

High Correlation Between Responses to *Juniperus ashei* (Mountain Cedar) Pollen in a Pollen Challenge Chamber versus Seasonal Exposure

Andrews CP, Ramirez DA, Harper N*, He W,* Rather C, Ahuja SK, Jacobs RL
 Biogenics Research Chamber, *University of TX Health Science Center and VA Center for Personalized Medicine, San Antonio Texas



ABSTRACT

BACKGROUND: The level of concordance between allergic symptoms induced upon exposure to pollen in a pollen challenge chamber (PCC) versus in the natural season has not been well studied.

OBJECTIVE: We tested the hypothesis that the symptom levels of allergic rhinoconjunctivitis elicited following out-of-season exposure to *Juniperus ashei* (mountain cedar) pollen in a PCC are highly correlated with those experienced during the natural season for mountain cedar.

METHODS: Twenty-two and 11 participants positive and negative, respectively, for skin test and allergy to mountain cedar were challenged in a PCC for 3 hours per day for 2 days. Seventeen of the twenty-two mountain cedar positive participants and seven of the mountain cedar negative participants recorded symptoms for 30 days during the natural mountain cedar season in San Antonio, Texas. Total symptom scores (TSS) for the chamber and natural season were calculated based on the sum of the total ocular symptom scores and the total nasal symptom scores.

RESULTS: The maximum TSS recorded in PCC and natural season were calculated for the twenty-four participants that took part in both PCC runs and natural season study. The maximum TSS-Natural vs. TSS-Chamber were plotted, and the overall correlation r^2 was 0.67. Using residuals for the $Y = X$ line (which represents perfect concordance) it was found that twenty-one out of the twenty-four participants (87.5%) had concordant maximum TSS in both the natural season and the chamber while three (12.5%) had discordant maximum TSS. The r^2 of the concordant groups was 0.82. Using linear regression on the concordant group, it was found that the slope was not significantly different from 1 (slope = 1.12; $P = 0.320$) and the intercept was not significantly different from 0 (intercept = 1.47; $P = 0.254$).

CONCLUSIONS: Our findings affirm our hypothesis that individuals will react similarly to mountain cedar pollen in a PCC as they do in the natural season, and highlight the utility of the PCC as a model system to explore novel therapeutics and the pathogenesis of allergic rhinoconjunctivitis.

INTRODUCTION

The mountain cedar tree is the only plant in the United States that pollinates in the winter. That heavy pollen season is utilized as a natural model for the study of seasonal allergic rhinoconjunctivitis.

Because of distinct advantages of controlling confounding factors, pollen challenge chambers (PCC) are being utilized more frequently to investigate the pathogenesis and novel therapeutics for seasonal allergic rhinoconjunctivitis.

This study compares allergic rhinoconjunctivitis elicited in PCC vs. the natural season to the same antigen.

METHODS

Study Subjects:

Chamber Study:

- 22 mountain cedar positive subjects and eleven mountain cedar negative subjects (controls) were challenged during the off-season for mountain cedar in the Biogenics PCC for 3 hours a day for 2 consecutive days.
- Average mountain cedar pollen counts in the PCC were 12,000 grains/mm³ (3 to 4 times the average in the natural season).
- During exposure, total nasal (TNSS) and total ocular (TOSS) symptom scores were recorded every 30 minutes and summed for total symptom scores (TSS).

Natural Season:

- 17 and 7 of the mountain cedar positive and negative participants, respectively, recorded symptoms for 30 days (Twice a day, AM and PM) during the mountain cedar season in San Antonio, Texas.

Inclusion Criteria for PCC

Negatives

- A negative reactivity skin test to mountain cedar.
- No other skin test reactions.
- No history of respiratory diseases (perennial allergic rhinitis, asthma, COPD).
- No chronic, non-allergic rhinitis symptoms.

Positives

- A positive skin test to mountain cedar.
- 2-year history of allergy symptoms during season.
- A wheal of 5 mm or larger than the negative control.
- Not currently on immunotherapy.

