# Housecalls

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INSIDE THIS ISSUE



PREVENTING CARDIOVASCULAR DISEASE

## The Polypill Approach

In these times of personalized medicine it seems a bit heretical to discuss a "one size fits all" strategy like the polypill, but a recent publication reminds us of the disease prevention potential of the approach. One of the original papers and the one naming the polypill was published in 2003. The authors proposed low dose medications to reduce cholesterol, blood pressure, serum homocysteine and platelet "stickiness" to reduce and delay the major killers — stroke and cardiovascular disease.

The recent study was a randomized prospective trial comparing a minimal care group (training on healthy lifestyle) and a group with lifestyle training and a daily polypill. The polypill group (those that took the pill) had a reduction in major cardiovascular events with a hazard ratio of .43 over the 60 months of follow-up when compared to the lifestyle only group.

There was no difference in adverse side effects with the polypill. This experiment took place in rural areas of a low to middle income country where access to personalized care may not be readily available. More studies are needed, but as obesity continues to increase in low and moderate income countries, a strategy like the polypill may be effective in counteracting the associated rise in cardiovascular disease.

In this edition of *Housecalls* Dr. Rosace discusses another "one size fits all" prevention strategy — routine vaccinations. She relates the importance of herd immunity and warns of a tipping point when we may see the re-emergence of some previously conquered diseases. I share a case of intracranial aneurysm with a family history, and Dr. Kadouch provides us with a challenging ECG.

**References**

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SCOR
The Art & Science of Risk

CASE #1

# An Unvaccinated Child

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**A life application is received for $500,000 on an eight-month-old infant. The amount is reasonable in comparison to the parents. This is the first child in this family. The child's birth and early physician checks were completely unremarkable except for the family's refusal to vaccinate their child at all. APS states that although the pediatrician encouraged routine immunizations, the family is part of an active anti-vax community in their town. Neither mom nor dad have been vaccinated.**

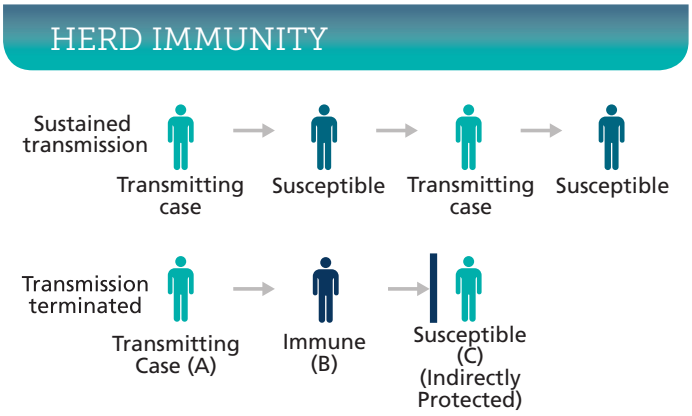
## Is this child at increased mortality risk compared to others who are receiving their vaccinations as scheduled?

## Principles of vaccination

The immune system's job is to recognize "self" and tolerate that substance and also to recognize and eliminate "non-self" material. Protection from infectious diseases is highly reliant on this system.

The infectious organism, be it viral or bacterial, should be recognized as "non-self" and eliminated. Immunity may be acquired **actively** by producing antibodies by the organism's own cells or **passively** by obtaining antibodies from some other place, such as from the mother through the placental circulation or from injections as with Intravenous Immune Globulin (IVIG) infusions. Although both are effective means of protection, **active immunity** tends to be longer lasting than **passive immunity**. Active immunity tends to last many years and is often lifelong. Passive antibodies degrade over time, and the individual's own cells have no way of producing more antibodies. The initial presentation of the foreign particle or **antigen** stimulates a host of reactions resulting in **antibody** formation. After a period of time, the level of antibodies may fall, but the reexposure of the immune system to the foreign substances reactivates the memory cells to very rapidly reestablish protection. Vaccinations work on this active immunity principle.

