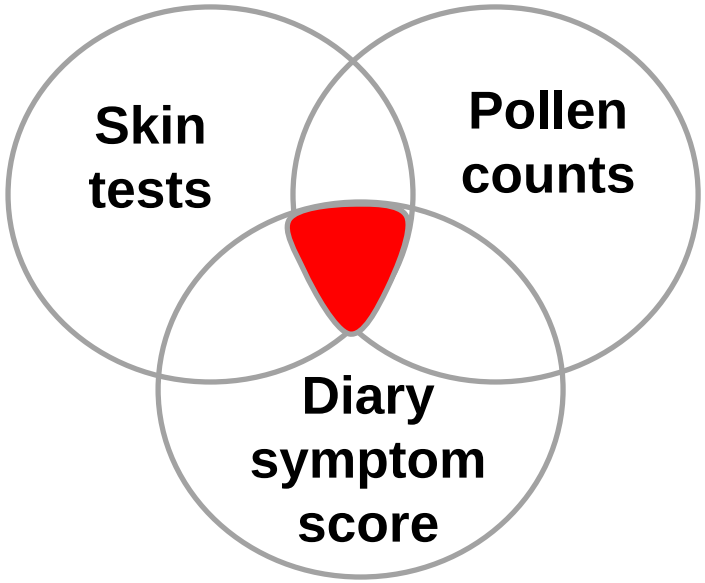
Alercon as a tool for allergists to improve the efficiency of immunotherapy in polysensitised pollinosis patients

Javier Subiza

AlerCon 2.0

AlerCon®: Conceptual Idea

Tools for assessing immunotherapy:



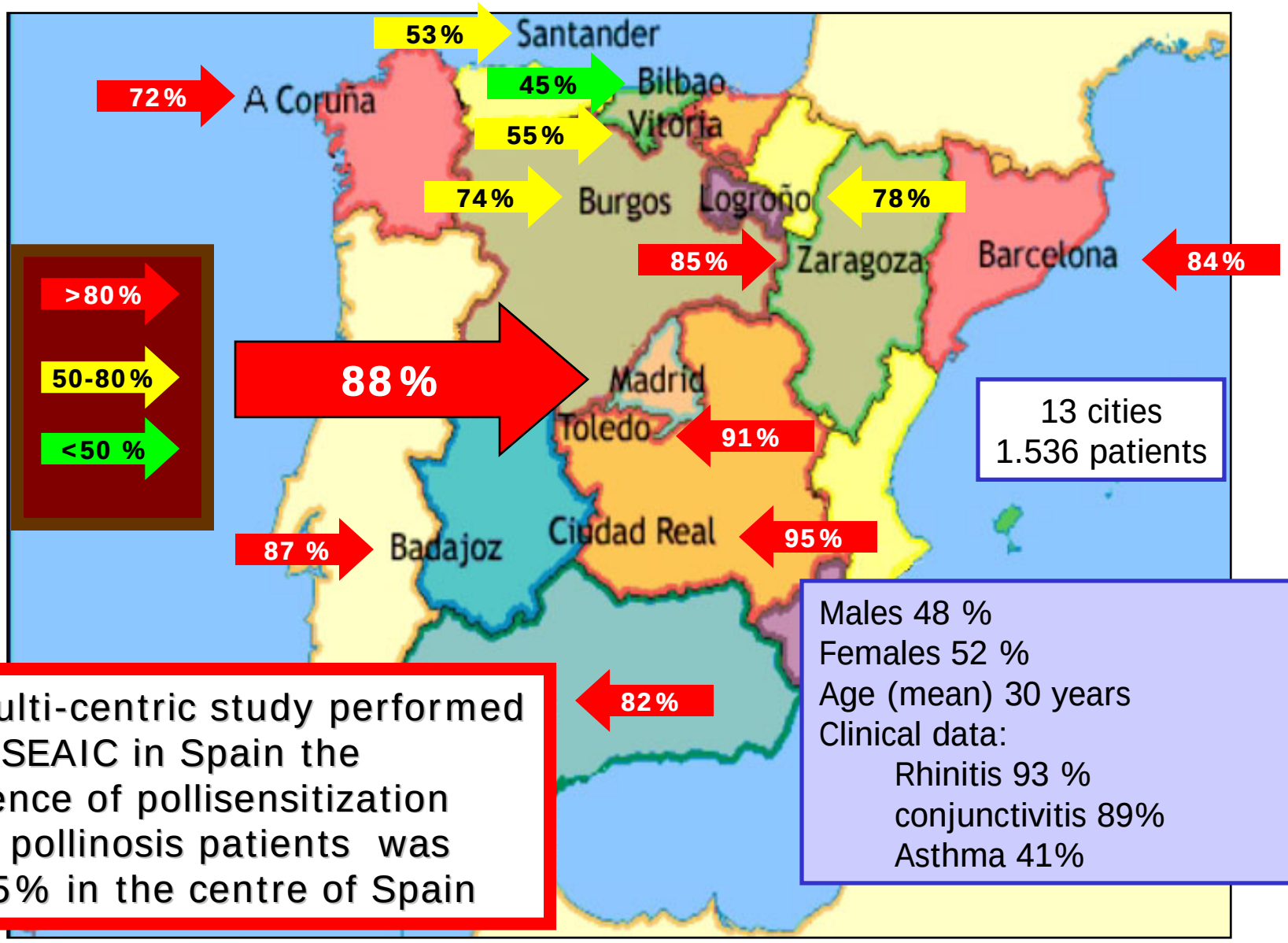
Alercon, a programme which automatically unifies

diary symptom score
pollen counts
and skin test

in order to try to improve the efficiency of immunotherapy in polysensitised pollinosis patients

Prevalence of pollen pollysensitization

within pollinosis patients in 13 Spanish cities



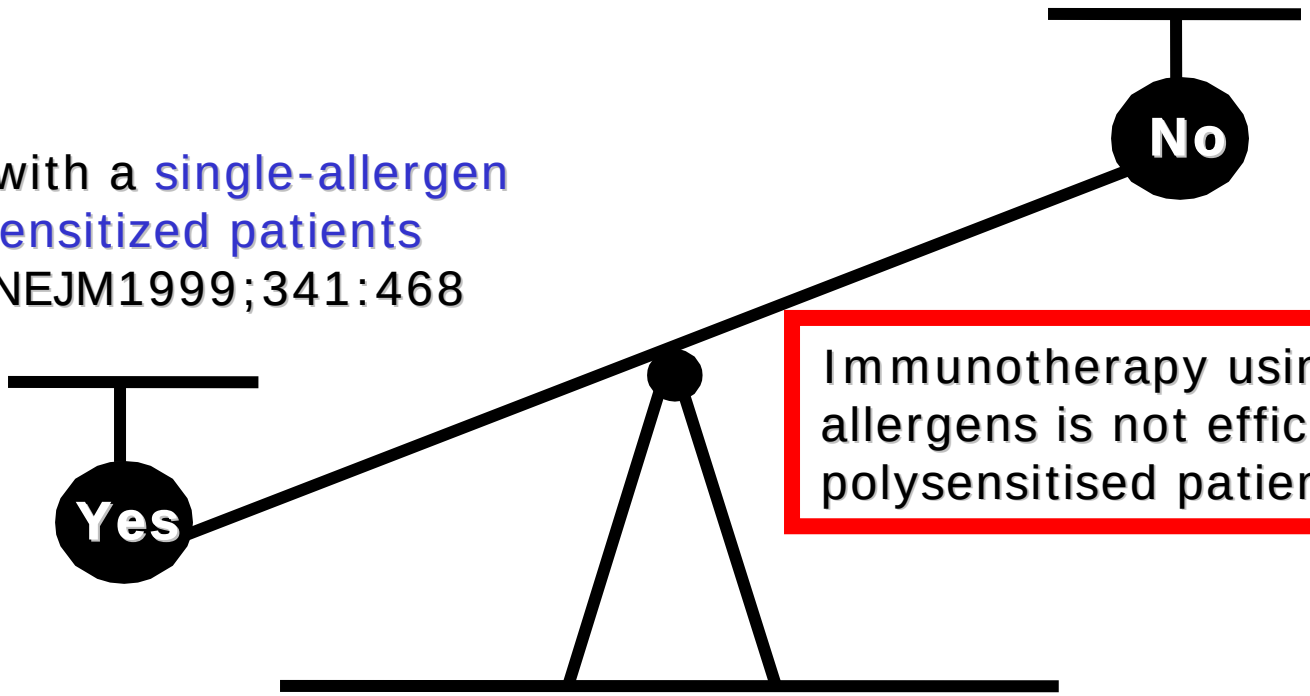
In a multi-centric study performed by the SEAIC in Spain the prevalence of pollisensitization among pollinosis patients was over 85% in the centre of Spain

Subiza J. Pola J, Feo F, Moral A, Bartra J. Pollinosis 2003. Aerobiological Committee of the SEAEIC

Problem

Extracts with multiple allergens in polysensitized patients
Adkinson NEJM1997;336:324

Extracts with a single-allergen in monosensitized patients
Durham NEJM1999;341:468

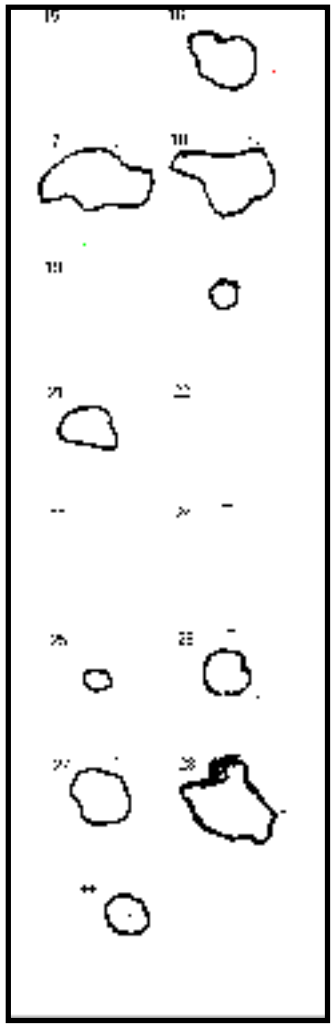


Immunotherapy using multiple allergens is not efficient in polysensitised patients

Immunotherapy efficacy

Example of skin prick tests on a pollinosis patient in Madrid

Immunotherapy? What can I do?



This is an Example of a typical pollinosis patient in Madrid: A 25 year old man with multiseasonal Rhino-conjunctivitis and showing a positive skin prick test to 5 different families of pollen

The question is ....What can I do?....because I can't prescribe 5 different vaccines; this is expensive, uncomfortable and most importantly, for some of them probably inefficient.

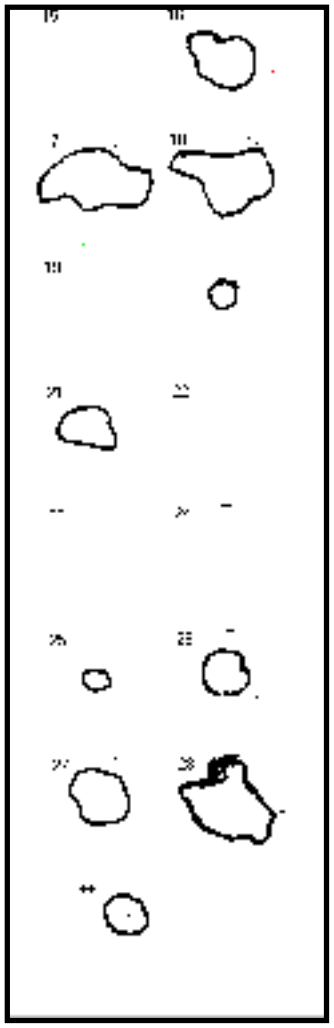
However the situation is not as bad as we might think, because normally only one or two of theses pollen types, contribute to the majority of the pollinosis symptoms. We name this pollen the "**DOMINANT POLLEN**", and we know this can vary between patients

For these reasons, when we observe a patient like this, firstly we try to detect the dominant pollen and secondly we try to perform a immunotherapy only with this pollen

Example of skin prick tests on a pollinosis patient in Madrid

Immunotherapy?

