Back in ancient times, quails' eggs were known to have anti-allergic therapeutic properties. Nowadays, the anti-allergic activity of quails' eggs has been proven by clinical studies carried out on large numbers of patients (J.C. Truffier).

In 1967 - following numerous comments from quail breeders who saw chronic asthma and permanent Dyspnea gradually disappear from their families - Dr. Truffier (who, at that time, coordinated more than 200 allergists) prescribed quail egg-based therapies for cases of Pollinosis or allergies from respiratory allergens.

At the time, more than 1,000 cases were followed by specialists in allergology, paediatricians or general practitioners with the diagnostic aid of skin tests carried out before and after treatment.

The standard treatment with quails' eggs involved adding a specific number of fresh quails' eggs to the diet in the following precise sequence:
- 6 eggs a day in a single administration, for 9 days
- Break of 9 days
- 6 eggs a day in a single administration, for 9 days
- Break of 9 days; if necessary, one could continue with consolidation therapy for another 6 days, or finish the therapeutic protocol and move on to control diagnostics.

Although it produced beneficial clinical results for the vast majority of patients, this protocol carried some unwanted side effects such as:
- weight increase in the patient
- Hypercholesterolemia
- Digestive problems
- Nausea when consuming the eggs.

Galenic forms were, therefore, researched in order to overcome these side effects and, finally, sublingual tablets made from B Mina family quails' eggs proved to be active and easy-to-digest.

It was therefore thought essential to test this new galenic form (ESOC) in a double-blind trial versus placebo, for the treatment of numerous allergic manifestations linked to Reagin (Type I allergy, according to Gell and Coombs classification) such as

- Asthma
- Rhinitis (annual or seasonal) linked to respiratory allergens, especially house dust mites and pollens.
ALLERGIES

Allergic Rhinitis

Seasonal Allergic Rhinitis (Spasmodic coryza or Hay fever)

Allergic Rhinitis is characterised by sneezing, Rhinorrhea, nasal congestion, irritation of the conjunctiva and larynx, and lacrymation.

It is generally a seasonal pathology linked to the aerial transmission of pollens; however, there can be variations and other etiologies.

The causes of this type of Rhinitis are the pollens from a relatively small number of plants - mainly from Gramineae, Betulaceae, Compositae, Plantaginaceae and Ambrosiaceae.

The pollination period for these varieties of plant varies little between one year and the next in the same location, but it can alter in another climate.

Persistent Allergic Rhinitis

This is caused by allergens that are present throughout the year such as epithelial desquamation, feathers, industrial chemical products, house dust and work environments.

The content of these dusts can vary a great deal and may include mites.

The capacity of these allergens to cause Rhinitis rather than to affect the inner parts of the respiratory apparatus, can be attributed to the fact that they are retained in the nose as a result of their fairly large size (10-100nm).

Allergic Asthma

Seasonal Allergic Asthma

This is linked to an IgE response controlled by the T and B Lymphocytes, followed by the interaction of IgE with the Antigen on the surface of the Mastocytes.

The majority of allergens that cause Asthma originate in the air. In order to create "sensitization", there has to be quite a large amount of allergens over quite a prolonged period. However, once sensitization is established then just the tiniest quantities of the causal agent can cause serious asthma attacks.

Non-seasonal Allergic Asthma

Asthma can also be caused by allergies to feathers, animal fur and other antigens that are constantly found in the environment.

Exposure to allergens causes an immediate typical response, establishing a "temporary" bronchoconstriction in just a few minutes.
In 30-50% of cases, a second "delayed" bronchoconstriction appears between 6 to 10 hours later.

This can be the only response in the minority of patients.

DOUBLE-BLIND CONTROLLED CLINICAL STUDIES VERSUS PLACEBO INTO ALLERGIC PHENOMENA LINKED TO IgEs (REAGIN)

Characteristics of the studies

Five different clinical studies were undertaken - one on Allergic Asthma from dust mites in children, three on Seasonal Rhinitis from pollens and one on annual Rhinitis linked to domestic respiratory allergens.

They were all double-blind, randomised, placebo-controlled and multicentric studies.

The inclusion criteria for the 5 studies always included the measurement of IgE. The total value of IgE for the patients participating in the study was greater than 300 Ul/ml for all those included.