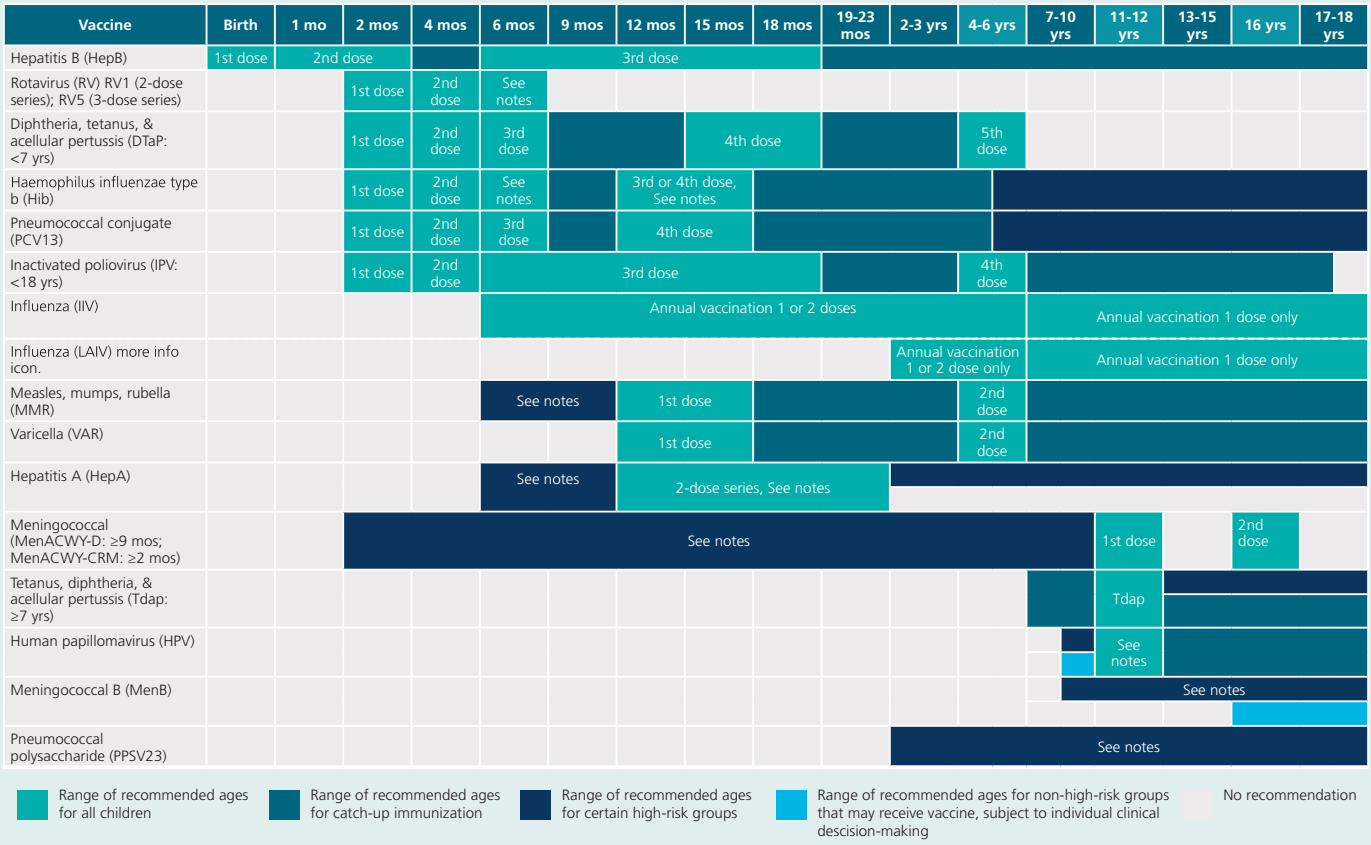
**Community or herd immunity** provides indirect protection from a pathogen. It describes resistance of circulation of a disease due to a sufficient number in the community with immunity to that particular disease. This offers protection to those not immune, such as newborns, the chronically ill or the unvaccinated, from encountering the disease because those who are immunized do not spread the disease. The percentage required to be immune to prevent disease varies by infectious agent. Measles and rubella outbreaks have occurred in communities with 85-90% immunization levels. The principle holds that as immunization levels drop below a certain threshold, the non-immune will no longer benefit from the indirect protection.




Source: *CDC*

## Recomended child and adolescent immunzation schedule for 18 years or younger United States, 2019

These recommendations must be read with the Notes on the CDC webstie (www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html). For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the dark teal bars in Table 1. chool entry and adolescent vaccine age groups are shaded in light teal..