What can I do?



Approaches to find the DOMINANT POLLEN

1. Perform Nasal provocations with pollen extracts?
2. Detect sensitization to recombinant allergens?
3. Using pollen counts and symptoms diary cards

Approaches to find the DOMINANT POLLEN

Nasal Provocation

Subiza J, et al. Cluster immunotherapy... Clin Exp Allergy. 2008;38:987-94

Serial dilutions of the allergen extract (206, 617, 1852, 16067 and 50000 BU/mL)

Allergen (0.2 mL/nostril) was then nebulized at increasing concentrations into each nostril (every 15 minutes with a DeVilbis atomizer

In-Check Nasal inspiratory flow meter

a decrease in PNIF of 40 % from postsaline

at least 0.5 g of nasal secretions (evaluated by weighing tissue

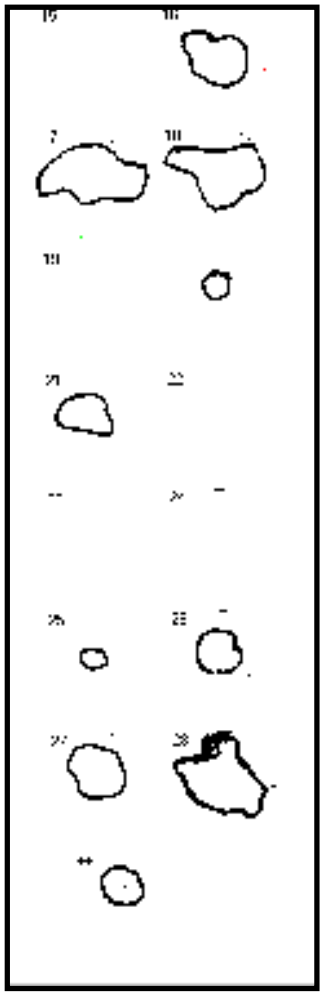
5 or more sneezes over a period of 10 minutes

Positive Nasal provocation based on the presence of at least 2 of the 3 criteria

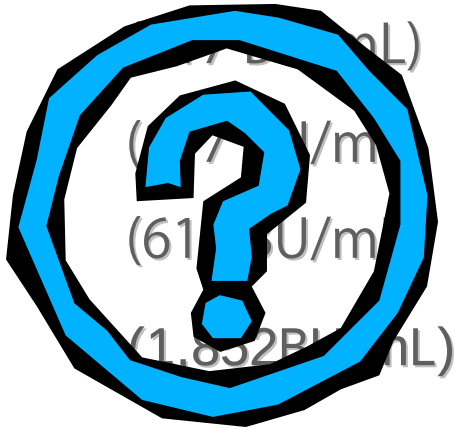
Approaches to find the DOMINANT POLLEN

Nasal Provocation

Subiza J, et al. Cluster immunotherapy... Clin Exp Allergy. 2008;38:987-94



	SPT	Nasal Provocation
Cupressus arizonica	3+	+
Platanus hispanica	4+	+
Phleum pratense	3+	+
Olea europaea	3+	+
Chenopodium a.	4+	+ (617 BU/mL)



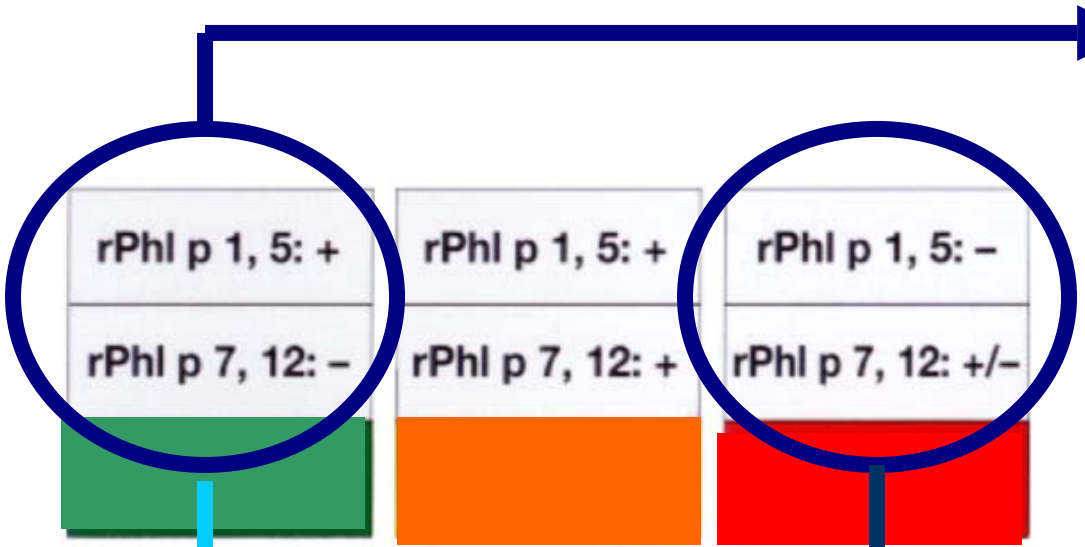
We cannot find a dominant pollen using nasal provocations

Approaches to find the DOMINANT POLLEN

Detect sensitization to recombinant allergen components

Phadia suggest, that if the polysensitised pollinosis patient shows a PSP to grass pollen, we can identify (using recombinant allergens) whether this grass sensitization is caused by

major (rPhl 1, 5) or minor (rPhl 7, 12) grass allergens



We can observe subclinical sensitization to rPhl p1, 5

We cannot find a dominant pollen using only recombinant allergens

Approaches to find the DOMINANT POLLEN

Using pollen counts and symptoms diary cards

A possible way to identify this dominant pollen is through the association of the results of:

1. **Period of symptoms**
2. **Period of pollination**
3. **Skin tests**

I would like to explain this last point, using these 3 clinical cases that we published in the Clin Exp Allergy many years ago. They are 3 patients which came to our Centre in 1992 because they suffered asthma symptoms during the spring time. As is typical in these patients, they couldn't specify the exact period of the year for the symptoms.

However, as all showed positive skin prick tests to grasses, and we know that grasses are the principal cause of seasonal asthma in our area, we prescribed them a grass immunotherapy

Additionaly, diary cards were kept daily by the patients from January 1993 until July 1993.

Subiza et al. Seasonal asthma caused by airborne *Platanus* pollen. Clin Exp Allergy 1994;24:1123-9.

2M y 1F 41-56-46 years old. Positive skin prick tests to *Dactylis*

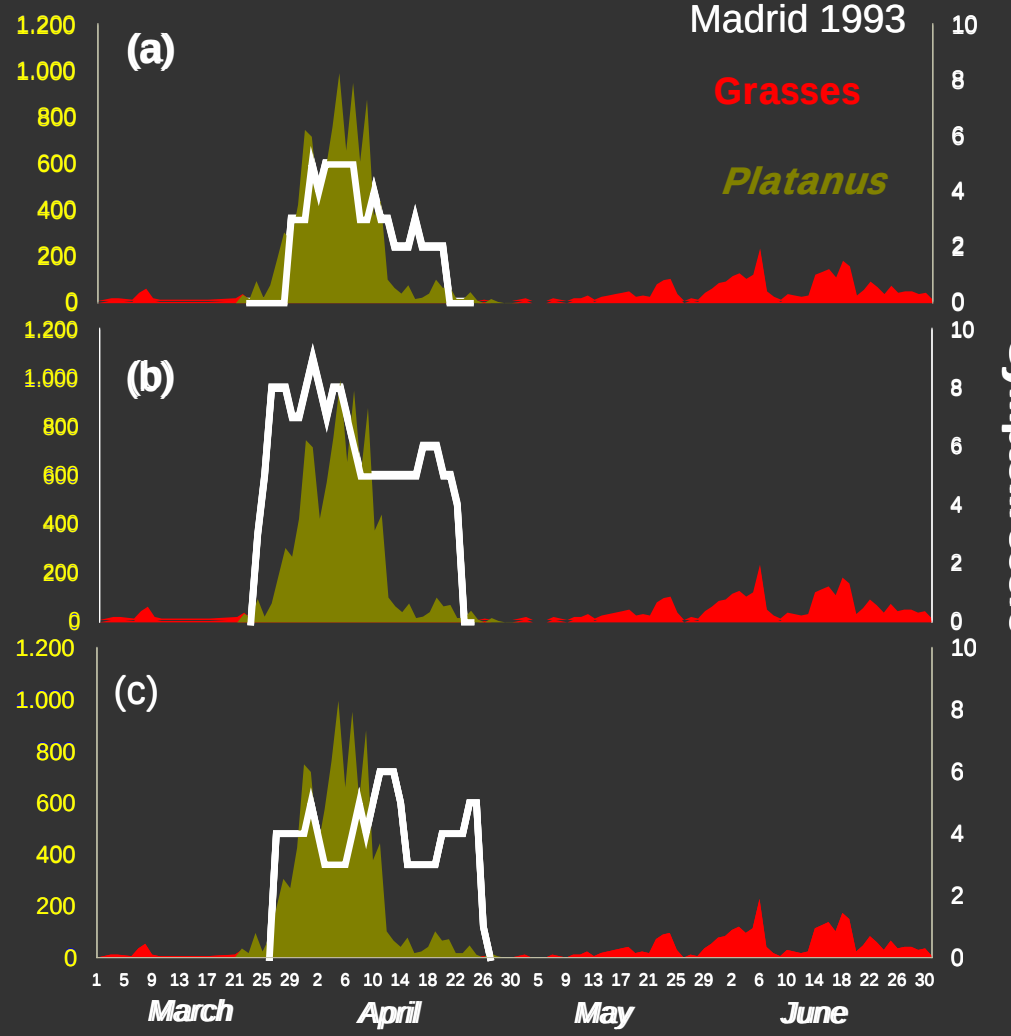
When, in July 1993, we could observe their diary cards, we could see with surprise that the asthmatic symptoms appeared in March and April instead of May–June, which is the period of the grass season in Madrid.

Furthermore we could observe that the asthma symptoms correlated very well with *Platanus* counts.

For this reason we made a *Platanus* pollen extract and we could obtain with it in the three patients a very strong response to the skin test and to the bronchial provocation.

Subiza et al. Seasonal asthma caused by airborne *Platanus* pollen. Clin Exp Allergy 1994;24:1123-9.

2M y 1F 41-56-46 years old. Positive skin prick tests to *Dactylis*



At that moment, these cases were very interesting to us because, until that moment, *Platanus* pollen was considered to have a very minor importance as a cause of pollinosis.

In following studies we could learn that at least in Madrid, and also in other cities in Spain, *Platanus* pollen is an important cause of pollinosis.

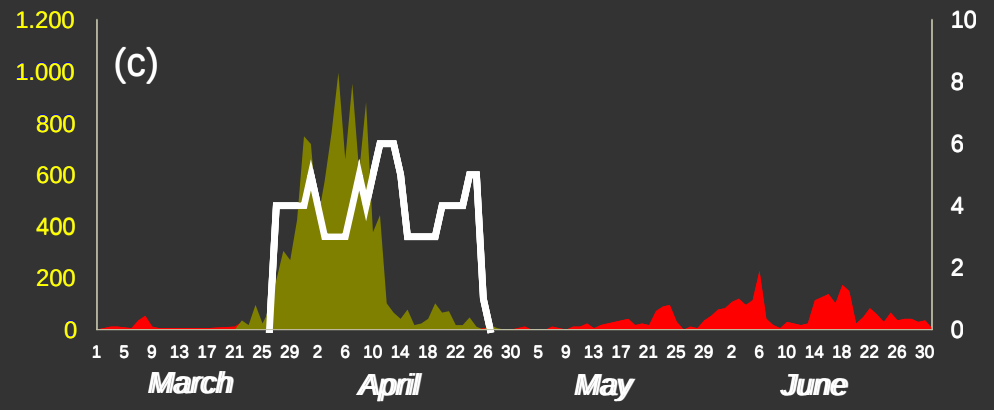
But more importantly we also learned that this **correlation between symptoms and pollen counts is useful to differentiate clinical from subclinical sensitization in polysensitised pollinosis patients.**

Subiza et al. Seasonal asthma caused by airborne *Platanus* pollen. Clin Exp Allergy 1994;24:1123-9.

