[13,14] In another study of aluminum adjuvants, up to 60% and 70% of aluminum in adult vaccines was urinary excreted by 1 week and 5 weeks, respectively.[15] Thus vaccine-injected aluminum is so rapidly excreted, that it produces minimal if any elevations in serum aluminum concentrations, and only for a few days, and definitely not near any toxic range, from the total possible 500 mcg injected over a 6-month period. Thus it accumulates little more than the infant's 6 months oral total (38,000 mcg-117,000 mcg) of daily regular dietary ingestion of aluminum via formula with a 1% absorption rate.[16]

SEARS' VACCINATION RESTRICTIONS

Dr. Sears has espoused the following restrictions upon alternative infant vaccinations.[7]

- Give only one aluminum containing vaccine at a time;
- Receive no more than 2 vaccines at a time;
- Delay shots for "milder" diseases or non-infant diseases, specifically hepatitis A and hepatitis B, respectively. Hepatitis A vaccine may be given at 12 and 21 months. For day care requirements, hepatitis B vaccine (HBV) may be given at 1 month, with a second dose at 3 months and a third dose at 9 months. (Sears still otherwise recommends hepatitis B as a preschool vaccine);
- Give only one live-virus vaccine at a time;
- Receipt of MMR at 12 months is adequate for him, but Sears prefers giving patients separate monovalent components, which he acknowledges is not going to happen. Varicella vaccine is typically given at 15 months. Both vaccines need to be given at least 3 months apart. [Per the CDC, MMR vaccine is currently recommended to be administered separately from varicella vaccine anyway. So the risk is minimal for merely another 3 months delay, and it is still compatible with the ACIP schedule].

He also discusses 3 different possible delayed vaccine schedules at 6 months, or 12 months or 24 months, for those parents who insist upon it. These would never be palatable for many pediatric practices.

Almost timely and tenable? If parents are adamant and balk about the irrational and totally disproven association of MMR with autism, then reverse the order. Give MMR at 15 months instead, and varicella at 12 months (see Table 2 [above] and Table 3 [page 403]). This is still within the

ACIP guidelines, but does allow the child to have an extra 3 months unprotected from measles and mumps. If a child does not show signs of autism by 15 months, then they are extremely unlikely to have this disorder.

ISSUES WITH SEARS' ADOLESCENT SCHEDULE

But, I have several major issues with his adolescent schedule, for example, adherence to and the scheduling of the several shots, and the use of only a single dose MCV4 at age 16 years old — by then it's just too late. I suggest that he watch our video on National Public Broadcasting Network's program: "Healthy Bodies/Healthy Minds" regarding the prevention of meningococcal disease in preteens as well.[17]

Finally, his discussion of the HPV4 vaccine is too biased and will lead to tragic outcomes. It is fraught with errors and background "noise" (claims of pregnancy issues, severe reactions, autoimmune disorders, and serotype replacement issues) and creates a dangerous mindset medicolegally for you. It particularly downplays the terrible consequences of severe female HPV disease (over 330,000 surgeries for CIN 2/3, etc) and cancers (over 20,000 cervical, vaginal, vulvar and rectal and possibly oral), three-quarters of which will be preventable with HPV vaccine.[18] His book seems to be advocating the failed and dubious "just say no" policy for teens. This is unlikely to work in real life for HPV, as has been reported in college freshman students,[19,20] and the staggering fact that up to 25% of people will become infected with preventable high-risk types of HPV. We all need to investigate HPV vaccine better by catching-up on the huge available data sets showing the extreme safety of HPV4 in true scientific studies.[21-24]

TABLE 3.

Alternative Infant Vaccine Schedule Using Pediarix When Pentacel Is Unavailable (Not Preferred by Dr. Sears' Schedule Due to High Aluminum Content in Pediarix (850 mcg)

Age	Alternative Age (months)	Main Vaccine	Concomitant Vaccines
4 weeks	1 month	Hepatitis B vaccine*	
6 weeks	2 months	Pediarix	
10 weeks	3 months	PVC13	HIB vaccine, RV5 or RV1
14 weeks	4 months	Pediarix	RV5 or RV1
18 weeks	5 months	PCV13	HIB vaccine, RV5 or RV1
22 weeks	6 months	Pediarix	RV5
26 weeks	7 month	PCV13	HIB vaccine, RV5
9 months/10 months		Flu vaccine (preservative free)†	Hepatitis B vaccine
12 months		MMR	PCV13
13 months		(Hepatitis A vaccine)‡	
15 months		HIB vaccine	Varicella
18 months		DTaP	IPV

**Hepatitis B is administered at 1 month for those infants enrolling in day care, although no hepatitis B vaccine is supposed to be administered in the first 2 years to accommodate Dr. Sears' usual schedule.*

†The intranasal vaccine is only FDA approved after age 24 months, and definitely should NOT be given as early as age 9 months, as stated by Dr. Sears, due to increased risk of hospitalization under 12 months.[29]

‡First dose of Hepatitis A vaccine can be given as late as 24 months, and still "almost" be within the ACIP guidelines, unless an outbreak occurs.