## Vaccine hesitancy or refusal

In the United States, all states have laws requiring some immunizations for school entry. However, all states allow medical exemptions, and most allow religious or philosophical exemptions. The American Academy of Pediatrics' website has an interactive map listing the percent of children immunized by vaccine type and state as well as whether or not the state allows nonmedical exemption. The range of nonmedical exemptions varied by state in 2016-2017, from <0.1 – 7.5%. Parental objections to vaccination also vary.

Nonmedical parental objections to vaccine:

- Concern for vaccine safety, perceived or real
- Lack of efficacy
- Belief that natural illness is better
- Fear of overwhelming an infant's immune system
- Unaware of seriousness of an illness
- Lack of trust in authority figures (medical, public health, pharmaceutical companies)
- Religious or moral objectives

## 2019 child & adolescent immunization schedule

The recommended child and adolescent immunization schedule for 2019 (shown above) has been approved and promoted by the CDC, the American Academy of Family Physicians and the American Academy of Pediatrics. Canadian recommendations are similar, though not exactly the same, and they vary by province.

In general, the first immunization is received in the hospital after delivery, Hep B #1, and then the shots are obtained at roughly two, four and six months of age, followed by doses between 12-18 months with boosters given at around five years before school attendance. There is a little variation in the 12-18 month range, particularly if there are local "epidemics" of a specific illness. Some of the ranges noted in the chart have to do with the specific formulations of vaccines that are available at the time of vaccination. These schedules have been studied extensively. The timing of the inoculations is such to optimize the child's immunologic response while trying to have protection in place at the age when disease spread is most prevalent and/or most dangerous to an individual.

Continued

CASE #1

# An Unvaccinated Child

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Some childhood vaccinations are recommended to protect patients from chronic illness or cancers in their adult years, such as **Hepatitis B (HepB)** vaccine and **Human Papilloma Virus (HPV)** vaccine. They are in place in childhood because some viruses that are found to cause cancers in later adulthood are actually acquired asymptomatically at very young ages. Because of these facts, variations to the schedule are not encouraged. There is a separate "catch up" schedule which can be found on the CDC's website for those who were not vaccinated on schedule. Again, timing of the vaccines is very important for an optimal immunologic response.

## Impact of vaccines in the 20th & 21st centuries

**Comparison of 20th century annual morbidity and current morbidity: vaccine-preventable diseases**

| Disease | 20th Century Annual Morbidity* | 2017 Reported Cases† | % Decrease |
|---|---|---|---|
| Smallpox | 29,005 | 0 | 100% |
| Diptheria | 21,053 | 0 | 100% |
| Pertussis | 200,752 | 18.975 | 91% |
| Tetanus | 580 | 33 | 94% |
| Polio (paralytic) | 16,316 | 0 | 100% |
| Measles | 530,217 | 120 | >99% |
| Mumps | 162,344 | 6,109 | 96% |
| Rubella | 47,745 | 7 | >99% |
| CRS | 152 | 5 | 97% |
| Haemophilus influenza | 20,000 (est.) | 33 § | >99% |

Source: *www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/e/impact.pdf*

* JAMA. 2007;298(18):2155-2163

† CDC. National Notifiable Diseases Surveillance System, 2017 Annual Tables of Infectious Disease Data. Atlanta, GA. CDC Division of Health Informatics and Surveillance, 2018. Available at: www.cdc.gov/nndss/infectious-tables.html. Accessed on December 3, 2018. NNDSS finalized annual data as of November 28, 2018.

§ Haemophilus influenzae type b (Hib) <5 years of age. An additional 10 cases of Hib are estimated to have occurred among the 203 notifications of Hi (<5 years of age) with unknown serotype.

**Comparison of pre-vaccine era estimated annual morbidity with current estimate: vaccine-preventable diseases**

| Disease | Pre-vaccine era annual estimate | 2016 estimate | % Decrease |
|---|---|---|---|
| Hepatitis A | 117,333* | 4,000† | 97% |
| Hepatitis B (acute) | 66,232* | 20,900† | 68% |
| Pneumococcus (invasive) - All ages | 63,067* | 30,400† | 52% |
| - <5 years of age | 16,069* | 1,700¶ | 89% |
| Rotavirus (hospitalizations <3 years of age) | 62,500* | 30,625 § | 51% |
| Varicella | 4,085,120* | 102,128†† | 98% |