Subiza et al. Allergenic pollen and pollinosis in Madrid. J. Allergy Clin. Immunol 1995;96:15-23

Varela et al. Platanus pollen an important unrecognized cause of pollinosis. J Allergy Clin Immunol 1997;100:748-754

Subiza et al. Pólenes alergénicos y polinosis en 12 ciudades españolas. Rev Esp Alergol Inmunol Clin 1998; 13: 45-58



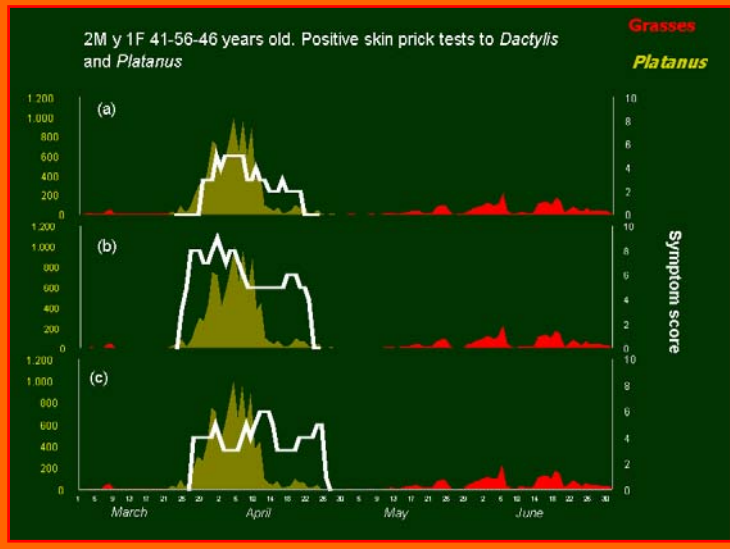
Question

can we use the "**dominant pollen**" to perform a successful **immunotherapy** in polysensitised pollinosis patients?

Perhaps we can answer this question by returning to the 3 patients with a clinical sensitisation to Platanus and sub-clinical sensitisation to grasses.

In one of them, we prescribed a immunotherapy with *Platanus* pollen.
This was the only prophylactic treatment that we used in the patient.

Of course we also used the paper diary card to follow his asthmatic symptoms.



In this graph we can see the *Platanus* pollen counts threshold to produce asthma symptoms in the patient before and after 5 years of immunotherapy.

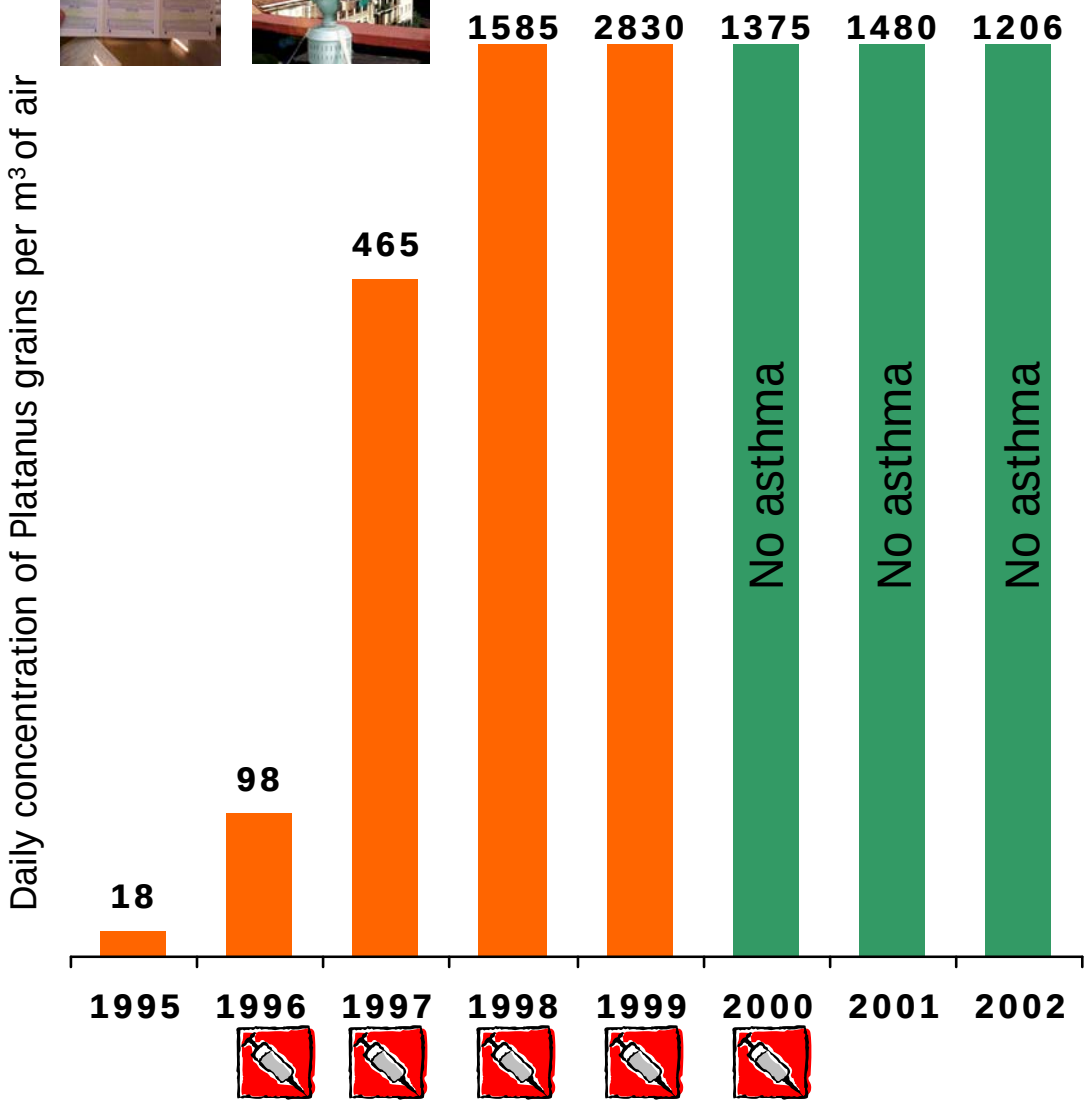
As you can see before the immunotherapy only 18 grains of *Platanus* counts were able to produce asthma symptoms.

On the contrary, in the following years this threshold kept increasing year by year to nearly 3000 Platanus counts after 4 years of immunotherapy

In 2001 we stopped the vaccination, and as you can see in 2000, 2001 and 2002 the patient did not show asthmatic symptoms in spite of the *Platanus* counts being over 1.000 grains/m^3 of air

Platanus pollen counts threshold to produce asthma symptoms before and after 5 years of immunotherapy

Subiza J. et al Update in allergy 2007



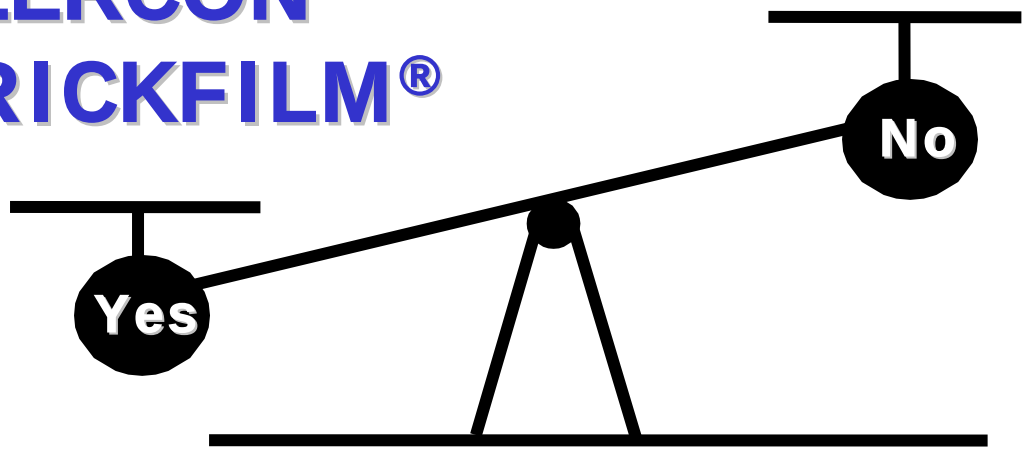
Question

IDENTIFICATION OF DOMINANT POLLEN IN CLINICAL ROUTINE?

Alercon and PrickFilm are 2 software programs that introduce the pollen counts, daily symptoms and skin prick test results automatically, into a data base

LACK OF PATIENT TIME
LACK OF MEDICAL TIME:
1) INTRODUCE DATA IN THE COMPUTER:
POLLEN COUNTS
DIARY SYMPTOMS
SKIN PRICK TESTS
2) PERFORM STATISTICAL STUDIES

ALERCON®
PRICKFILM®

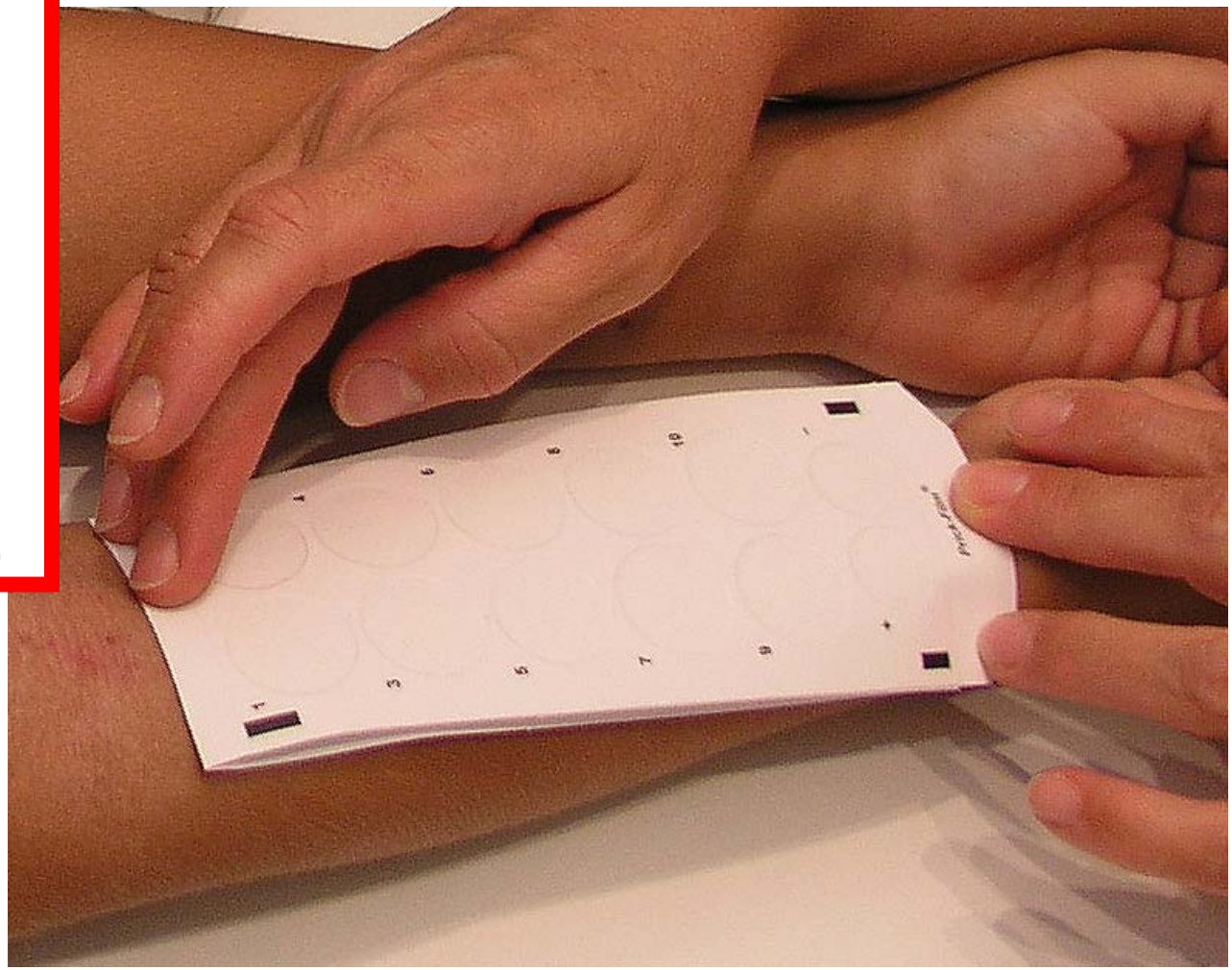


AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

This device basically consists of 2 different layers. A paper layer that we use to perform the prick and a plastic layer that we use to perform the reading.

AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

Firstly we stick the paper layer on the forearm thanks to a medical adhesive which is present in the corners.



AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

Secondly, we put the different drops of allergen extracts and controls, in the small holes

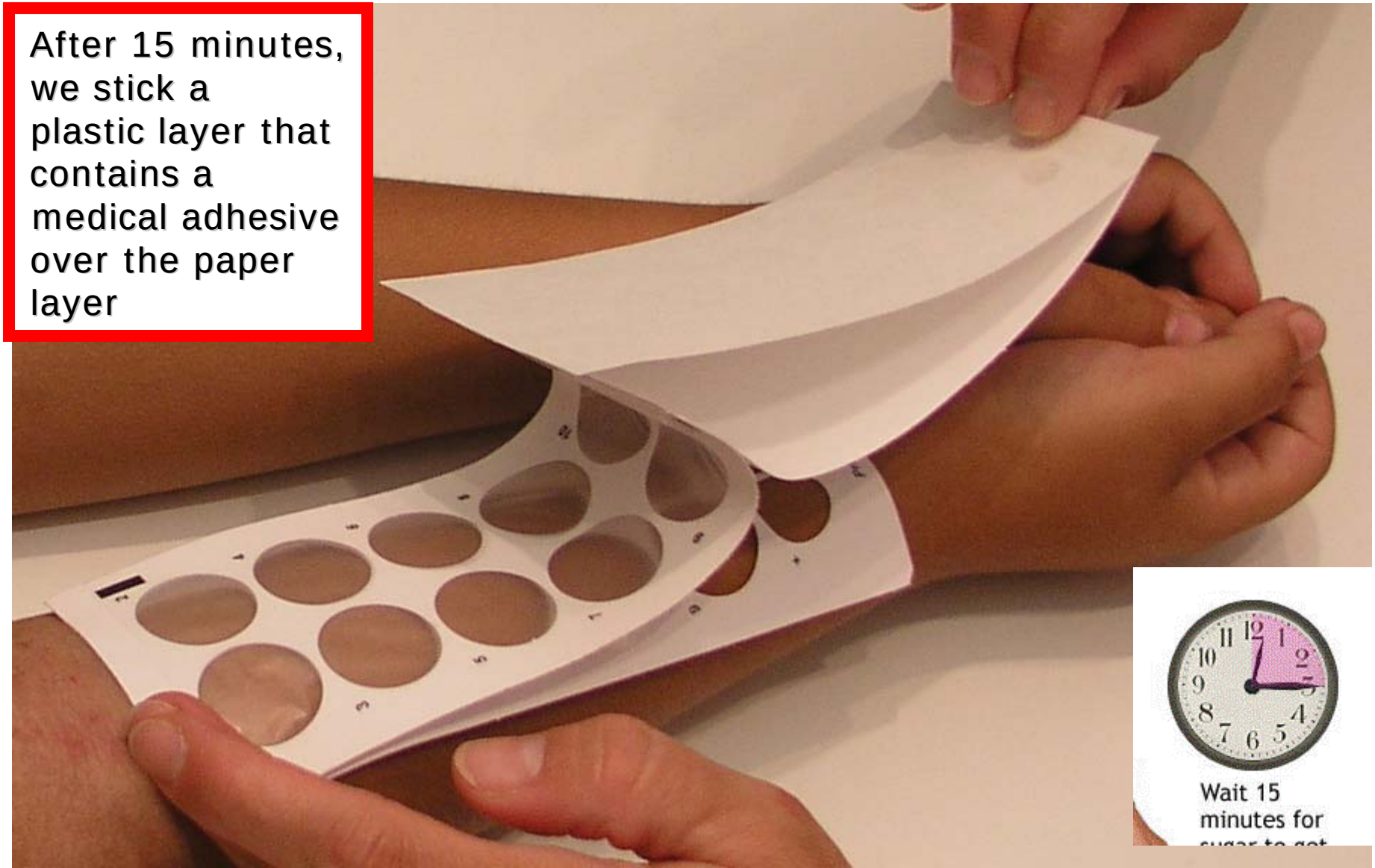

Thirdly we perform the prick using a lancet for each drops to avoid cross contamination

AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

Fourthly we remove the excess of extract with a drying paper

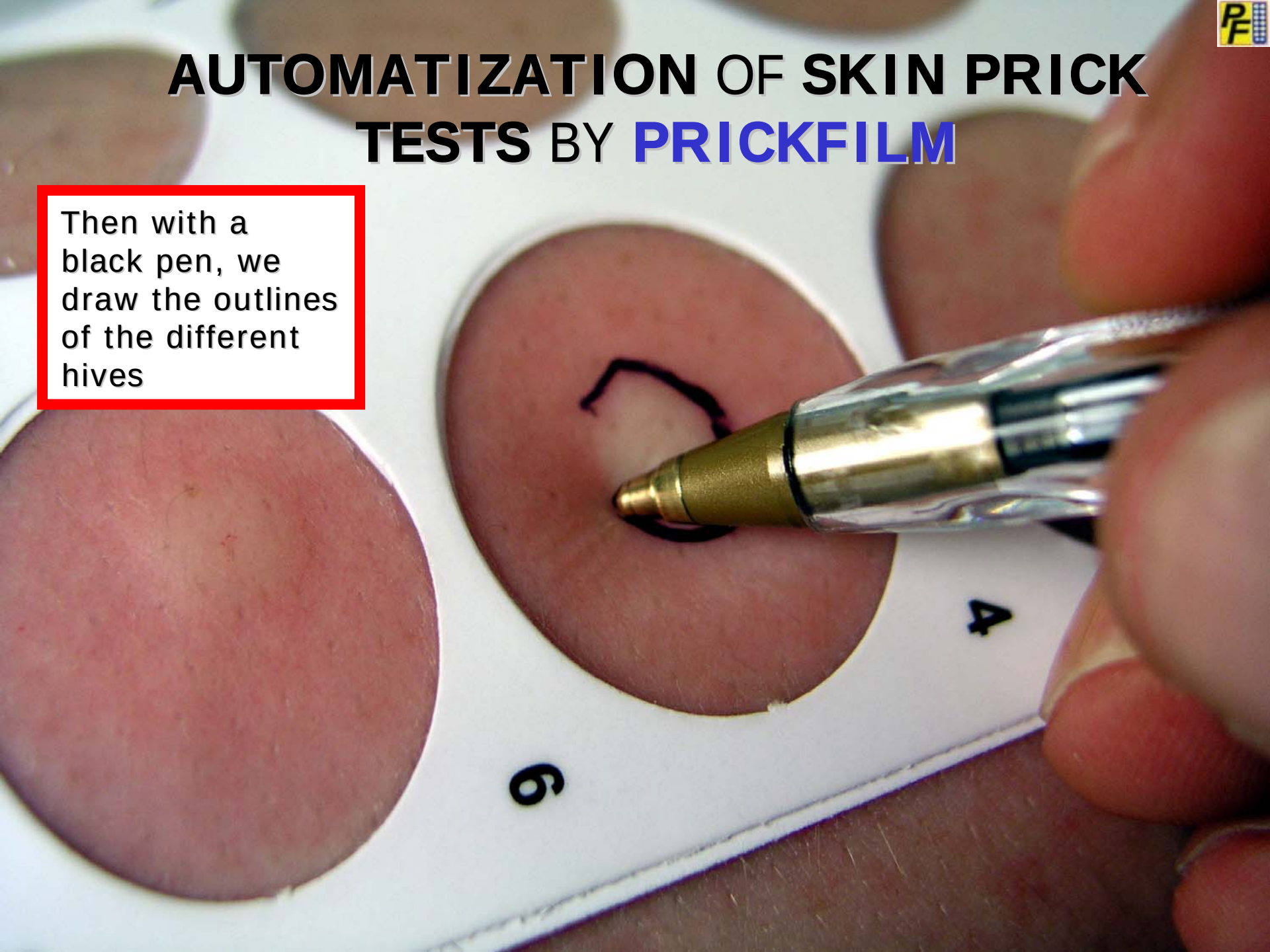
AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

After 15 minutes, we stick a plastic layer that contains a medical adhesive over the paper layer



AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

Then with a black pen, we draw the outlines of the different hives

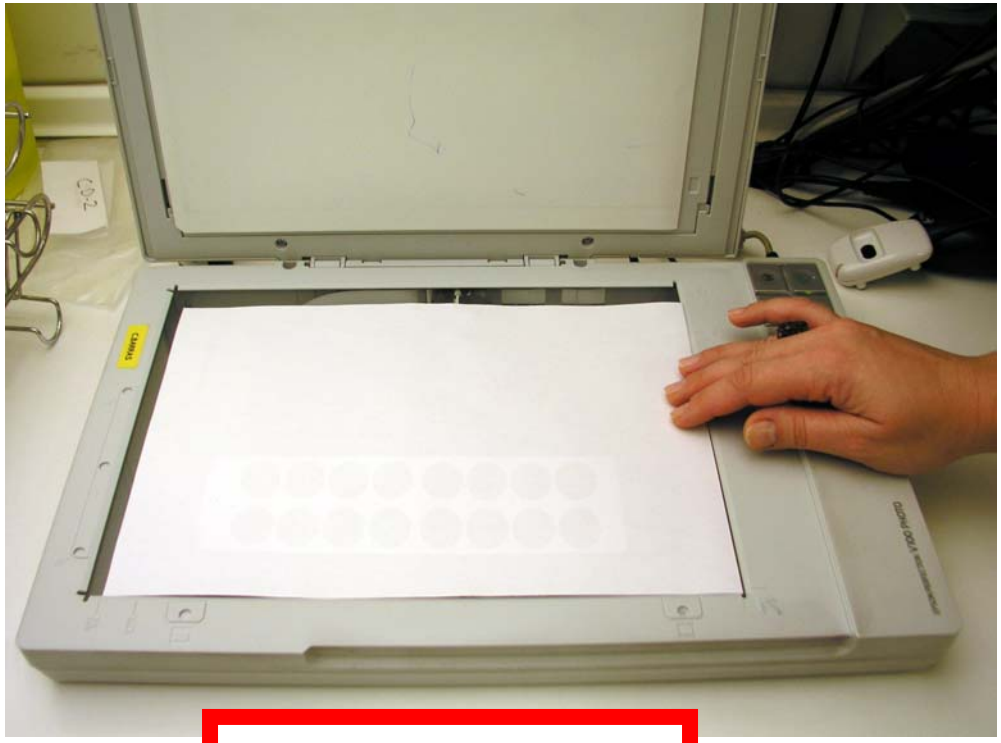


AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

We remove the plastic layer from the forearm

AUTOMATIZATION OF SKIN PRICK TESTS BY PRICKFILM

we stick the plastic layer on an page that contain a bar code indicating the type of battery

