# Case Report: Diamine Oxidase Deficiency as a Proposed Mechanism for Anaphylaxis after the Third Stage of Labor

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## Background

Previous case reports have demonstrated postpartum anaphylaxis associated with breastfeeding thought to be due to destabilization of mast cells. However, anaphylaxis after delivery of the placenta is much less commonly seen in the literature. (1) Investigating the cause of such postpartum anaphylaxis warrants a closer look at maternal-fetal histamine and diamine oxidase production and regulation.

The enzymes diamine oxidase (DAO) as well as L-histidine decarboxylase (HDC) are produced in high amounts by the placenta suggesting a physiologic role, yet need for tight control, of histamine during pregnancy. DAO functions extracellularly to degrade histamine into imidazole acetaldehyde and to provide a metabolic barrier to prevent excessive histamine from entering maternal or fetal circulation. (Fig. 1)

Complications in pregnancy may arise when histamine-DAO levels become unbalanced via two major mechanisms: histamine intolerance (HI) or decreased DAO levels or activity. It is known that DAO levels are 50-times higher in maternal circulation compared to that of the fetus for ~2 weeks following delivery in uncomplicated pregnancies. (2) A precipitous drop in DAO levels or decreased activity is associated with several maternal-fetal conditions (Table 1), and we propose decreased DAO levels may also increase hypersensitivity and risk of postpartum anaphylaxis in susceptible individuals. Currently it is unknown what causes low DAO activity or levels, but some thought has been given to genetic mutations in the DAO gene.

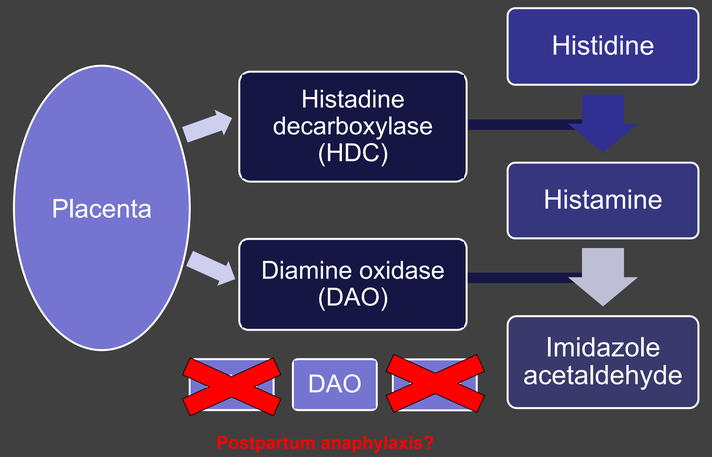


Figure 1. Proposed mechanism of decreased DAO leading to postpartum anaphylaxis.

| Table 1. Conditions associated with low DAO plasma levels[2] |
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| Premature rupture of membranes |
| Pre-eclampsia |
| Diabetes |
| Prematurity |
| Threatened, habitual, or missed abortions* |
| Trophoblastic diseases (Hydatid mole, Chorioncarcinoma) |
| *due to histamine's direct contractile effect on myometrium and indirect production of prostaglandins |

## Case

A 29-year-old G5P3 presented to labor and delivery at 39w1d with ruptured membranes. Her obstetrical history is significant for 3 vaginal deliveries with subsequent anaphylaxis after delivery of the placenta and premature rupture of membranes (PROM) with her second delivery. Medical history includes sensitive skin, seasonal allergies, and negative allergy testing. During her first two deliveries, she had eye and lip swelling after delivery of the placenta. She required steroids and oxygen following her second delivery. After her third delivery, she required oxygen due to throat edema with minimal improvement from Diphenhydramine. The reaction was not associated with timing of narcotics. With her third delivery, the patient was given 125 mg IV Solumedrol (methylprednisolone) two hours prior to her vaginal delivery in addition to IV Diphenhydramine intrapartum. Two hours after delivery, she complained of angioedema with eye and lip swelling and throat itchiness. She remained hemodynamically stable and did not require supplemental oxygen. She had received a second dose of IV Diphenhydramine, which was not relieving her symptoms. Due to her history, 0.3 mg epinephrine IM was given and resolved patient's symptoms.

## Conclusion

A proposed mechanism of decrease of diamine oxidase after delivery of placenta may provide insight into the maternal – fetal immune system interface. This could lead to future efficacious therapies (e.g. DAO administration) for high risk pregnancies.

References
[1]Gupta et al. "postpartum anaphylaxis: universal but successful management protocol should not deter appreciation of underlying etio-pathogenesis plethora." Clinics and Practice 2012; 2:e43.
[2]Maintz et al. "Effects of histamine and diamine oxidase activities on pregnancy: a critical review." Human Reproduction Update, Vol.14, No.5 pp. 485–495, 2008.