Statistical Analysis

- The maximum value of TSS within each environment (PCC or natural season) that was within two standard deviations (SD) from the mean TSS was considered as maximum TSS.
- Hierarchical clustering was used by taking into account the maximum TSS in the chamber and natural season. Any value within two standard deviation from the perfect line ($Y=X$) line were considered as concordant, and the remainder as discordant.
- Linear regression was used to examine the relationship between maximum TSS in the chamber and natural season among subjects categorized to the concordant and discordant groups.

RESULTS

Fig. 1 Flow chart of the studies subjects

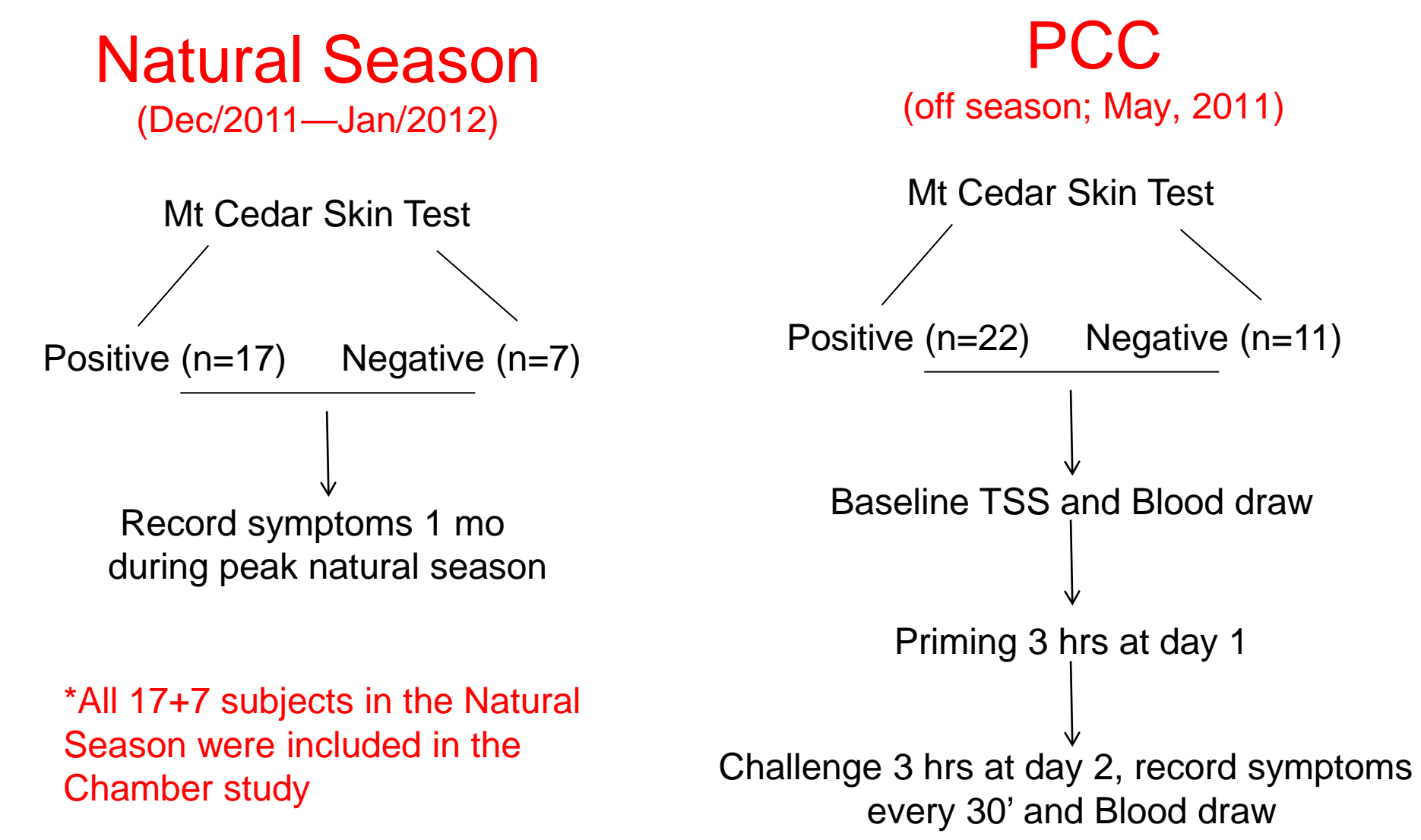


Fig. 3 TSS (mean ± 2SD) in PCC

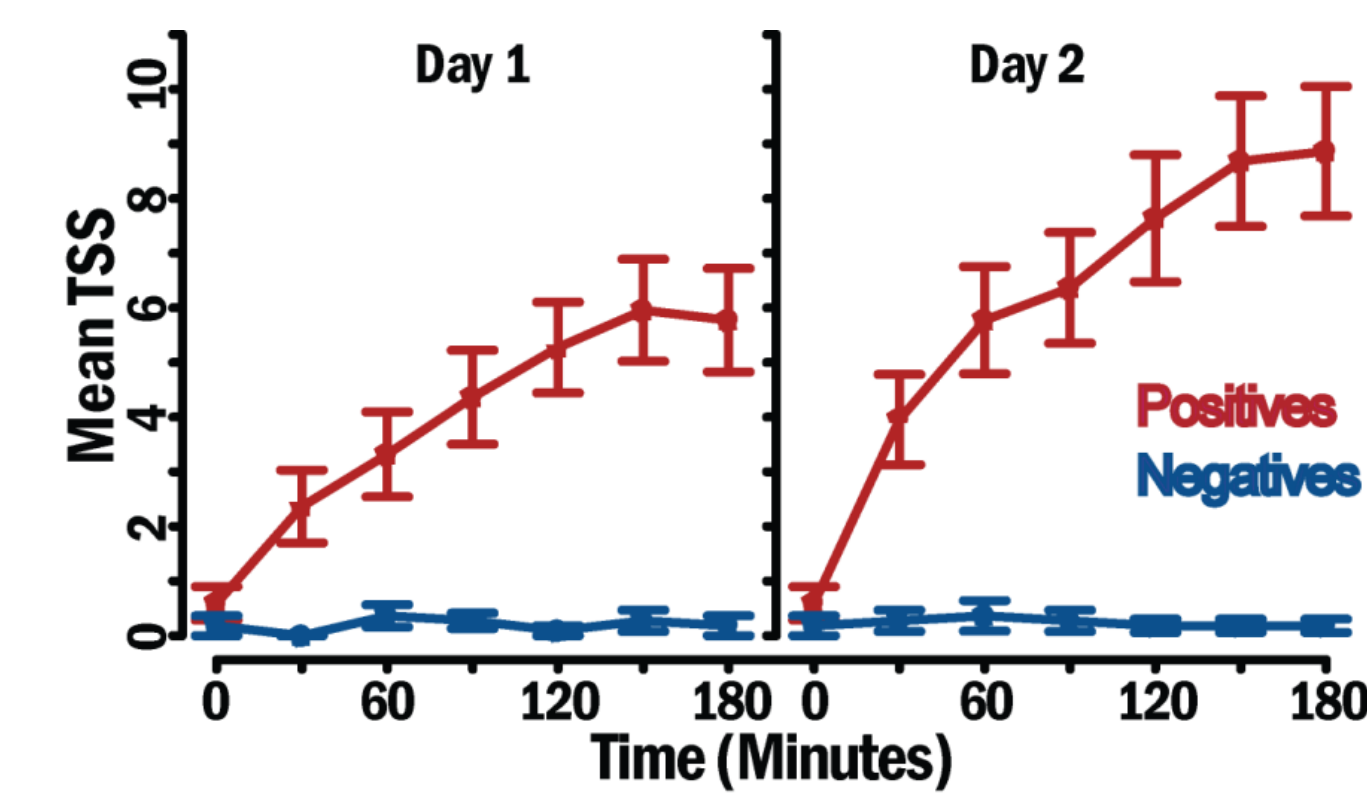
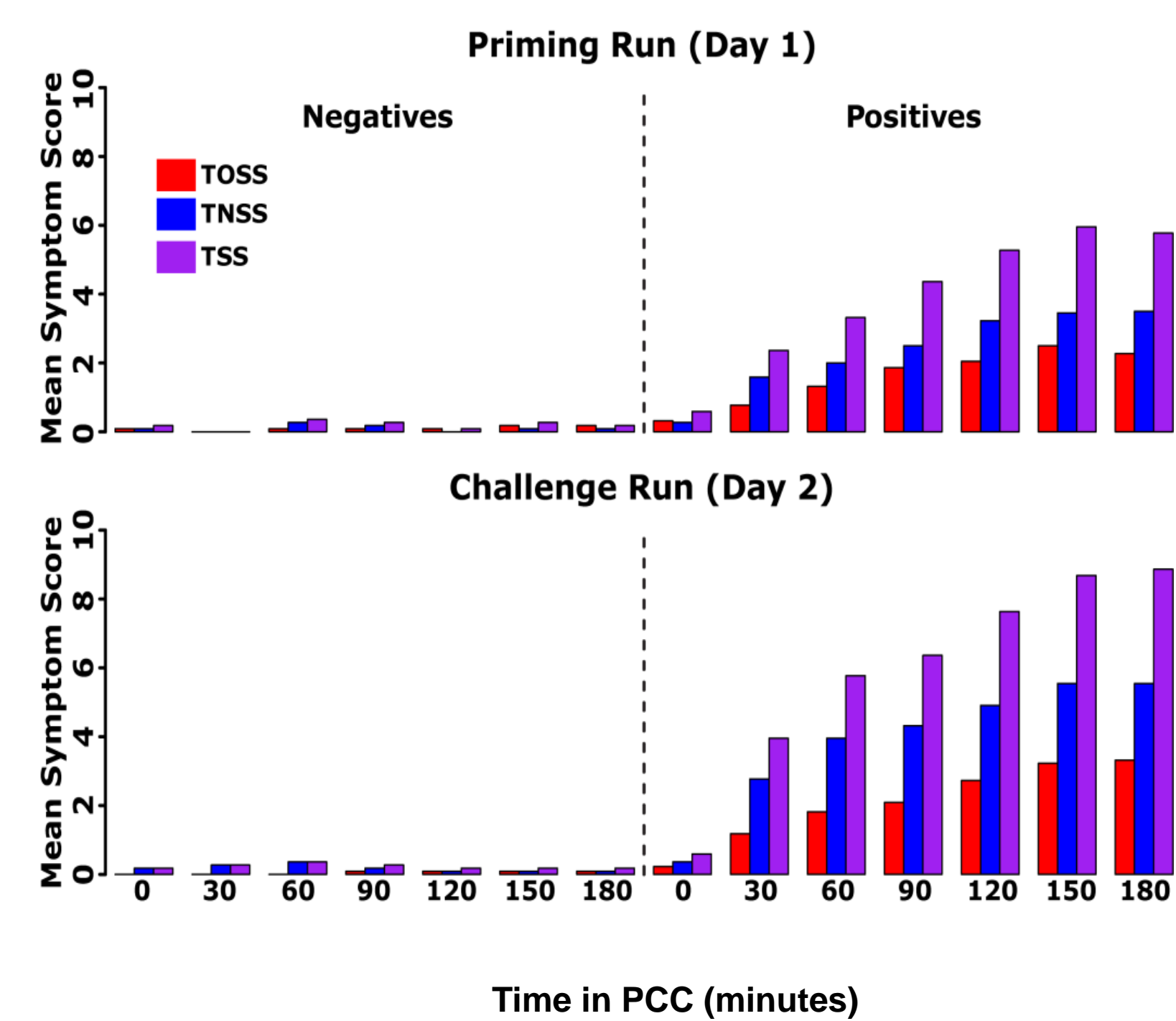