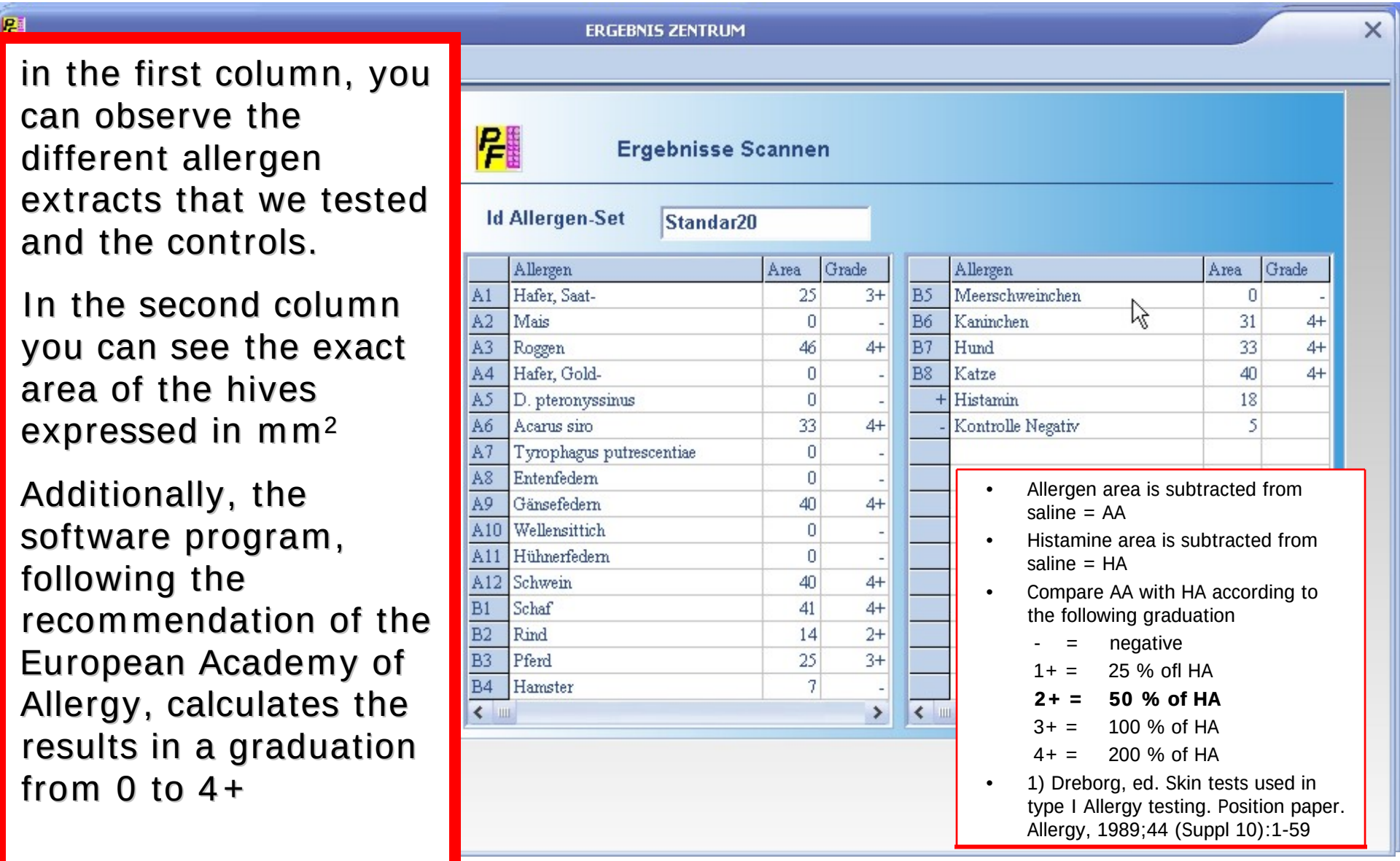


we scan the page and in this way we obtain reading results immediatelly

in the first column, you can observe the different allergen extracts that we tested and the controls.

In the second column you can see the exact area of the hives expressed in mm^2

Additionally, the software program, following the recommendation of the European Academy of Allergy, calculates the results in a graduation from 0 to 4+



	Allergen	Area	Grade
A1	Hafer, Saat-	25	3+
A2	Mais	0	-
A3	Roggen	46	4+
A4	Hafer, Gold-	0	-
A5	D. pteronyssinus	0	-
A6	Acarus siro	33	4+
A7	Tyrophagus putrescentiae	0	-
A8	Entenfedern	0	-
A9	Gänsefedern	40	4+
A10	Wellensittich	0	-
A11	Hühnerfedern	0	-
A12	Schwein	40	4+
B1	Schaf	41	4+
B2	Rind	14	2+
B3	Pferd	25	3+
B4	Hamster	7	-

	Allergen	Area	Grade
B5	Meerschweinchen	0	-
B6	Kaninchen	31	4+
B7	Hund	33	4+
B8	Katze	40	4+
+	Histamin	18	
-	Kontrolle Negativ	5	

- Allergen area is subtracted from saline = AA
- Histamine area is subtracted from saline = HA
- Compare AA with HA according to the following graduation
  - \- = negative
  - 1+ = 25 % ofl HA
  - **2+ = 50 % of HA**
  - 3+ = 100 % of HA
  - 4+ = 200 % of HA
- 1) Dreborg, ed. Skin tests used in type I Allergy testing. Position paper. Allergy, 1989;44 (Suppl 10):1-59

Hauttest

Bericht Nr: 1674568 Testnummer: 6
Patienten: **Weiss, Alfred**, 62 , Geschlecht: M

Klinik für Allergologie Dr. Klein
Pfostenbergweg, 12
76543 Riederich
Telefon: 76547898
Fax: 87560876
Email: drklein@drklein.de

Datum: 05/09/2006 8:10:04

Angefordet von: Dr. med. Marcus Klein

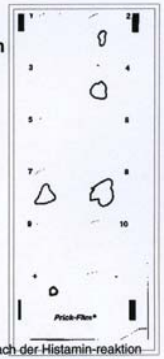
Test-Methode: Prick-Test
Lanzetten-Typ: 1 mm DHS

Dermographismus: -

Motiv: Asthma

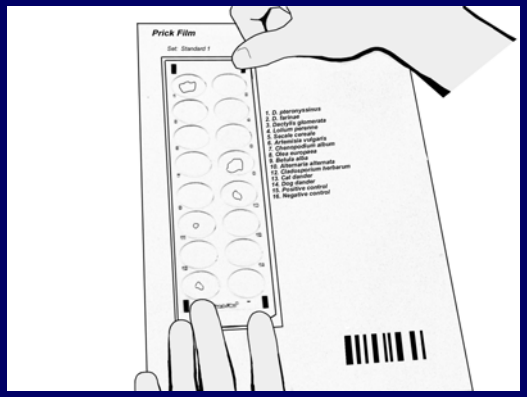
Satz: Standard-1K

	Allergene	Fläche	0-4+	Konzentration
A1	Alternaria alternata	0 (0/0)	-	30 HEP
A2	Ulme	23 (4/7)	3+	1/20 W/V
A3	Birke	0 (0/0)	-	50 HEP
A4	D. farinae	53 (8/8)	4+	50 HEP
A5	D. pteronyssinus	0 (0/0)	-	50 HEP
A6	Gänsefuss	0 (0/0)	-	50 HEP
A7	Beifuss	60 (10/9)	4+	50 HEP
A8	Roggen	105 (11/13)	4+	50 HEP
A9	Gerste	0 (0/0)	-	50 HEP
A10	Wiesenlieschgras	0 (0/0)	-	50 HEP
+	Histamine	15 (4/4)		10 mg/mL
-	Saline	0 (0/0)		



A 1:2

Umfangsbereich der Quaddel in Quadratmillimeter
Grad ausgedrückt nach der spezifischen Fläche (Allergene minus Salinisch) kalkuliert nach der Histamin-reaktion
-(<25%), 1+(25 - 50%), 2+(50 - 100%), 3+(100 - 200%), 4+(>200%)
Man beurteilt als positiv die Werte > 1+
Auslegung

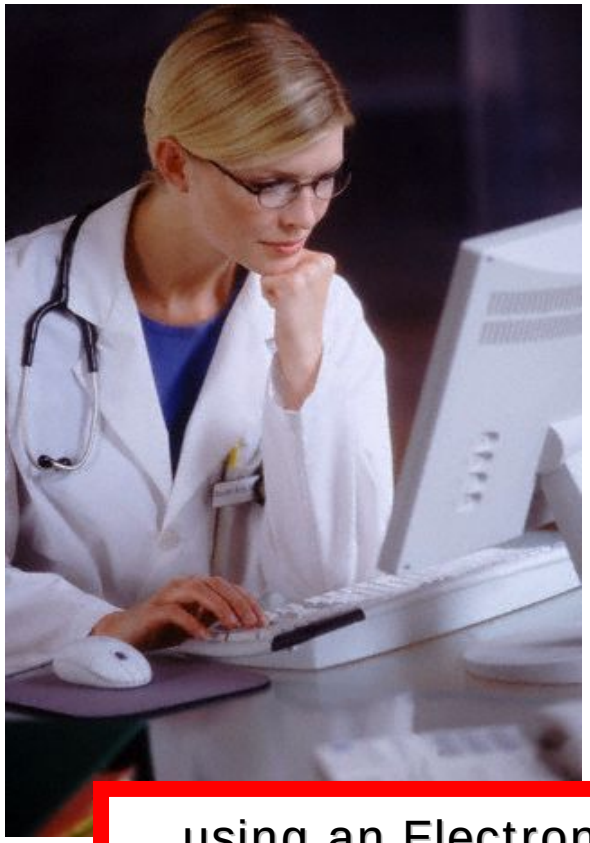


The program is able to generate a report of the skin prick test.

But the most important thing, is the fact that all the skin prick test results are now stored in a data base that we can use with the Alercon program to perform the correlations with the symptoms.

