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# Protocol: Extrinsic Allergic Alveolitis- A Systematic Review of HLA-DR in Pigeon Breeder's Disease

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**We use this protocol and it's working**

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## Disclaimer

No Disclaimer

## Abstract

Pigeon Breeder's Pneumonitis' complex pathogenesis affects a specific exposure group, as well as a potential genetic predisposition varying the immune response to these antigens. Previous research has begun to categorize affected individuals possessing HLA sequences as compared to normal population. This HLA meta-analysis with Pigeon Breeder's Pneumonitis will offer a broad scope analysis of these alleles, and serve as a further prognostic application. Earlier identification of the predisposition towards Pigeon Breeder's Pneumonitis will also serve as an opportunity for potentially disease course altering treatment earlier in it's pathogenesis.

## Troubleshooting

## Administrative Information

### 1 Title

Protocol: Extrinsic Allergic Alveolitis- A Systematic Review of HLA-DR in Pigeon Breeder's Disease

### 2 Registration

Registration is via protocols.io

### 3 Authors

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### 4 Amendments

None

### 5 Support

Sources: No financial sources utilized

Sponsor: Lake Erie College of Osteopathic Medicine- Bradenton

Role of sponsor: Research oversight

## Introduction

### 6 Rationale

Pigeon Breeder's Pneumonitis' complex pathogenesis affects a specific exposure group, as well as a potential genetic predisposition varying the immune response to these

antigens. Previous research has begun to categorize affected individuals possessing HLA sequences as compared to normal population. This HLA meta-analysis with Pigeon Breeder's Pneumonitis will offer a broad scope analysis of these alleles, and serve as a further prognostic application. Earlier identification of the predisposition towards Pigeon Breeder's Pneumonitis will also serve as an opportunity for potentially disease course altering treatment earlier in it's pathogenesis.

## 7 **Objective**

To conduct a meta-analysis to ascertain how the various HLA-DR alleles are linked with odds of developing Pigeon Breeder's Pneumonitis.

## Methods

### 8 **Eligibility criteria**

Only studies published after 1975 will be included for analysis purposes. Studies that cannot be accessed, do not provide adequate data on the experimental or control population, or contain data that is difficult to interpret will not be used.

### 9 **Information Sources**

PubMed, Google Scholar, ScienceDirect, and Cochrane Library will be utilized as databases for data acquisition. Institutional access will be used for data acquisition however no attempts to contact authors will be made if access is not available. This data will be gathered for approximately 1 month.

### 10 **Search Strategy**

Searching will be conducted using the following terms "HLA and Pigeon Breeder Pneumonitis", "HLA-DR and Pigeon Breeder", "HLA-DR1 and Pigeon Breeder", "HLA-DR3 and Pigeon Breeder", "HLA-DR4 and Pigeon Breeder",. When an available database feature is available, both HLA and Pigeon Breeder will be required to appear in the title in order to limit the search. One researcher, Ryan Witcher will be assigned the role of searching and data collection. Dylan Thibaut and Ryan Witcher will collaborate for the statistical analysis.

### 11 **Study Records**

#### **Data Management**

The data collected during the search process will be housed in google sheets for analysis with statistical software.

#### **Selection Process**

Studies will be included in the event the relevant data is readily accessible in the publication, with the minimum requirement being the presence or absence of disease

among an experimental and control group. Although data will be recorded on any HLA allele that meets the aforementioned criteria, only alleles that are represented at the minimum of three times will be included in the meta-analysis. Acceptable control groups will include exposed pigeon handlers with no presence of pigeon breeder's pneumonitis, or unrelated and unexposed normal individuals.

A control group that consists of individuals that are familially related to a pigeon breeder's pneumonitis individual (but with no exposure to pigeons) is not an acceptable control group and will be excluded from the present analysis. If the data does not directly link the presence of an HLA allele to Pigeon Breeder's Pneumonitis, or if the publication was created prior to the 1975 earliest date acceptable, the data will not be included. Finally, if a study only assessed the allelic frequency of specific subtypes of HLA alleles, and those subtypes corresponded to identical serotypes, the data will not be included. For example, if an individual study included genotypic frequency on both HLA-DR4\*0407 and HLA-DR4\*0405, these data cannot be consolidated under a single serotype HLA-DR4 and therefore will be excluded.

### **Data collection Process**

Data will be collected by two researchers onto one Google Sheets. If the legitimacy of data or the study being assessed is questionable, the other researchers will be polled on their opinion about its inclusion or exclusion. If a consensus is not reached, the PI will be consulted for the final decision.

#### **12 Data items:**

Data collected included the number of cases of Pigeon Breeder's Pneumonitis with the presence or absence of specific HLA alleles, as well as the healthy controls with the presence or absence of the specific HLA alleles. Odds ratios and confidence intervals that were found were also recorded.

#### **13 Outcomes and Prioritization**

All HLA data will be collected regarding their frequency with pigeon breeder's pneumonitis. Data will only be included if at least 3 acceptable separate publications included the HLA allele and if the statistics show a significant odds ratio interval. Significance will be determined based on odds ratio confidence intervals, effect size, and heterogeneity measured with I squared.

#### **14 Risk of bias in Individual Studies**

Risk of bias is assessed through the NIH Quality Assessment Tool of Case Control Studies (cited below). A generated DOI plot will also be made if possible with MetaXL.

National Heart, Lung, and Blood Institute. Study Quality Assessment Tools. Available from: <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>. Updated 2021 July.

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### **Data Synthesis**

A: Revman 5.4 software (cited below) will be used for statistical analysis. The number of cases with a discrete HLA, total case number, the number of control with a discrete HLA will be inputs for forest plot analysis.

B: The odds ratios and their confidence intervals of each individual study will be assessed to form a single, combined odds ratio and confidence interval for each allele. Data will then be assessed with  $I^2$  as a measure for heterogeneity. Heterogeneity above  $I^2$  of 25% will be considered moderate or high.

C: Sensitivity analysis may be performed via Revman or other software such as MetaXL.

D: See above.

Review Manager (RevMan) [Computer Program]. Version 5.4, The Cochrane Collaboration, 2020.

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### **Meta-bias and Confidence in Cumulative Evidence**

GRADE criteria will be used (cited below).

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schünemann HJ, Edejer T, Varonen H, Vist GE, Williams JW Jr, Zaza S; GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ*. 2004 Jun 19;328(7454):1490. doi: 10.1136/bmj.328.7454.1490. PMID: 15205295; PMCID: PMC428525.