Source: *www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/e/impact.pdf*

* JJAMA. 2007;298(18):2155-2163

† CDC. Viral Hepatitis Surveillance – United States, 2016

¶ CDC. Unpublished. Active Bacterial Core surveillance. 2016 ‡ CDC. MMWR. February 6, 2009 / 58(RR02); 1-25

§ New Vaccine Surveillance Network 2017 data (unpublished); U.S. rotavirus disease now has biennial pattern

†† CDC. Varicella Program 2017 data (unpublished)

## Protecting individuals and groups

Some vaccinations are put in place to protect the individual from an illness that can vary from mild to severe but, more importantly, to protect a susceptible group from serious illness. This would include **pertussis**, in which mortality is disproportionately borne by the very young who cannot mount an immune response, and **rubella**, which is most devastating to pregnant women and their unborn fetuses. **Congenital Rubella Syndrome (CRS)** was a major cause of fetal loss and neonatal morbidity with life-long implications in the pre-vaccine era.

Vaccines and screening programs are put in place as a response to current threats and concerns. They must be economical and beneficial. There must be a benefit to morbidity, mortality and/or financial loss to remain efficacious. **Tetanus, diphtheria, measles, mumps, polio, hepatitis A, influenza, rotavirus, Hemophilus influenza B** and **pneumococcal disease** all fit into this category. These diseases are still present throughout the world, even though they may be greatly contained in developed countries with high immunization rates. As such, travel, immigration and waning immunity from low vaccination rates are all that are needed to reintroduce these pathogens or accelerate their transmission in previously well controlled regions.

As with treatments, one must balance the risk versus benefits. How much is too much? Can a young child respond immunologically to the vaccine? Do the short-term costs (in money and time) outweigh the long-term benefits (lack of acute illnesses or future cancers)?

Several vaccines have been developed and successfully implemented with positive results only to find that immune-protective properties wane over time. That is how some recommendations have changed from single vaccines or initial series to a series that is followed by a booster several years later. Most are familiar with tetanus shots. In general, a **tetanus** shot is recommended every 10 years in an otherwise healthy individual, but if five years have passed since the last immunization and a patient presents with a serious or potentially soil-contaminated wound, a tetanus booster shot is given. Similarly, **measles, mumps, varicella** and **pertussis** vaccines, while initially recommended as only a single vaccine or a short series, now all have the recommendation of future booster injections. Time has proven that immunization wanes, and protection is much less complete than hoped for at times distant from initial inoculation.

The charts on the opposite page obtained from the Centers for Disease Control and Prevention website demonstrate both the reduction in incidence of vaccine responsive illness and the effect on mortality.

## Returning to the case

In this case, there appear to be both favorable and unfavorable signs. On the positive side, the family sees the pediatrician regularly and likely seeks care when needed. On the negative side, the parents are unvaccinated and are part of a vibrant non-vax community, so the child is less likely to benefit from community or herd immunity. Overall, given the levels of vaccination in the US and the incidence of vaccine preventable illnesses in the past few years, there is likely little to no increased mortality risk in this individual case. However, the overall vaccination situation needs to be monitored. With lower levels of vaccination in the community, one would expect increased risk in the vulnerable populations.

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CASE #2

# Intracranial Aneurysm

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**A 49-year-old man, asymptomatic and a runner, applied for life insurance. His mother died of a ruptured cerebral aneurysm (age at death not provided). Two years prior to the application, he was having some headaches and a magnetic resonance angiography (MRA) was performed. It showed a 4-mm aneurysmal dilatation of the middle cerebral artery. No further treatment or follow-up was reported.**

## What is the significance of a 4-mm intracranial aneurysm and the family history of rupture?

Intracranial or Cerebral Aneurysms (ICA) were found in 1.8% of asymptomatic individuals in the population-based Rotterdam study. There is a slight female preponderance for having ICA.

The prevalence increases with age and with certain conditions like adult polycystic kidney disease. The prevalence ratio was reported as 3.4 when there was a family history of aneurysm or subarachnoid hemorrhage. Another study found a prevalence of ICA in 8.7% of first-degree relatives of patients with ICA.

While some connective tissue diseases such as Ehlers-Danlos and pseudoxanthoma elasticum do show an association with ICA, only a small fraction of familial cases have an identifiable heritable syndrome. It has been suggested that aneurysms occur in similar locations in families and that they tend to rupture at a smaller size. Besides family history, other factors that increase the risk of aneurysms and subarachnoid hemorrhage are cigarette smoking, hypertension, estrogen deficiency and coarctation of the aorta.