Fig. 5 TOSS and TNSS symptoms in PCC



RESULTS(cont')

Fig. 2 Average symptoms and pollen count during the natural season

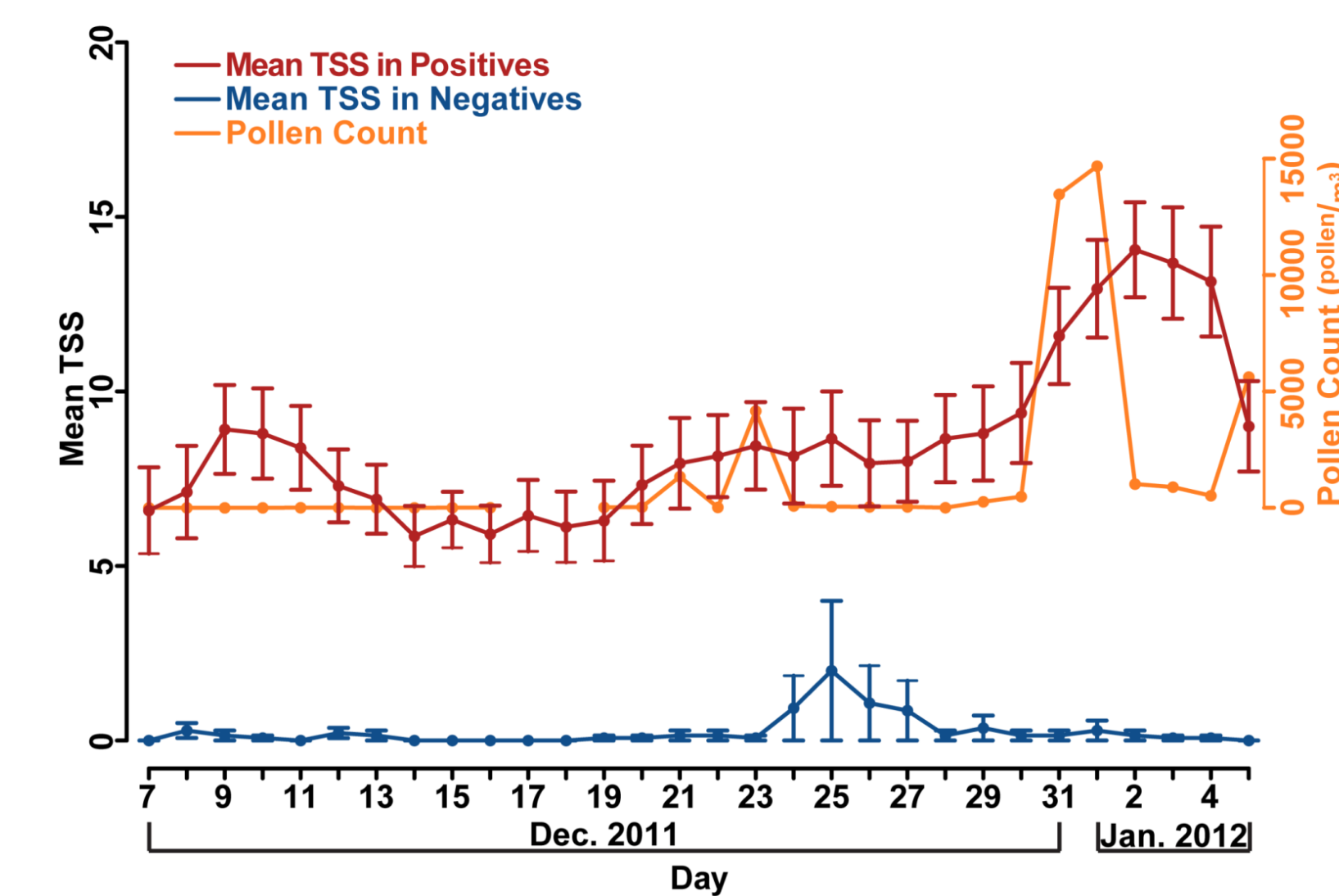


Fig. 4 TOSS and TNSS symptoms in natural season (positives only)

