Literature Review: Antibody Production in Mice in Response to Aspergillus fumigatus Inhalation

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Antibody production in mice in response to *Aspergillus fumigatus* inhalation

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Background Information

- ***Aspergillus fumigatus*** is a commonly inhaled respiratory fungal pathogen and an allergen found in flooded indoor environments, household dust, soil, and plant matter. *A. fumigatus* is relevant because if inhaled it poses a threat to weakened immune systems due to the potential of infection in the lungs or sinuses which can spread to other areas of the body.
- **The mouse genome** is 99% similar to the human genome, and therefore they serve effectively in modeling the effects of inhaled *A. Fumigatus* in humans (National Human Genome Research Institute, 2010). Good models are necessary to know what kind of effects *A. Fumigatus* could have on humans. It is also unethical to perform these tests on humans for cause and effect relationships. This would help in diagnosing and designing a treatment plan in humans for *A. fumigatus*.
- **Inhalational** route of exposure to *A. fumigatus* in mouse models is relevant since it is the most similar to how we as humans would be exposed (Ralph & Sheppard, 2021). Inhalation exposures have also been found to provide a more representative analysis of immune responses to *A. fumigatus* or similar fungal contaminants (Buskirk et al., 2014).
- **Antibodies** are proteins in the body that is released in response to fungus, bacteria, or viruses to help fight them off. *A. fumigatus* can cause specific antibodies to be released. It is important to know and understand the antibodies which are most often elicited in response to *A. fumigatus* in mice, since mice are one of the most common models for *A. fumigatus* exposure. This data will help inform the optimization of mouse procedures for *A. fumigatus* exposure, that are critical for developing treatment and diagnostic options for humans.

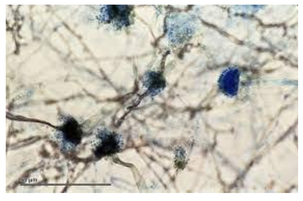


Illustration 1: A microscopic picture of *Aspergillus fumigatus*. Photograph by Reischig, distributed under a CC-BY 2.0 license. https://commons.wikimedia.org/wiki/File:Aspergillus_fumigatus_(257_15).jpg

Illustration 2: A laboratory mouse model. Photograph by Rama, distributed under a CC-BY 2.0 license. https://commons.wikimedia.org/wiki/File:Lab_mouse_mg_3263.jpg.

Methods & Research Questions

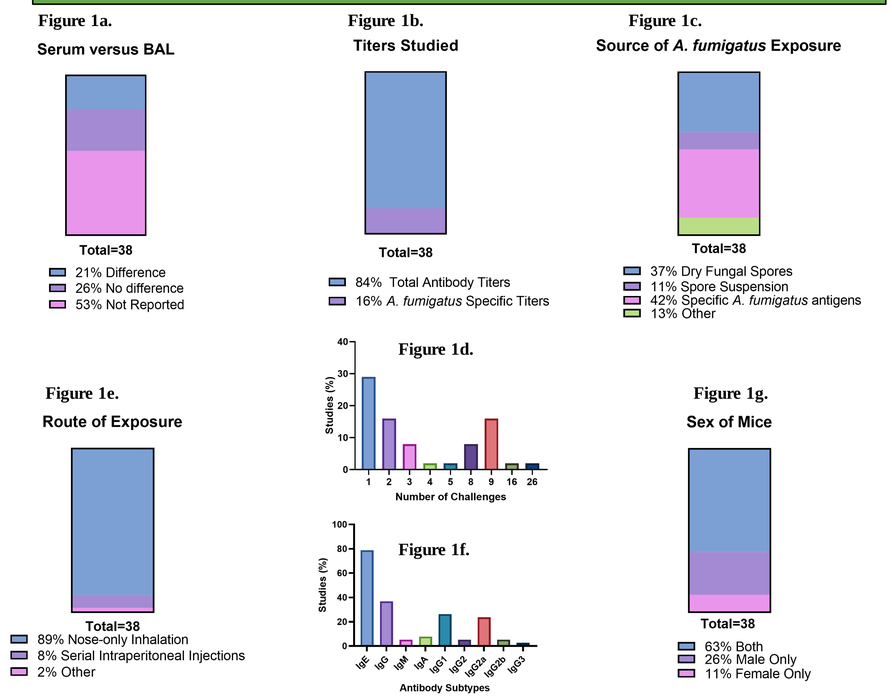
PubMed search keywords *Aspergillus fumigatus*, **mice, inhalation, antibodies** → **38 relevant articles**

Articles mined for the following 8 questions:

- What types of antibodies are measured in response to *A. fumigatus* in mice?
- Is there any difference between antibody titers in serum versus BAL in response to *A. fumigatus* inhalation?
- Have these studies measured total antibody titers or *A. fumigatus* specific titers?
- In these studies - have they used dry fungal spores or spore suspensions or specific antigens from *A. fumigatus*?
- In these studies what is the route of exposure?
- Have these studies parsed out the data for male and female mice?
- How many challenges (total # of exposures) were administered to the mice?
- At which timepoints were the mouse samples analyzed?