Approximately 85% of ICAs are in the anterior circulation of the Circle of Willis. Sites at the junction of two arteries are the most common. Intracranial aneurysms may be described as saccular or fusiform. Saccular aneurysms are thin-walled and more prone to rupture. Most ICAs are asymptomatic, although rarely they can place pressure on a nerve causing a cranial neuropathy.

There is also an increased risk (2x or more) of ICA rupture in the posterior arterial system (vertebrobasilar, posterior cerebral arterial system or posterior communicating arteries) as compared to the anterior system (anterior communicating, anterior cerebral or internal carotid arteries). When there was a family history of subarachnoid hemorrhage and an ICA, there was an observed rupture rate of 1.2% per year which was 17 times higher than the rate observed in the International Study of Unruptured Intracranial Aneurysms (ISUIA).

Treatment of ICA is not without risk. One meta-analysis of reports found a 1.7% mortality risk of aneurysm clipping and 6.7% rate of unfavorable outcomes (morbidity). There are reports that endovascular repair, as opposed to surgical repair, results in better mortality and morbidity outcomes. Indications are that older age patients (>70) do not fare as well as younger patients. Smaller aneurysms (<7 mm) are generally not repaired due to the lower risk of rupture. Age and location of the aneurysm as well as risk factors and patient preferences all play a role in determining treatment.

| Aneurysm size | Frequency of enlargement over 47 months |
|---|---|
| < 8mm | 7% |
| 8-12mm | 25% |
| >12mm | 83% |

| Aneurysm size | Frequency of rupture over 5 years |
|---|---|
| 7-12mm | 2.6% |
| 13-24mm | 14.5% |
| >24mm | 40% |

**Aneurysm growth and rupture is more common in larger aneurysms.**

## Returning to the case

A 4-mm intracranial aneurysm is considered small and at low risk of rupture. However, the family history increases the risk of both growth and rupture. At a minimum it would be prudent to have at least one follow-up evaluation by a neurologist to determine if there is any growth or development of additional findings.

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SOLVE

# ECG Puzzler

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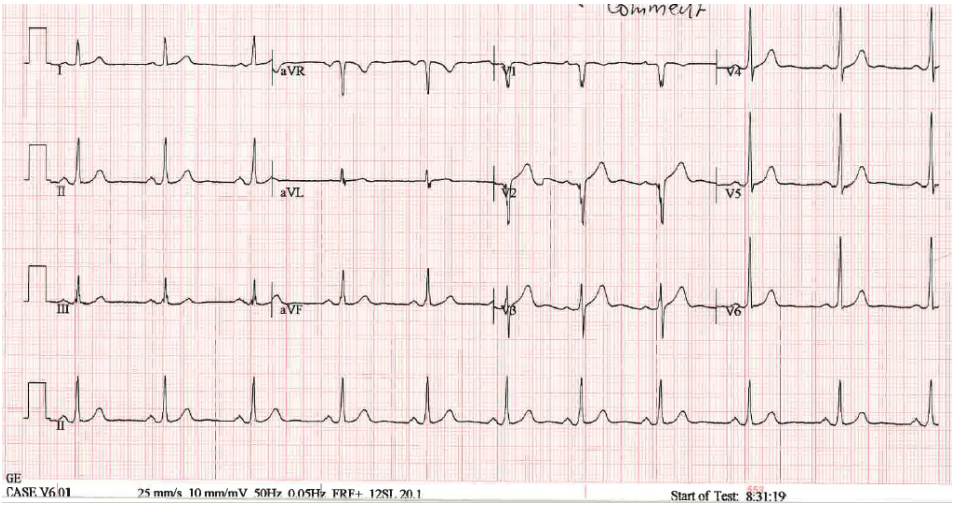
Here is the latest ECG Puzzler to solve.

A 44-year-old male applies for insurance. He has no adverse cardiac history personally or in his family. He has no cardiovascular risk factors except a slightly elevated total cholesterol at 6 mmol/L with LDL at 3.11 mmol/L but HDL at 1.41 mmol/L and total/HDL ratio at 4.3.

A recent stress test was reported as normal. An echocardiogram was normal, and his CT calcium score was 0. His ECG is shown at right.

Visit the *Housecalls* page on our website (www.scorgloballifeamericas.com) to find the answer. Click on Fall 2019 Puzzler to confirm your findings.

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