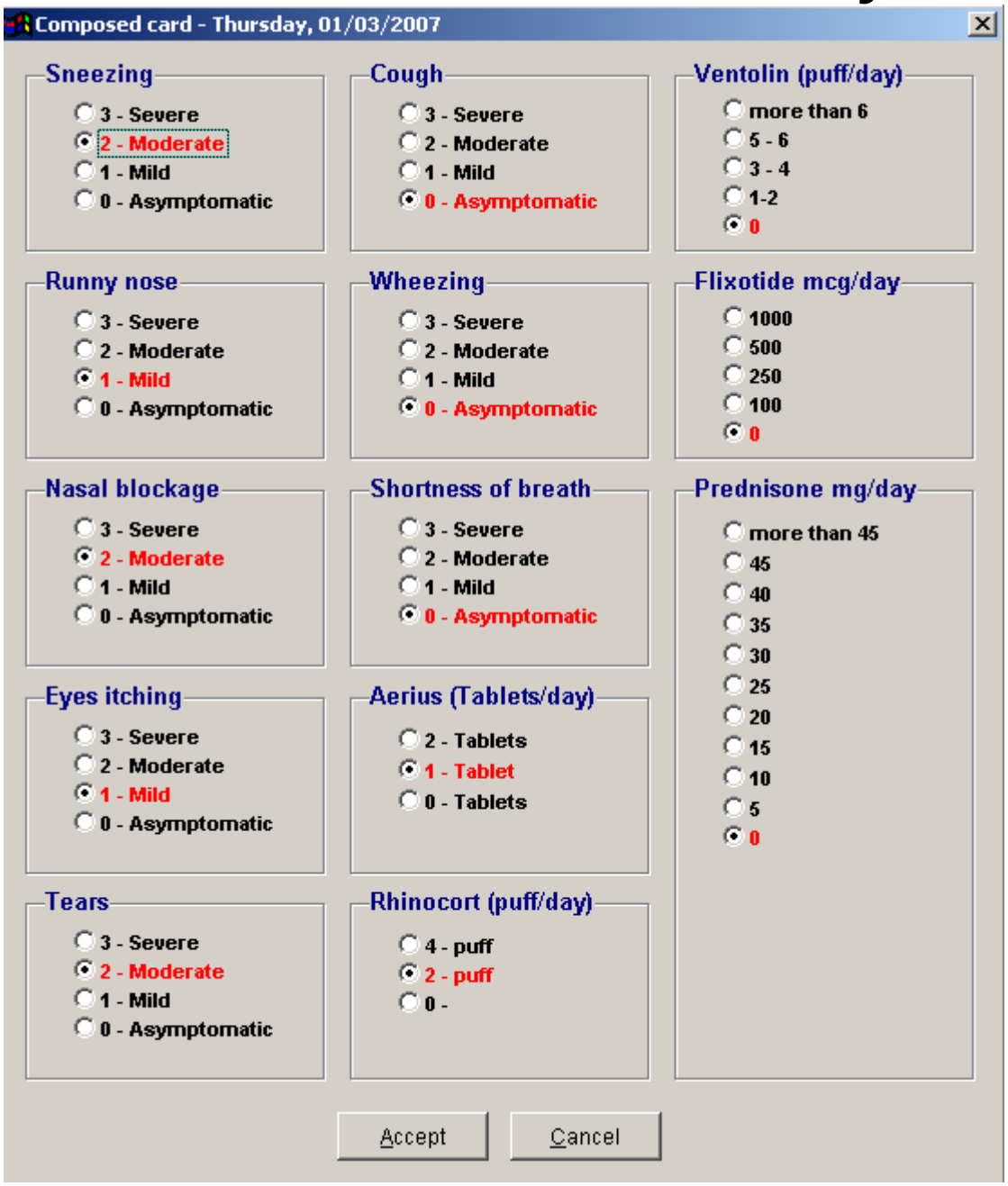
HOW CAN WE **AUTOMATIZE** THE **DIARY SYMPTOM SCORE**?

Alercon Electronic Diary Card



...using an Electronic Diary Card. This is in reality a simple program that we generate from the Alercon and is automatically sent to the patient by email. When the patient receives this email in their PC, the program is automatically installed in their computer.....

Alercon Electronic Diary Card



..from this moment, whenever the patient starts the computer, a calendar appears, with a notice indicating that the patient needs to fill in the electronic diary card...

SQL Server

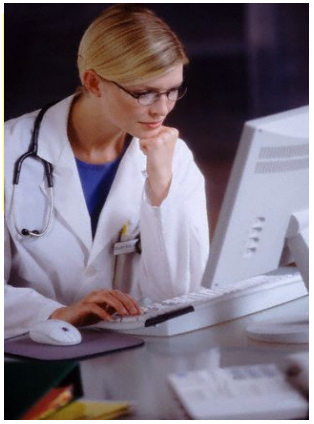
MySQL

Data update

Data Sent

Patient's PC

Doctor's PC



Alercon

Pollen counts

Electronic Diary Card

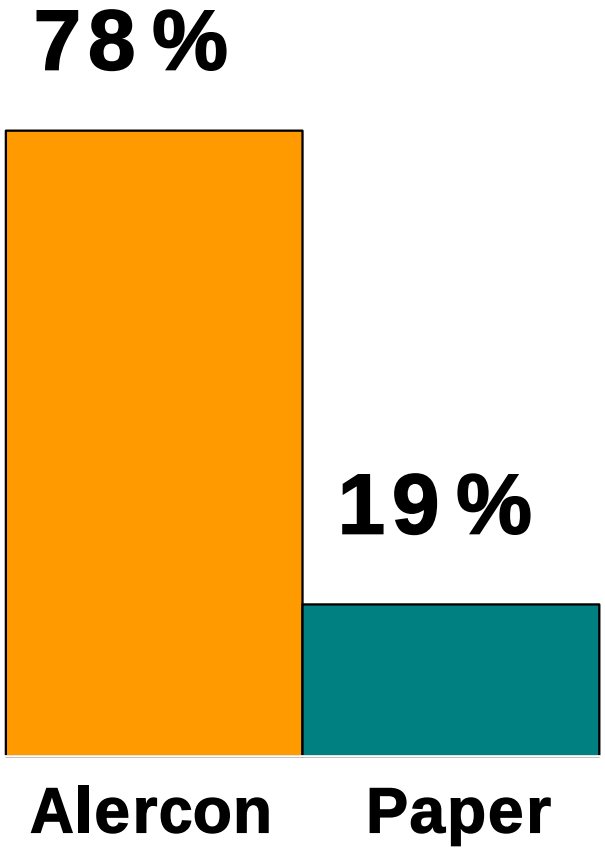
Patient's daily symptoms

PrickFilm

Patient's skin tests

..when the patient closes the electronic diary card program, all data on the electronic diary card are automatically sent to a central server. Additionally, when the doctor starts the Alercon in his PC, he automatically obtains both the patient's data and pollen counts, along with the skin prick test results from the prickfilm.

Patient compliance
Alercon Diary Card *versus* Paper Diary Card



n=146 n=40
From January to December 2007

Patient compliance has been a traditional problem using the paper diary card.

On the contrary when using the Electronic diary Card we could see that the percentage of compliance is as high as 75%. In spite of the fact that patients must fill in the diary card for many months.

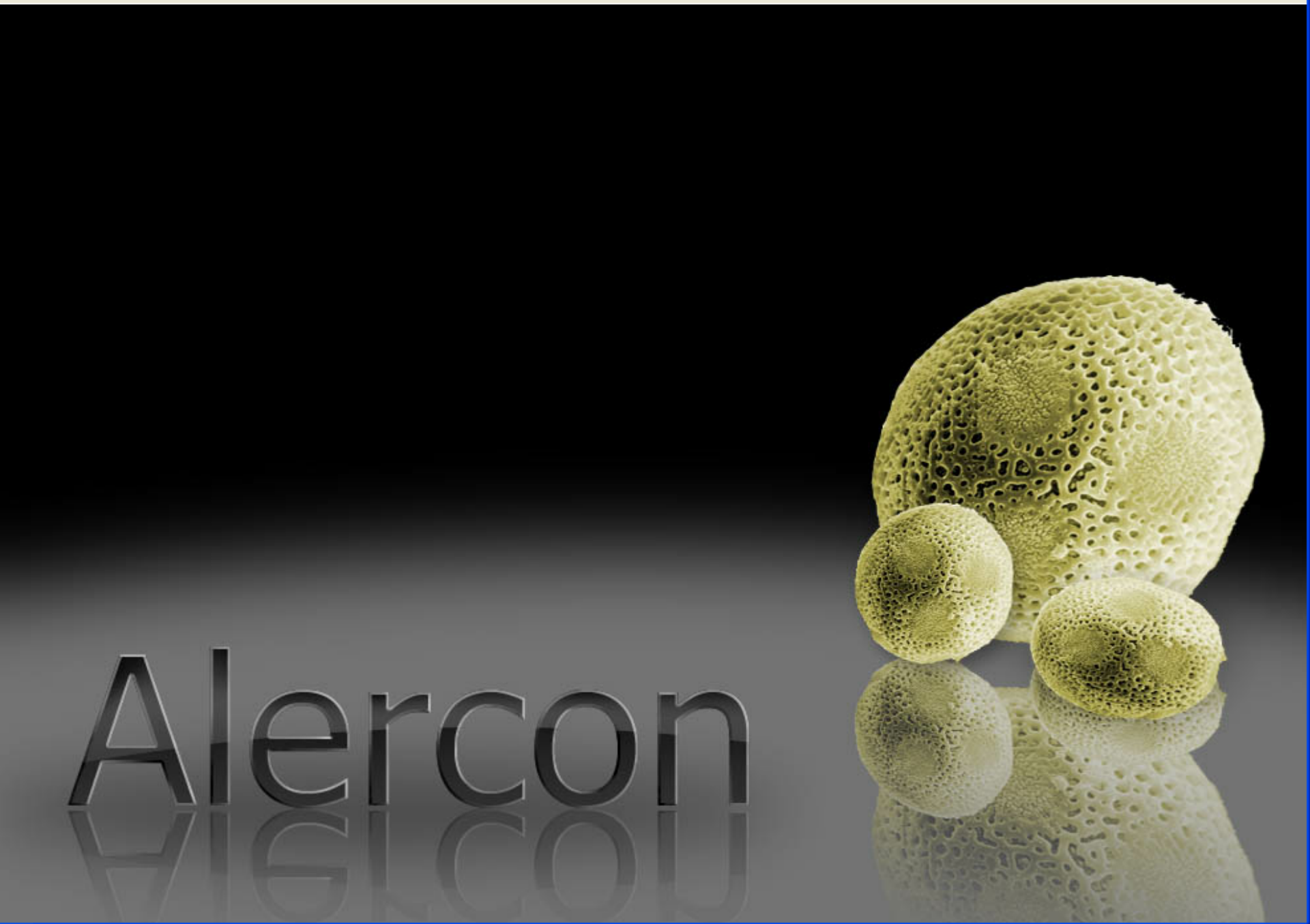
CLINICAL CASE USING ALERCON

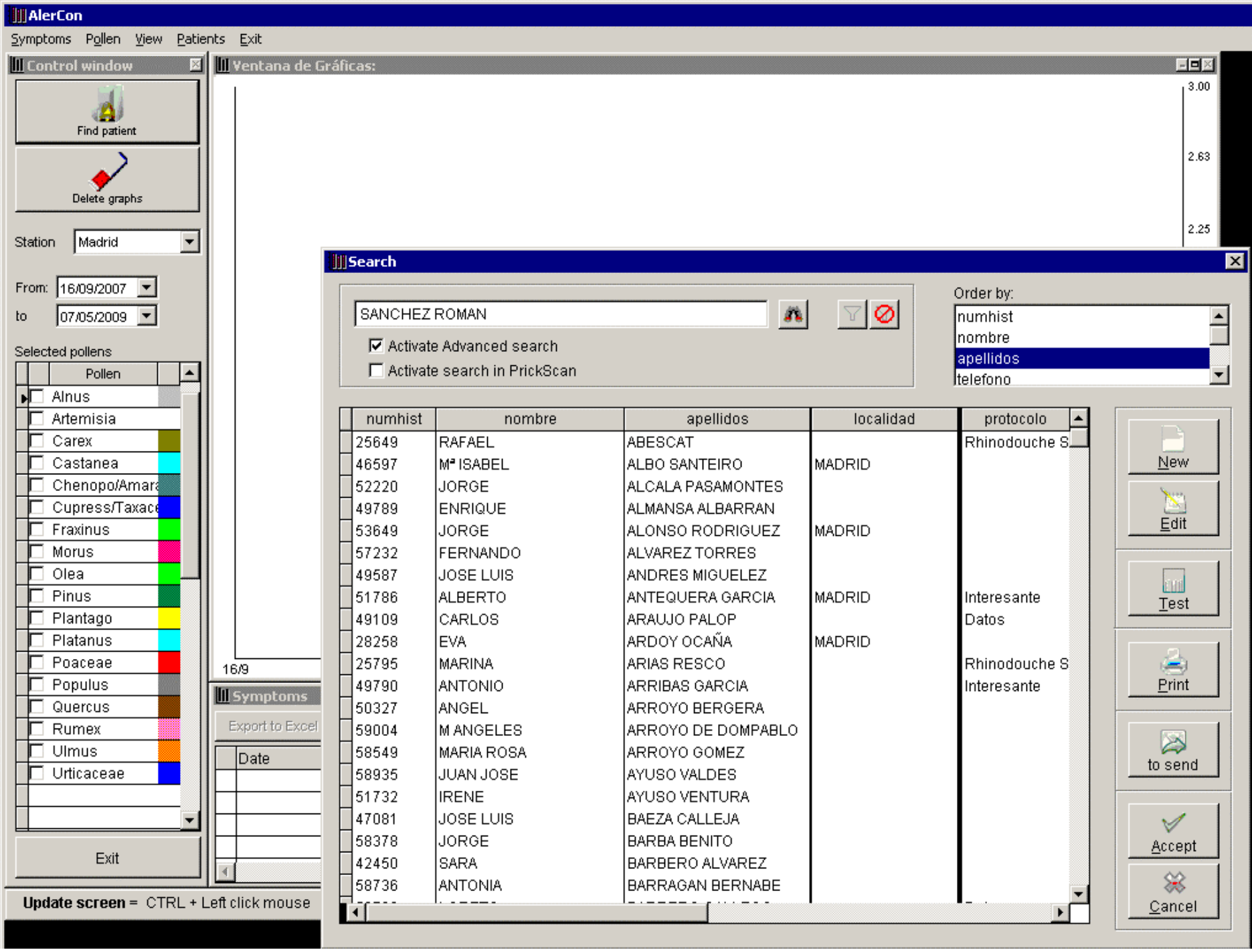
Patient 1 — A 22 year old man
RC Symptoms: multi-seasonal