Other tests were used to select patients by assessing their allergic terrain: positive skin tests; being at least Class 2 Specific IgE positive (mites, pollens), according to the RAST (Radioallergosorbent Test) or FAST (Fluoroallergosorbent Test) Test; the "allergy" having been diagnosed for at least 2 years.

The criteria for the efficacy of the therapy were based on the development of symptomology; evaluation of the overall efficacy seen by both the doctor and the patient; the reduction in the administration of "emergency" medication and varied tolerability to the latter.

The results of each of the 5 studies were examined according to medical statistics (Chi2 test or Analysis of Variance).

Patients and posology

690 patients were studied: 394 of these patients (average age = 30), 115 of which were children (average age = 9), received placebo.

In four studies - i.e. those for Seasonal Rhinitis, Rhinitis from pollens and Asthma from dust mites - the patients included were asymptomatic and were not taking any medication.

The posology of ESOC was as follows:

- 1 tablet per day
(N.B. - the therapy was started between 30 and 60 days before the onset of the attacks, so that the body was protected by ESOC. The duration of treatment could therefore vary between 75 and 450 days).

In the fifth study - i.e. Perennial Rhinitis from domestic respiratory allergens – only those patients with active attacks and those who were not using any other medication, except emergency medication, were included.

The posology for this group was 2 tablets per day.

The treatment in this case began immediately and lasted for 42 days.

**EFFICACY OF ESOC AGAINST REAGINIC ALLERGIES**

**Allergic Asthma from dust mites**

180 children were observed.

The recovery of the functioning of the respiratory mechanics and the extent of maximum respiratory volume (VEMS) were assessed.

For the patients to be included in the study, this parameter (VEMS) had to be greater or equal to 85% of its theoretical value and show an increase of 15% under therapy with 200 µg of a β-2 stimulant bronchodilator (Boehringer-Ingelheim Fenoterol inhaler).

An increase of more than 20% in VEMS was regarded as an excellent therapeutic result.

Other parameters were also taken into consideration, such as the frequency and intensity of the attacks, the symptomology and decrease in the use of emergency inhalers (Fenoterol).

In this study, the results obtained with ESOC were significantly better than placebo, with a 77.7% (p<0.0001) reduction in the number of attacks by the end of treatment.

The use of emergency medication was reduced by 58.6% using ESOC.

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**Seasonal Rhinitis caused by pollens**

(Gramineae, Betulaceae, Compositae, Plantaginaceae and Ambrosiaceae)

Three studies were carried out on this pathology - 435 patients were assessed for these studies. 208 of them had taken ESOC.

The studies provided:

- an assessment of the efficacy of ESOC on true Rhinitis from pollens. In this case, 80 patients in the "verum" group took ESOC for 90 days and these patients continued to be observed for a further 30 days.
- an assessment of the efficacy of ESOC on Allergic Rhinitis from pollens. In this case, 48 patients in the "verum" group took ESOC for 60 days and continued to be observed for another 15 days.
- an assessment of the efficacy of ESOC on Rhinitis from pollens in patients presenting with an annual allergic terrain. In this case, 90 patients took ESOC for 90 days and continued to be observed for a further 30 days.

In all these studies, the patients were asymptomatic on admission to the study; the study began between 30 and 60 days before the predicted onset of pollinosis, so as to ensure that the body was adequately protected, and that a good clinical result was produced.

There were no "drop outs" from the study, as patients were able to resort to their emergency medication.

The efficacy of ESOC was assessed via an examination of clinical symptoms, the intensity of the Rhinitis (sneezing, nasal congestion, nasal irritation) and the intensity of the conjunctival inflammation, the appearance of the nasal mucosa and a quantitative assessment of the use of emergency medication.

These assessments highlighted:
- a statistically significant reduction in the intensity of the Rhinitis in the treated group compared with the placebo group \((p<10^{-4})\), with an improvement in all the symptoms examined.
- A significant improvement in the state of the nasal mucosa \((p<10^{-4})\) in comparison with the placebo group.
- A significant reduction in the use of emergency medication \((p<10^{-4})\), represented in this case by Terfenadine tablets (Teldane® - Lepetit).

These results were also produced at the height of the pollen season, i.e. between 60 to 90 days from the beginning of treatment.