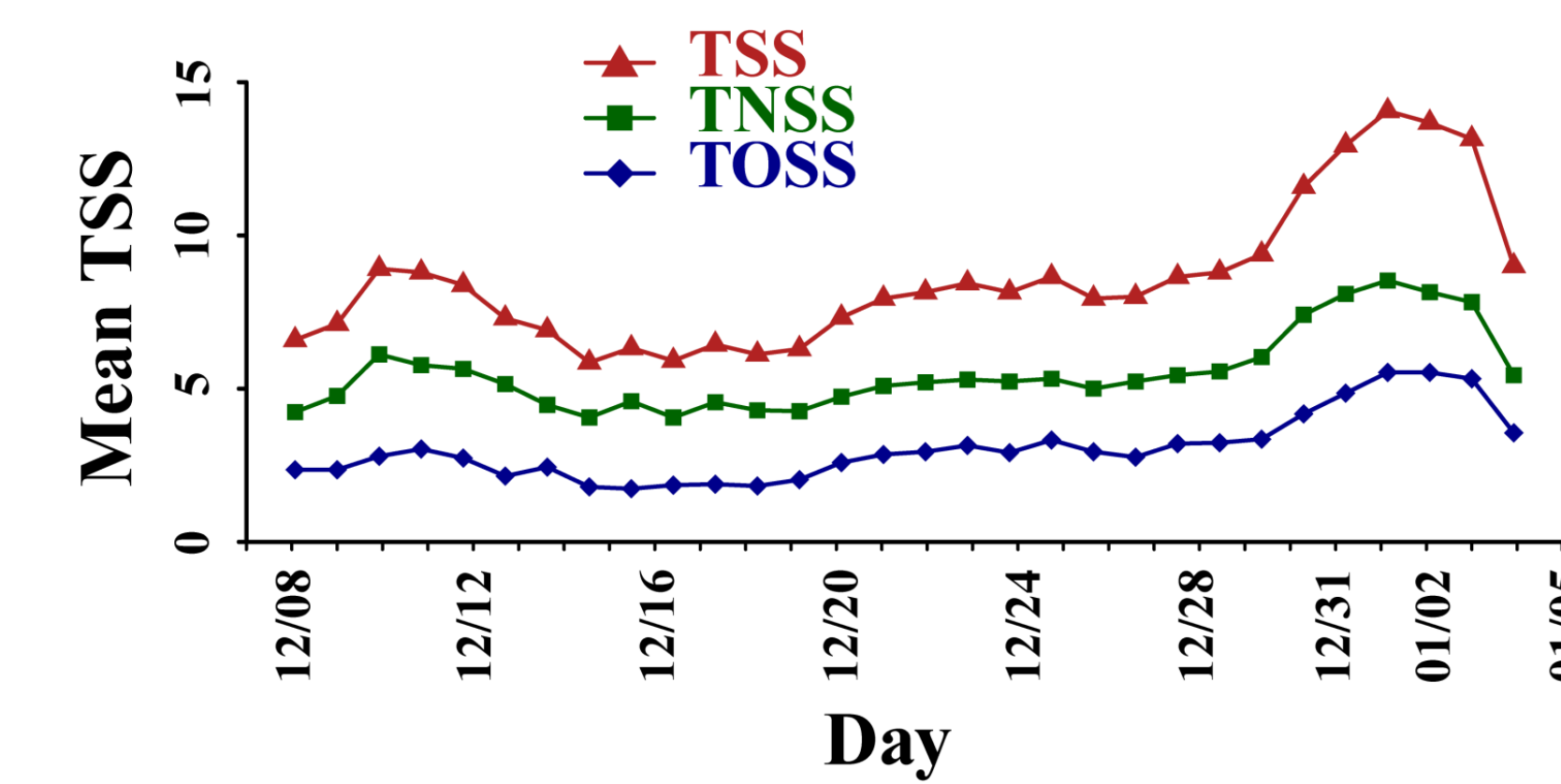