Excel data organization and analysis → **Data figures and statistical analysis using Graph Pad Prism 9.**

Results



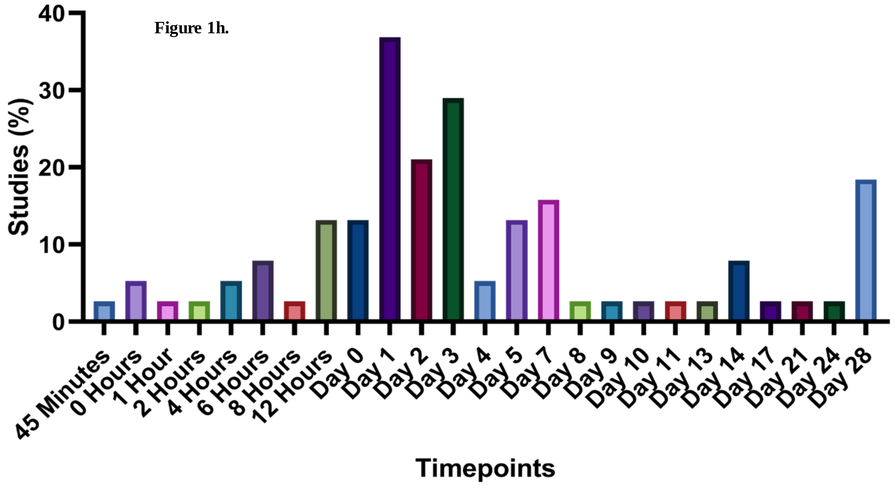


Figure 1: Analysis of the 38 articles in regards to our 8 questions. Figure 1a. Serum versus BAL was considered in about half the articles. **Figure 1b.** 84% of the articles studied total antibody titers. **Figure 1c.** Specific *A. fumigatus* antigens at 42% and dry fungal spores at 37% were the most common sources of exposure. **Figure 1d.** the number of challenges was often 1, but ranged to 26. **Figure 1d.** The number of challenges was often 1, but ranged to 26. **Figure 1e.** Nose-only inhalation was the primary route of exposure by almost 90%. **Figure 1f.** IgE and IgG antibodies were the most common types of antibodies reported as elicited in response to *A. fumigatus*. **Figure 1g.** Both sexes of mice were utilized for over half the studies. **Figure 1h.** Timepoints for challenges were commonly one, two, and three days for most of these studies.

Discussion & Conclusion

- **Our questions** were designed to be able to collect the most relevant and useful data. It is important to consider many factors for infectious disease biology because immune responses differ dependant on a wide variety of factors.
- **Host-sex** has a considerable effect in shaping the immune response, so most of the studies we found had good representation of both male and female mice (Schaefer et al., 2020). Having data with both sexes would rule out a possible difference between male and female mice based on differences of sex hormones, X vs. Y chromosomes, and epigenetics.
- **Timepoints** are important to consider because different white blood cells and antibodies would be present at different timepoints. Early responders will try to kill the fungus quickly, but responders around on day 28 might employ different strategies to rid of the fungus.
- **Source of exposure** is a crucial factor in creating studies which are relatable to how humans would be naturally be exposed to *A. fumigatus* (Buskirk et al., 2014). Dry fungal spores would be the type of exposure in this case that would most closely replicate how the fungus would be in the environment when humans come into contact.
- **Route of exposure** for *A. fumigatus* would similarly be important in how the fungus would enter the human system (Buskirk et al., 2014). Nose-only inhalation, rather than injections, would be the most natural way *A. fumigatus* would enter the body.
- **Serum vs. BAL** was a considerable factor in our review since BAL is expected to have high levels, but it's also important to study the serum levels to see if the infection had spread to the whole system (Verbout et al., 2013).
- **Antibody titers** studied is an essential factor to understand in our studies because those unspecific to *A. fumigatus* may not be helpful to fighting the infection.
- **Number of challenges** is helpful to understand how antibodies deal with the fungus over different time periods.
- **Subtypes of antibodies** elicited in response to A. fumigatus is crucial to know how the body is reacting. The high prevalence of IgE and IgG antibodies indicates their large role in attacking the fungus and treatment methods can be designed accordingly (Müller et al., 2006).
- **All of these factors** were considered to ensure data collected was valid in relating how A. fumigatus infections displayed in mice would be displayed in humans.

References

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