In the study on Allergic Rhinitis from pollens, the results given above were already proving significant 45 days after treatment commenced. The efficacy was assessed using the above criteria, but the overall efficacy was analysed not only by the doctor but by the patient as well.

**“Verum” Group (ESOC):**
25 children - 23 adults

**“Placebo” Group:**
25 children - 22 adults

The efficacy of the product, in comparison with the placebo, was recognised as much by the doctor as by the patient.

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<tr>
<th>Doctor’s verdict:</th>
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<tbody>
<tr>
<td><strong>ESOC:</strong></td>
<td><strong>76% of children effective</strong></td>
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<tr>
<td></td>
<td><strong>61% of adults effective</strong></td>
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<tr>
<td><strong>Placebo:</strong></td>
<td><strong>12% of children effective</strong></td>
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<td><strong>13% of adults effective</strong></td>
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Patient’s verdict:

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<tr>
<td></td>
<td><strong>ESOC</strong>:</td>
<td><strong>Placebo</strong>:</td>
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<tr>
<td></td>
<td>78% of children</td>
<td>16% of children</td>
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Periannual Rhinitis from domestic respiratory allergens (dust, mites, feathers and animal fur)

This multicentric study, carried out at 33 Allergology centres, examined the activity of ESOC in 41 patients in this group during 42 days of therapy.

In this case, to ensure patients were suitable for inclusion, obviously symptomatic patients were chosen.

The posology of ESOC was set at 2 tablets per day.

The results confirmed the conclusions of the studies previously mentioned - i.e. the product was effective in the treatment of Allergic Rhinitis and associated symptoms.

Using the dose of 2 tablets per day, 42 days after treatment had commenced, the assessments by both the doctor and the patient showed a number of much more significant successes in the ESOC group in comparison with the Placebo group.

Doctor’s verdict:

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<tr>
<td></td>
<td><strong>ESOC</strong>:</td>
<td><strong>Placebo</strong>:</td>
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<td></td>
<td>63% of patients</td>
<td>27% of patients</td>
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Patient’s verdict:

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<tr>
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<td><strong>Placebo</strong>:</td>
</tr>
<tr>
<td></td>
<td>65% of patients</td>
<td>25% of patients</td>
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</table>

- According to the doctor, ESOC is already effective by the 28th day of treatment, for both nasal congestion and conjunctivitis.
- According to the patient, ESOC is already effective by the 28th day in the treatment of Rhinorrhoea, sneezing and nasal congestion.

We should also point out that in this experiment, some observers did not comply with the basic inclusion criteria.

In the ESOC group, therefore, the results of 22 patients were not taken into account for the following reasons:

- 10 patients presented with pollinosis
- for some of the patients, the laboratory analysis did not confirm any allergy (completely normal IgE, negative specific IgE, negative skin tests)
- there were inflammatory phenomena on an infectious base for 3 patients (2 sinusitis and 1 polymicrobial vaccinotherapy)
- 3 patients left the study through personal choice.

We should emphasise that, in any case, 7 out of the 10 patients presenting with pollinosis had made a clinical improvement by the end of the study.

In conclusion, the efficacy of ESOC in the treatment of the reaginic pathologies studied, Rhinitis and Asthma, has been clinically proven to be significant, whatever the offending allergens and the clinical symptomology and regardless of the age of the patient.

THE EFFICACY OF ESOC

The treatments usually used in allergy therapy are both etiological and symptomatic.

Immunotherapy, or desensitization, involves carrying out repeated subcutaneous injections at progressively increasing concentrations of the allergens responsible for the symptoms. It is particularly recommended to the patient that they avoid any exposure to the allergens in the attack period.

In contrast to using ESOC, they provide for strong treatments with secondary effects (focal, general and anaphylactic reactions).

The symptomatic treatments resort to active principles such as antihistamines (collateral effects: general sedation, digestive problems), the local use of α-adrenergics (Drawback: rapid vasodilatation), or corticosteroids, with the unwanted systemic effects that we know all too well.

With regard to specific gamma-globulins (Standard therapy: 12 units/ml of anti-pollen antibodies and 16 units/ml anti-mite antibodies), we can now see that these therapies have a very time-limited efficacy as well as serious contraindications, such as sensitivity to the mercury contained in products and the presence of anti-IgA antibodies.

In addition, these products are painful when they are injected.

