EAACI Clinical Fellowship 2025 Final Report

Project Title: Cotrimoxazole hypersensitivity and diagnostic test outcomes

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Type, Duration, and Location of Fellowship: Short-Term Clinical Fellowship, 1 May 2025 – 31 July 2025 (3 months), Sorbonne University Tenon Hospital, Paris, France

Host Institution and Supervisor Name: Sorbonne University, Department of Dermatology and Allergology, Tenon Hospital, Paris, France — Prof. Dr. Annick Barbaud

Summary of the Clinical and Academic Activities Undertaken During the Fellowship

It was a distinct honor to be awarded the 2025 Clinical Fellowship by the European Academy of Allergy and Clinical Immunology (EAACI). I had the invaluable opportunity to complete this fellowship at Sorbonne University, Tenon Hospital, Paris, France.

During the fellowship, I engaged in a wide range of clinical activities, primarily focusing on drug allergy patients. I significantly expanded my knowledge and experience, particularly regarding severe delayed hypersensitivity reactions and perioperative allergies. Besides drug allergy cases, I also evaluated numerous patients with urticaria, atopic dermatitis, food allergies, and venom allergies.

My responsibilities included observing and assisting in patient evaluations, performing diagnostic procedures, and participating in multidisciplinary discussions of complex cases alongside leading clinicians and researchers in the field. Working at a center of excellence and reference (EAACI & UCARE & ACARE) greatly contributed to my clinical and academic development in this field.

Clinical Activities and Observations

During this period, I observed approximately 450 patients, averaging 30–50 patients per week over the course of 12 weeks. Each workday lasted about 8 hours, resulting in an effective working time of approximately 40 hours per week. I participated daily in

outpatient clinics from 09:00 to 17:00, accompanying patient examinations. In addition to routine clinic hours, I also took part in the following specialized programs:

Monthly workshops: I also actively participated in a monthly practical workshop organized by Sorbonne University, focusing on applied clinical skills. During these sessions, I gained valuable hands-on experience with skin prick tests, intradermal tests, and patch tests.

Weekly Schedule and Activities:

- **Monday, Tuesday, Wednesday, Thursday, Friday (08:00–10:00) — Drug Provocation Tests:**

I observed and participated in various provocation tests, primarily for antibiotic, NSAID, and contrast media allergies. On average, six patients per day underwent drug provocation tests. This experience enhanced my knowledge of managing reactions during provocation and exposed me to diverse clinical approaches. Additionally, I gained experience with food desensitization in adults.

- **Tuesday (09:00–12:00) — Immunotherapy Day:**

I focused on both the initiation and maintenance phases of immunotherapy, closely observing the procedures involved at each stage. Observing these procedures provided valuable insights into patient selection, preparation, and follow-up, as well as the importance of patient education and adherence. This experience greatly enhanced my understanding of the practical application and clinical management of immunotherapy in allergic diseases.

- **Tuesday (14:00–17:00) — Severe Drug Allergy Council & Telemedicine Consultations:**

I regularly attended weekly multidisciplinary meetings dedicated to the discussion of severe drug reactions, which significantly enriched my clinical knowledge. The opportunity to observe and learn from esteemed experts in the field during these case discussions provided invaluable insights into the evaluation and management of complex allergic reactions. Furthermore, the telemedicine consultations, which frequently involved cases of malignancy-related and chemotherapeutic agent hypersensitivity, were particularly instructive, offering a broader perspective on the challenges and approaches to managing such patients in a remote setting.

- **Wednesday (09:00–17:00) — Consultations with Prof. Dr. Annick Barbaud:**

I had the privilege of working closely with Prof. Dr. Annick Barbaud during the Wednesday consultation sessions. Throughout the day, I observed her clinical approach to evaluating and managing complex dermatologic and allergic conditions, benefiting greatly from her vast experience and nuanced decision-making. After the official clinic hours, Prof. Barbaud kindly provided additional theoretical instruction, elaborating on the cases we had seen, discussing relevant literature, and addressing my questions in depth. This mentorship not only enhanced my clinical knowledge but also deepened my understanding of the underlying principles guiding diagnostic and therapeutic choices in the field.

Research Project

Title: Cotrimoxazole Hypersensitivity and Diagnostic Test Outcomes

Cotrimoxazole (CTX) is a first-line antibiotic with a key role in the management of various patient populations, particularly for the prophylaxis of opportunistic infections in immunosuppressed individuals. CTX is a fixed-dose combination of sulfamethoxazole (SMX) and trimethoprim (TMP) in a 5:1 ratio and is a broad-spectrum sulfonamide widely used in the treatment of bacterial, fungal, and protozoal infections. Cutaneous adverse drug reactions (CADRs) associated with CTX occur in approximately 2% of treated patients, with a significantly higher frequency observed among those living with HIV infection. The incidence of cutaneous eruptions due to CTX increases from 2–5% in HIV-negative individuals to as high as 40–80% in HIV-positive patients, and previous studies have suggested that HIV status and higher CTX doses may represent risk factors for the development of severe CADRs.

