It's No Yolking Matter: Reaction During Insemination

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While artificial insemination has been a common procedure in humans for over 30 years, few adverse allergic reactions have been described or well documented in the medical literature.

Anaphylaxis occurs mainly with the following allergens:

- latex,
- a 14KD protein found normally in human spermatic fluid,
- penicillin, streptomycin, and other drugs added in the sperm processing media, and
- bovine serum albumin (BSA), used to protect the sperm from damage due to the freezing procedure.

Tracy's Exception

Tracy, 27, has been diagnosed with polycystic ovary syndrome (confirmed by laparoscopy). Her husband is infertile. Since 1999, she has had nine attempts at artificial insemination. In each instance, within a few minutes of injecting thawed semen directly into the uterus, she experienced severe lower abdominal pain described as "excruciating menstrual cramps" lasting between 20 minutes and two hours. These episodes were also accompanied by pallor and malaise.

Her medical history is remarkable for allergic rhinoconjunctivitis to cats, dogs, dust mites, and grass pollens starting at age 17. She also has occasional asthma with prolonged contacts with animals. Previously, it was judged these reactions were attributable to some type of vasovagal reaction.

On the tenth attempt, Tracy experienced the same reaction. However, three minutes later, she developed generalized pruritis, followed by weakness, vomiting, and diffuse urticaria and angioedema. She was rapidly transferred to the emergency department. She nearly fainted en route, having difficulty breathing due to a cough and wheezing.

She immediately received intramuscular (IM) epinephrine, intravenous

(IV) diphenidramine, and solumedrol with 2L of normal saline, in addition to salbutamol aerosol. She gradually recovered within 30 minutes and left the hospital eight hours later with a tapering course of benadryl and prednisone for five days. She had no further complications, but failed to conceive once again.

She was seen one month later for a followup.

Digging deeper

Upon reviewing Tracy's chart, it was discovered that every sperm donor was used more than once.

Close questioning revealed that, while Tracy never had eczema nor anaphylactic food or drug reactions, she hasn't been able to eat liquid eggs for the past five years because of a tingling sensation in her mouth and a tight throat. Similar symptoms were noted with the injestion of mayonnaise, a variety of sauces, and icings. She could, however, eat cakes, muffins, pancakes, and cooked eggs.

Why is this important?

To protect the sperm from damage due to the freezing procedure, sperm banks use two different types of mixture: in 30% of the cases, the semen is diluted in Sperm Freeze™ solution, while the remaining 70% is processed in Ackerman's medium.

The Sperm Freeze solution contain a HEPES buffered medium with 0.4% human serum albumin. The Akerman's medium is made of the following ingredients:

- 40 mL sterile egg yolk 50%,
- 30 mL glycerol,
- 2 g of glycine,
- 2.6 g of glucose,
- 2.3 g of sodium citrate, and
- 130 mL deionized water.

Tracy always received semen samples cryopreserved in Ackerman's medium.

Table 1 shows the results of Tracy's allergy prick skin test and fluoroenzyme-immuno-assay specific IgE (UniCAP®) test completed for latex, egg antigens, and spermatic fluid.

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What do the tests reveal?

Tracy's skin tests were positive for only egg white and egg yolk, while the UniCAP-specific IgE was positive at a low level for egg yolk.

What does it all mean?

Tracy's life-threatening anaphylaxis during intrauterine insemination was triggered by egg yolk, which was used as an alternative animal protein to BSA for cryopreservation of sperm.

Previously, hypersensitivity reactions occurring after intrauterine placement of spermatozoa or embryos were attributed to cells being processed and transferred in media containing trace amounts of either antibiotics or foreign proteins.

Even though the specific IgE to egg yolk was rather low, Tracy most likely sustained a severe reaction because the allergen was injected close, or directly into, the blood vessels.

Table 1

Results of Tracy's diagnostic tests

Reagents	Skin prick test (mm of induration)	UniCAP®[3] KUA/L	UniCAP®[3] Class (0 to 6)
Latex[1] (crude resine in 50% glycerine)	0	< 0.35	0
Egg white (1:10 w/v)[2]	4	< 0.35	0
Egg yolk (1:10 w/v)[2]	8	0.43	1
Ovalbumin	ND	< 0.35	0
Ovomucoid	ND	< 0.35	0
Spermmatic fluid	ND	< 0.35	0
Histamine (1mg/mL, 50% glycerine w/v)	4	ND	
Diluent (normal saline, 50% glycerine with human serum albumin and phenol 0.4%)	0	ND	

1. Allergi-Lab, Quebec, Canada
2. Omega Laboratoires, Montreal, Canada
3. Pharmacia Diagnostics AB, Uppsala, Sweden
ND: Not done
w/v: weight/volume

Three months after the anaphylactic event, Tracy underwent an artificial insemination using semen in Sperm Freeze, in which no allergic reaction or abdominal discomfort was noted. Unfortunately, the fertilization attempt was again unsuccessful.

What are the chances?

Egg allergy is extremely uncommon in adults (< 0.1%). In young children, the prevalence is considerably higher, reaching a maximum of 1.6% at two years of age. In allergic children, the prevalence of egg allergy is around 5% to 6%. In those with moderate to severe eczema, the prevalence reaches approximately 40%.[1] Although it is said most adolescents

Take-home message

- Egg allergy is extremely uncommon among adults (< 0.1%).
- Still, egg and other allergens can be found in:
  - vaccines,
  - injectable medecines,
  - biological products,
  - general anesthetic (propofol),
  - intravenous hyperalimentation (intralipid),
  - some cryopreservatives of human cells.
- It is important to always question patients about food allergies, especially when dealing with the above-mentioned treatments and prescriptions.

will outgrow the allergy, its exact prevalence in atopic adults is unknown.

How does it apply to your practice?

Enquiring about food allergies remains an important part of all medical questioning, particularly before prescribing injectable medicines or biologic products, as measurable quantities of animal protein allergens may be found in some of them. It is also important to keep in mind that egg allergens constitute a fraction of some vaccines (*e.g.*, inluenza, yellow fever, mumps, and rabies) and are also found in general anesthetic (propofol), IV hyperalimentation (intralipid), and some cryopreservatives of human cells. CME

References
1. Zeiger RS: Current issues with influenza vaccination in egg allergy. J Allergy Clin Immunol. 2002; 110(6):834-40.

Further references available—contact ***The Canadian Journal of CME*** at **cme@sta.ca**.