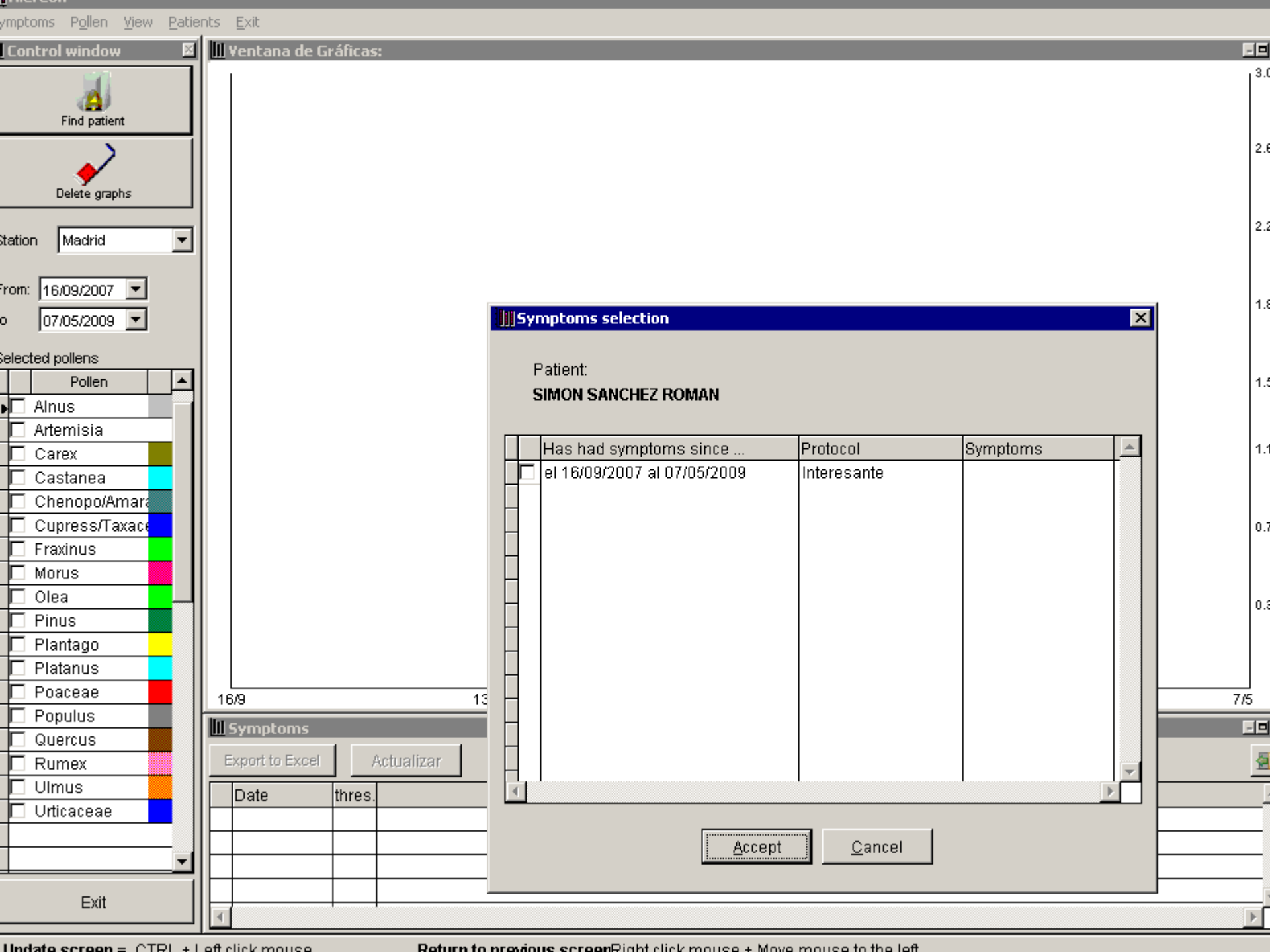
	SPT	CAP (kU/L)	Nasal Provocation
Cupressus arizonica	4+	1.34	Positive (1.852 BU/mL)
nCup a 1		9.13	
Phleum pratense	3+	0.53	Positive (16.677BU/mL)
rPhl p 1		0.81	
Olea europaea	3+	1.92	Positive(206 BU/mL)
nOle e 1		0.86	
Chenopodium album	2+	nd	non done

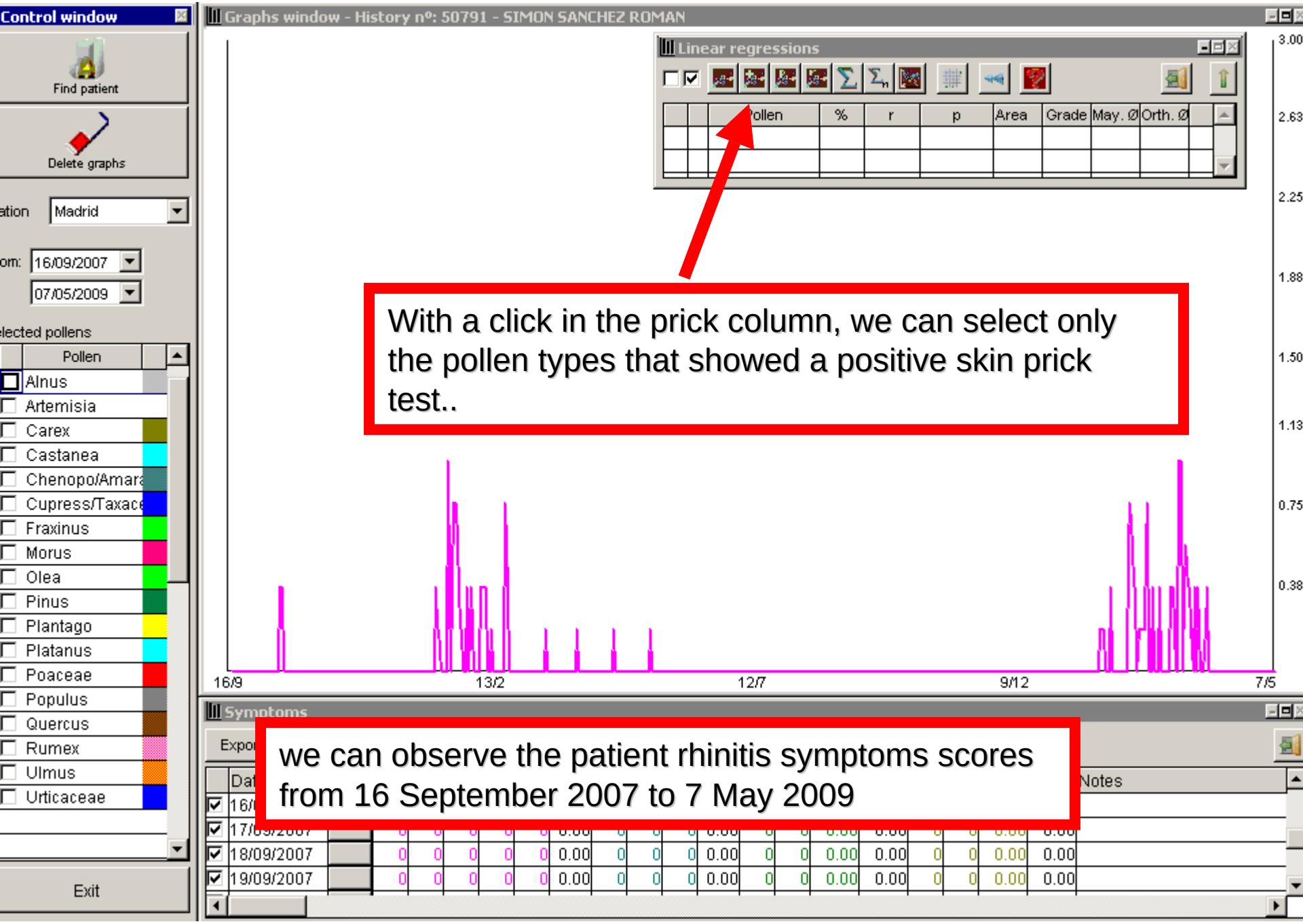
AlerCon 2.0 - Despacho3

Graphs Reports Utils Help Exit

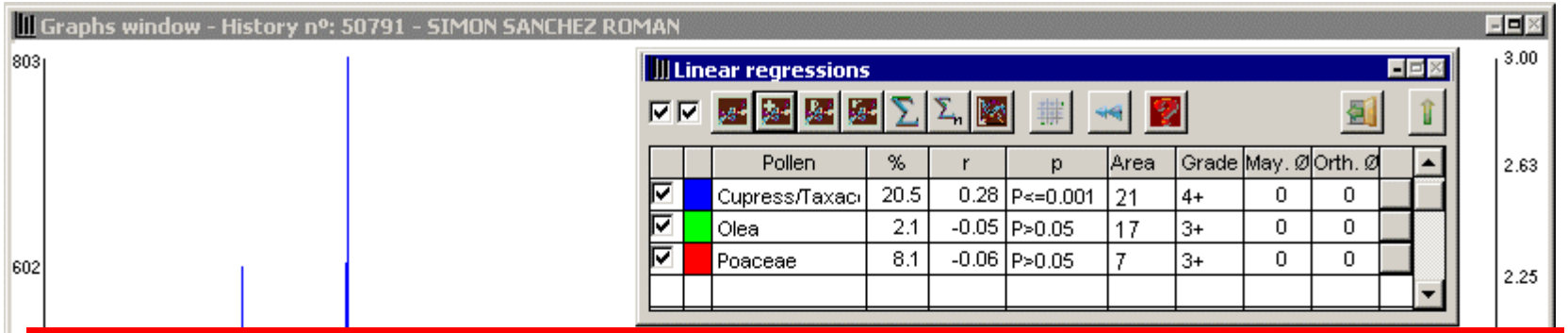



AlerCon
Symptoms Pollen View Patients Exit
Control window
Find patient
Delete graphs
Station Madrid
From: 16/09/2007
to 07/05/2009
Selected pollens
Pollen
Alnus
Artemisia
Carex
Castanea
Chenopo/Amara
Cupress/Taxace
Fraxinus
Morus
Olea
Pinus
Plantago
Platanus
Poaceae
Populus
Quercus
Rumex
Ulmus
Urticaceae
Exit
Update screen = CTRL + Left click mouse
Ventana de Gráficas:
3.00
2.63
2.25
16/9
Symptoms
Export to Excel
Date
Search
SANCHEZ ROMAN
Activate Advanced search
Activate search in PrickScan
Order by:
numhist
nombre
apellidos
telefono
numhist nombre apellidos localidad protocolo
25649 RAFAEL ABESCAT Rhinodouche S
46597 Mª ISABEL ALBO SANTEIRO MADRID
52220 JORGE ALCALA PASAMONTES
49789 ENRIQUE ALMANSA ALBARRAN
53649 JORGE ALONSO RODRIGUEZ MADRID
57232 FERNANDO ALVAREZ TORRES
49587 JOSE LUIS ANDRES MIGUELEZ
51786 ALBERTO ANTEQUERA GARCIA MADRID Interesante
49109 CARLOS ARAUJO PALOP Datos
28258 EVA ARDOY OCAÑA MADRID
25795 MARINA ARIAS RESCO Rhinodouche S
49790 ANTONIO ARRIBAS GARCIA Interesante
50327 ANGEL ARROYO BERGERA
59004 M ANGELES ARROYO DE DOMPABLO
58549 MARIA ROSA ARROYO GOMEZ
58935 JUAN JOSE AYUSO VALDES
51732 IRENE AYUSO VENTURA
47081 JOSE LUIS BAEZA CALLEJA
58378 JORGE BARBA BENITO
42450 SARA BARBERO ALVAREZ
58736 ANTONIA BARRAGAN BERNABE
New
Edit
Test
Print
to send
Accept
Cancel