Treatment with ESOC is simple: 1 tablet, once a day; or 2-4 times a day if the treatment is being introduced to symptomatic patients.

During the treatment it is not necessary to avoid exposure to the offending allergen.

Treatment with ESOC is effective and also well-tolerated, as it has no unwanted effects.
TOLERABILITY OF ESOC

ESOC was administered to 249 patients - of which the 115 children were part of 5 controlled multicentric studies - under a double-blind trial versus placebo, with a posology of 1 or 4 tablets per day.

308 patients received 1 tablet per day
41 patients received 4 tablets per day

The duration of treatment varied between 42 days and 360 days.

In all the studies, tolerability was assessed by the researcher. Attention was given to all the unwanted effects reviewed in the allergologic literature. In particular, by examining the data from the therapeutic use of whole quails' eggs, weight increase, hypercholesterolemia and digestive problems were studied.

All 35 doctors who took part in the study assessed tolerability as being "very good".

The secondary effects encountered were not statistically different from those observed with the placebo. Even at a dosage of 4 tablets per day the difference was not significant, even though there were different results in the two groups.

A weight increase of 2 Kg was recorded in only 6 patients out of 349 (1.7%).

This result is not statistically significant, even with a dosage of 4 tablets per day. Other biological parameters were also studied statistically.

In particular, the study on Allergic Rhinitis from pollens (48 patients with 1 tablet per day, for 60 days of therapy) confirms the data from previous studies; the laboratory data for haematic, renal and hepatic function were studied, and these values remained normal.

There were no pharmacological interactions with the antihistamines, such as Terfenadine, which was given as emergency medication. Nor were there any interactions with the corticosteroids used in other studies.

Toxicological studies on rats proved that ESOC was harmless. Using single and repeat administration, it was established that there were no mutagenic or genotoxic properties, nor any sensitizing actions.

In conclusion, we can emphasise that the collateral effects produced by whole quails' eggs - i.e. weight increase and changes in some biochemical parameters, such as cholesterol and triglycerides, bilirubin, transaminase, creatine and urea – are definitely not produced by ESOC, which contains 0.750 mg of quail egg homogenate, with a posology of 1 or 4 tablets per day.

With these posologies, ESOC has a proven efficacy with excellent tolerability, and is therefore extremely safe for use with adults and children.
CONCLUSIONS

ESOC is a product aimed at preventing reaginic allergic manifestations, whatever the offending respiratory allergen. Until now, we were not completely clear about its mechanism of action.

Truffier hypothesises that ESOC could have a blocking action on specific antigens or an inhibiting action on specific anti-IgE antibodies fixed on the mastocyte, preventing them from degranulating.

The main indications for ESOC are reaginic pathologies such as:
- Allergic asthma from domestic respiratory allergens
- Seasonal allergic rhinitis (Hay fever)
- Annual allergic rhinitis due to domestic respiratory allergens.

ESOC must be administered 1 or 2 months before the onset of pollinosis (Rhinitis or Asthma) at a dosage of 1 tablet per day, half an hour before meals.

The treatment should last for another 1-2 months and should be repeated each year before the pollen season.

For annual manifestations (allergy to domestic respiratory allergens), doctors will decide whether to use a posology of 1 or more tablets per day according to the intensity of symptoms to be prevented or depending on whether there are any symptoms at the beginning of treatment.

Children should not exceed the dose of 1 tablet per day.

There are no restrictions on the use of ESOC.

Care should be taken with patients showing intolerance to eggs, bearing in mind that not everyone who is intolerant to hens' eggs will automatically be intolerant to quails' eggs.

Quails' eggs are not contraindicated during pregnancy, but there is not yet any documented experiment. Mothers who are breastfeeding can use ESOC without any problem, as it is a good alternative to any antihistamine or corticosteroid, which would certainly interfere with breastfeeding. Secondary effects are rare.

The clinical studies carried out recorded isolated cases of gastric problems, weight increase, cephaelea, bursts of heat and dryness of lips, phenomena that, nevertheless, could not have a cause and effect relation with ESOC.

No interaction with antihistamines and corticosteroids was recorded. These products can be used if necessary. ESOC can significantly reduce their use. There was no record of overdosage of ESOC.

In conclusion, ESOC has a favourable benefits/risks ratio. In comparison with existing treatments, it has the advantage of an excellent tolerability and is extremely simple to administer.