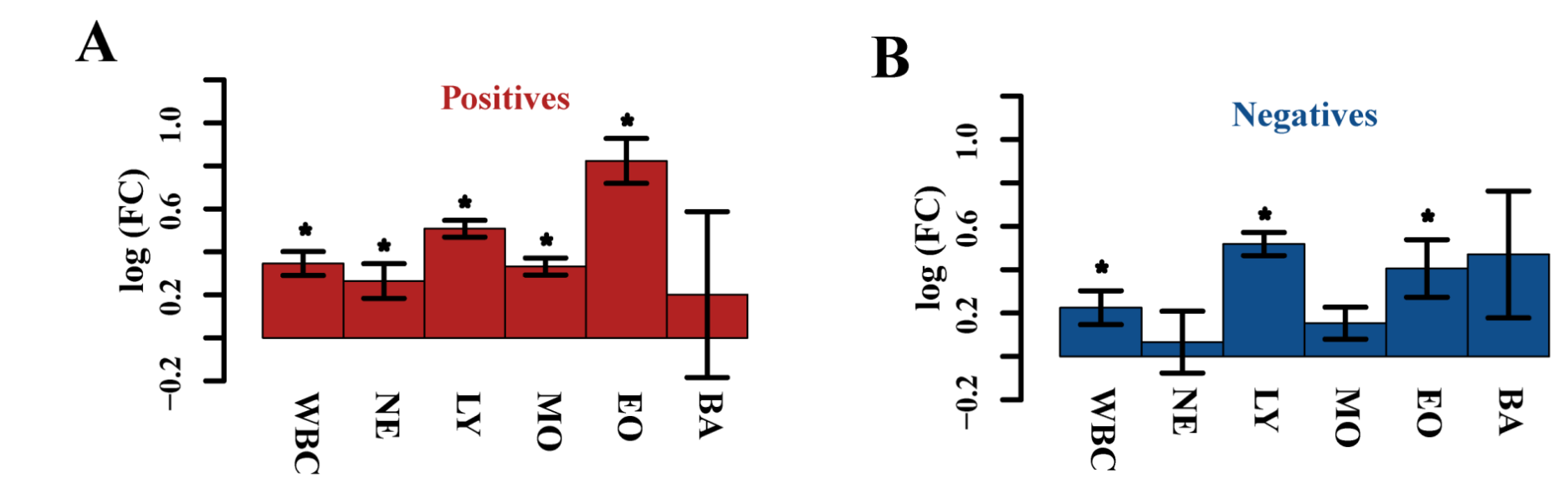