ymptoms Pollen View Patients Exit
Control window
Find patient
Delete graphs
Station Madrid
From: 16/09/2007
o 07/05/2009
Selected pollens
Pollen
Alnus
Artemisia
Carex
Castanea
Chenopo/Amara
Cupress/Taxace
Fraxinus
Morus
Olea
Pinus
Plantago
Platanus
Poaceae
Populus
Quercus
Rumex
Ulmus
Urticaceae
Exit
Ventana de Gráficas:
16/9
7/5
Symptoms selection
Patient:
SIMON SANCHEZ ROMAN
Has had symptoms since ...
Protocol
Symptoms
el 16/09/2007 al 07/05/2009
Interesante
Accept
Cancel
Symptoms
Export to Excel
Actualizar
Date
thres.
Update screen = CTRL + Left click mouse
Return to previous screenRight click mouse + Move mouse to the left


Control window
Find patient
Delete graphs
Madrid
16/09/2007
07/05/2009
Pollen
Alnus
Artemisia
Carex
Castanea
Chenopo/Amara
Cupress/Taxace
Fraxinus
Morus
Olea
Pinus
Plantago
Platanus
Poaceae
Populus
Quercus
Rumex
Ulmus
Urticaceae
Exit
Graphs window - History nº: 50791 - SIMON SANCHEZ ROMAN
Linear regressions
Pollen
%
r
p
Area
Grade
May. Ø
Orth. Ø
3.00
2.63
2.25
1.88
1.50
1.13
0.75
0.38
16/9
13/2
12/7
9/12
7/5
With a click in the prick column, we can select only the pollen types that showed a positive skin prick test..
Symptoms
Notes
18/09/2007
19/09/2007
we can observe the patient rhinitis symptoms scores from 16 September 2007 to 7 May 2009

Clinical case using Alercon (1)



Pollen	%	r	p	Area	Grade	May. Ø	Orth. Ø
Cupress/Taxac	20.5	0.28	P<=0.001	21	4+	0	0
Olea	2.1	-0.05	P>0.05	17	3+	0	0
Poaceae	8.1	-0.06	P>0.05	7	3+	0	0

..there were only 3 different types of pollen, *Cupressus Olea*, and grasses

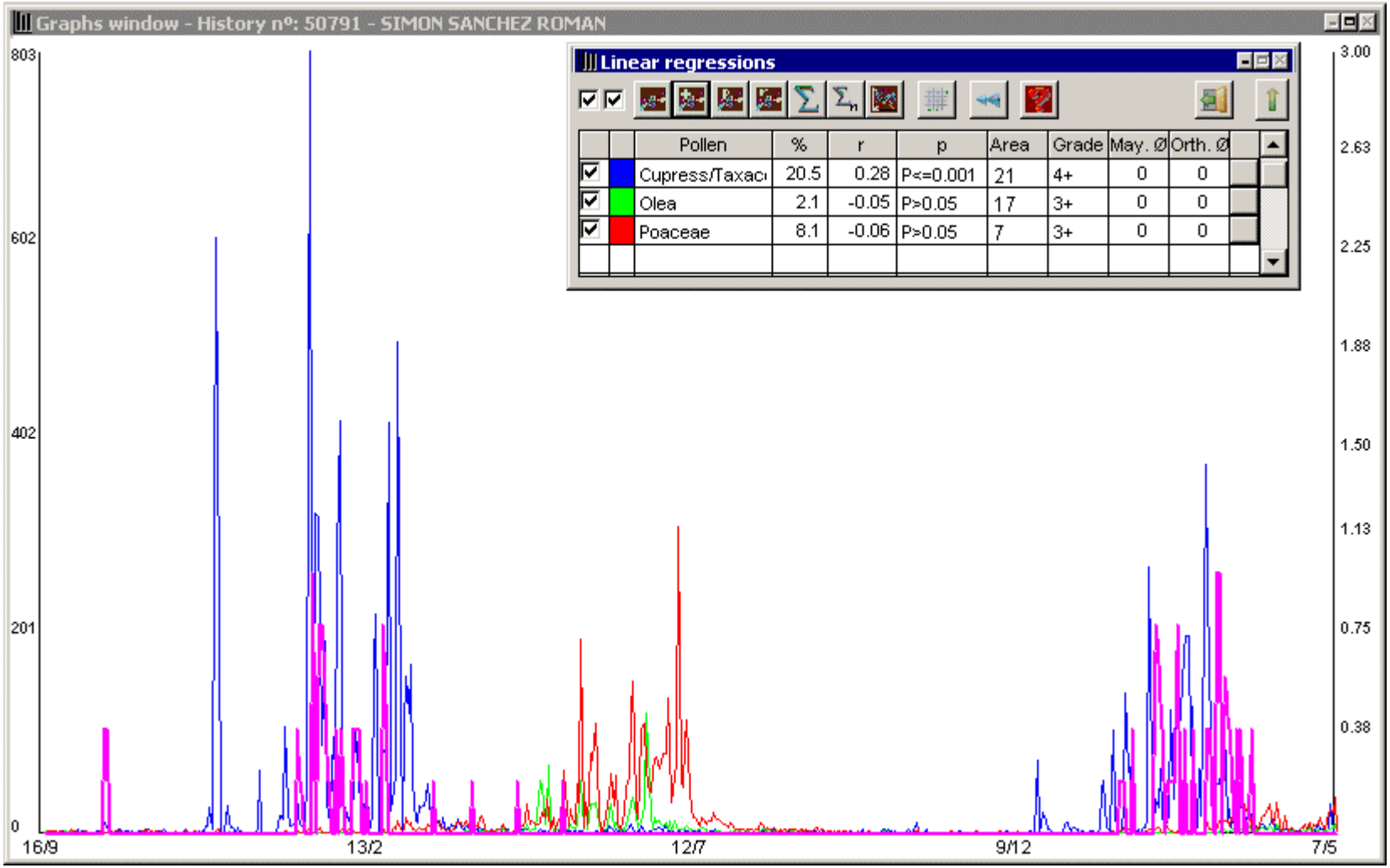
In the second column, we observe the atmospheric porcentual contribution of each pollen type in total pollen, during this period.

In the third and fourth column, we can see the correlation coefficient between symptoms and each type of pollen and the significant.

Finally, in the last columns we have the results of the skin prick tests

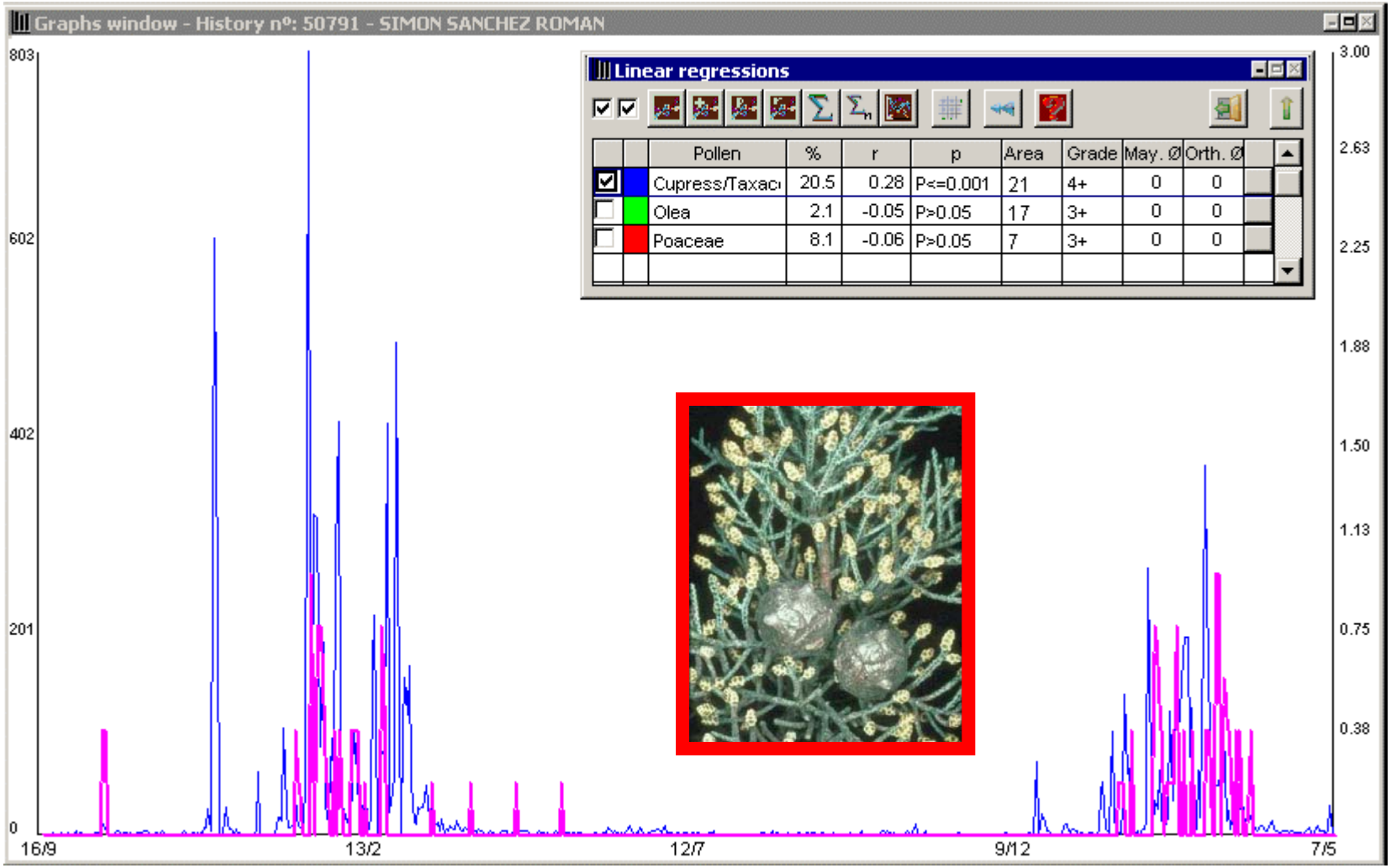
AlerCon 2.0

Clinical case using Alercon (1)



You can see that the Symptoms only showed a significant correlation with *Cupressus* but not with *Olea* and grasses counts in spite of the positivity in the skin prick tests

Clinical case using Alercon (1)



In this polysensitised patient, *Cupressus* is his dominant pollen, and we think he is a good candidate to try an immunotherapy only with this pollen.

And we could obtain this knowledge in a very easy way, thanks to Alercon.

Thank you for your attention