BLOCK ALMOST TIMELY AND TENABLE ALTERNATIVE TO SEARS SCHEDULE (BATTASS), OR THE PEDIATRICIAN'S ALTERNATIVE TO SEARS SCHEDULE (PASS) FOR INFANTS

The key to my compromise with the Sears schedule and my new BATTASS schedule (see Table 2) is his allowing the use of Pentacel (Sanofi Pasteur) in his second edition.[7] Sears states, "Pentacel is an OK choice, and it easily fits into an alternative vaccine schedule."[3] It has a much lower aluminum content than does Pediarix (GlaxoSmithKline) – 330 mcg versus 850 mcg, which he does not advocate except when Pentacel is not available. The good news for us "traditionalists" is that despite his multiple simultaneous antigen concerns, the two extra antigens in each of these vaccines do not preclude their beneficial utility for him. The much lower dose of aluminum in Pentacel is actually lower than giving the single component vaccines simultaneously. Thus he gives a waiver to Pentacel — which is almost perfect for us.

CAVEATS TO THE USE OF BATTASS

Adherence

When using BATTASS, parents must be willing to adhere to and be totally accepting of the clinician's vaccine timing. For those practitioners who are more compulsive about ACIP recommendations,[25] you can ask parents to come in for vaccines on the 4-week interval schedule in Table 2 (see page 402) and Table 3 instead. Thus, they will be finished with the primary series by 6 months as well. The vaccines at 12 to 15 months old in BATTASS are relatively the same as ACIP, except for the separation of MMR from varicella by 3 months, yet still fall within ACIP guidelines. Each physician will have to decide when to pull the plug on families who procrastinate too long for their comfort.

Costs

Parents must be willing to accept the extra visits and the additional slightly higher charge for first vaccine administration at the 3-, 5-, and 7-month visit as opposed to the reduced charge for simultaneous 2 to 4 vaccines at one visit. Many clinicians have a separate additional nurse visit charge for shots not occurring during a checkup. (Use CPT code 90471 [first shot] and CPT 90472 [additional shots]) Further "spacing out" of visits would not be acceptable.

Availability of Pentacel

Pentacel must be in full supply to make your and their acceptable transition to BATTASS fully work. At press time, shortages should be resolved. Using Pediarix could create significant friction for the family who still does not believe in low-dose aluminum safety. Pentacel reduces the number of shots by two for each of four visits — a real time/cost saver for our nursing staffs. Some offices may complain about the three to four possible extra visits and extra time in the room for vaccines. I sympathize. But it does not seem too much different than giving a child one or two weekly allergy shots apart from any office visit.

Hepatitis A and Hepatitis B Vaccines

Hopefully we can convince many of the delayers of the birth dose of hepatitis B vaccine, to receive the first dose at 1 month and the second dose by 9 months of age, and third dose after 15 months. The day care attendance policy requiring hepatitis B vaccine may be compelling for over half of the families. The delay of hepatitis A vaccine is an issue we will just have to possibly compromise with until the child is older, perhaps by 23 to 24 months — almost compliant with ACIP guidelines. For the missed birth-dose hepatitis B vaccine, you will need to have the family sign and acknowledge the AAP vaccine refusal form either at birth or within the first weeks of life.

Aluminum Toxicity

Arguing with families about this issue may be fruitless. We have minimal actual data on the pharmacokinetics of aluminum in pediatric vaccines but we have decades of post-vaccine observations from over an estimated billion injections which have shown no long-term toxicity.

CONCLUSION

In 2005 and 2009, the AAP Bioethics Committee said that, "continued [vaccine] refusal" after adequate discussion [between physician and parent] should be respected unless the child is put at significant risk of serious harm."[26,27] In our quest each day to "do no harm", I think we can do better than becoming a willing partner to needless severe or catastrophic illness and deaths because of untenable vaccine hesitation and refusal. You have seen my staid position on total vaccine refusal.[28]

However, when adopting a Physicians' Alternative to the Sears' Schedule (PASS), we are acknowledging both that we have found a way to compromise within limits, and that we still insist upon providing the best possible care for our patients, families and the community. By becoming a BATTASS, it allows you now to finally work with the numerous families who follow a frequently invoked, previously untenable "belief system." ■

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