Table. 1 Symptom correlations between natural season and PCC

Symptom Score comparison	correlation R	P value
TOSS components		
Eye itch	0.71	<0.001
Tears	0.60	<0.001
Redness	0.79	<0.001
TNSS components		
Congestion	0.70	<0.001
Sneezing	0.68	<0.001
Runny Nose	0.70	<0.001
Nasal Itch	0.73	<0.001
TSS Components		
TOSS	0.76	<0.001
TNSS	0.74	<0.001
TSS	0.82	<0.001

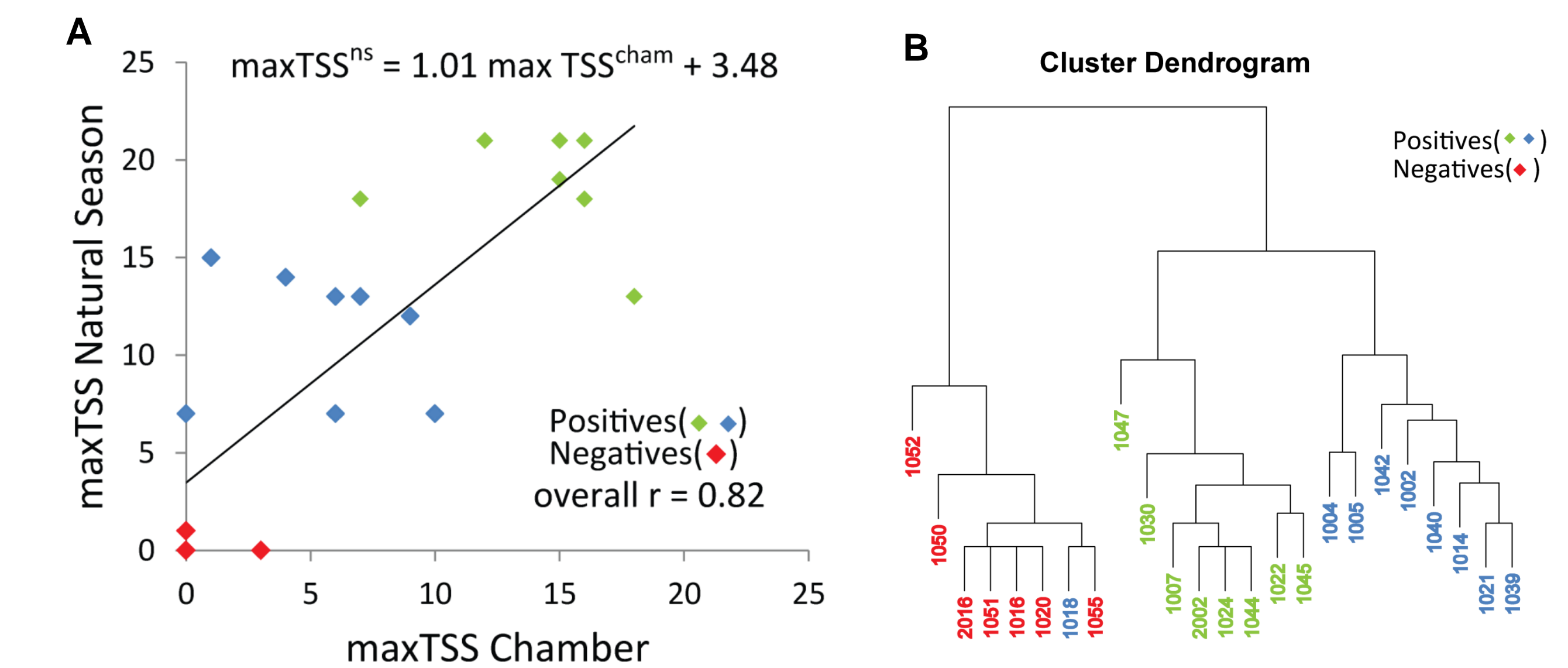
RESULTS(cont')

Fig. 6 Eosinophil counts increase in both positive and negative individuals following challenge with mountain cedar in PCC



Eosinophil counts increased significantly in both the positive (~1.8 folds increase) and the negative (~1.3 folds increase) individuals. * $P < 0.05$

Fig. 7 Correlation of TSS^{max} in natural season and PCC & cluster analysis.



(A) Correlation of TSS^{max} in the PCC and natural season. The positives could generally stratified into two groups: concordant with high TSS (green) and concordant with low TSS (blue). (B) Cluster analysis. Color corded shared between the 2 panels. The negative subjects are in one cluster with an exception of one positives.

CONCLUSIONS

- The hypothesis was confirmed that individuals will react similarly to mountain cedar pollen in a pollen challenge chamber as they do in the natural season.
- These results are in agreement with our recent study wherein we found high concordance of symptomology to Ragweed in both environments as well (JACI, 2012).
- We are investigating the mechanisms underpinning allergic rhinoconjunctivitis using the PCC model system.