The most common CADRs are non-immediate, T cell–mediated reactions such as maculopapular exanthema, although more severe and life-threatening reactions, including drug reaction with eosinophilia and systemic symptoms (DRESS) and Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), though rare, have also been reported. Patients with a history of non-severe delayed reactions, the most frequent clinical phenotype associated with CTX, or those with non-severe immediate reactions labeled as "sulfa allergic," can usually undergo a graded oral TMP-SMX challenge safely. To identify the causative agent in such non-immediate CADRs, CTX is commonly included in antibiotic patch test series; however, concerns have been raised regarding the low sensitivity and limited diagnostic utility of patch testing for this drug. Although antibiotic allergy testing (AAT), including skin testing followed by oral provocation, has demonstrated that most patients can be successfully desensitized, the benefits of AAT in immunocompromised populations remain unclear and supporting data are limited. Despite their greater need for suitable antibiotic alternatives, this high-risk patient group has often been excluded from studies investigating AAT. While hypersensitivity reactions to CTX

are relatively common, data on their clinical course as well as the diagnostic accuracy of skin tests and provocation tests in immunocompromised populations remain scarce in the literature.Given the limited data regarding the accuracy of skin tests and the outcomes of provocation tests, particularly in high-risk populations, we aim to evaluate the clinical features and diagnostic approaches of cotrimoxazole hypersensitivity reactions in patients admitted to the allergy clinics of Hacettepe University Hospital and Sorbonne University Tenon Hospital. The primary endpoint of the study is to evaluate the clinical characteristics of these allergic reactions and their management, while the secondary endpoints are to determine the skin test results in these patients.

We recorded data including patients' age, gender, family history, and underlying conditions (e.g., immunodeficiency, malignancy) in a pre-established database. The number of reactions, doses of suspected drugs, symptoms, and the time between reaction and allergological evaluation were documented. Results of skin tests and drug provocation tests were analyzed, and patients were classified accordingly.

These procedures were conducted independently at the Allergy Unit of Hacettepe University Hospital and the Allergy Unit of Sorbonne University Tenon Hospital. At Sorbonne, the records of 90 patients with cotrimoxazole hypersensitivity who had undergone skin testing and/or provocation testing during the fellowship program were retrospectively reviewed. Data from patients at Hacettepe University are currently being collected, and the combined analysis will be undertaken upon completion of data acquisition. The findings from this fellowship are planned to be presented at the EAACI Annual Congress 2026 in Istanbul.

Achieved Objectives:

I successfully accomplished the objectives set for theoretical knowledge, practical skills, and research activities in allergology during my fellowship at Sorbonne University Tenon Hospital. Through active participation in specialized clinics and discussions with leading experts, I deepened my understanding of allergic reactions. I also gained practical experience in procedures such as provocation tests and skin testing. This fellowship has significantly enhanced both my practical skills and my expertise in the field of allergology.

Conclusion

The academic and clinical experience provided by this fellowship at Sorbonne University Tenon Hospital has been truly invaluable. It significantly broadened my understanding of drug and skin allergic diseases and offered a unique platform to explore diverse approaches in the field. This experience greatly improved my ability to manage complex drug allergy cases, enhanced my confidence in performing diagnostic tests such as skin and provocation

testing, and strengthened my skills in international collaboration and interdisciplinary teamwork. I am deeply grateful to EAACI and the fellowship selection committee for granting me this exceptional opportunity.

Acknowledgements

I would like to express my profound gratitude to the entire team at Sorbonne University Tenon Hospital, with special recognition to my esteemed supervisor, Prof. Dr. Annick Barbaud, for her steadfast support, exceptional guidance, for introducing me to leading experts in the field, and for her invaluable mentorship throughout this project. I am also sincerely thankful to Prof. Dr. Angele Soria and Dr. Jean Eric Autegarden for kindly providing access to the project database, and to my home supervisor, Prof. Dr. Gülfem Elif Çelik, for her continuous support and encouragement. In addition, I greatly appreciate the financial support provided by the EAACI, which made this enriching experience possible.

Finally, I am deeply thankful to my mentors, Prof. Dr. Ebru Damadoglu, Prof. Dr. Gül Karakaya, and Prof. Dr. Ali Fuat Kalyoncu, for their invaluable guidance, encouragement, and unwavering support throughout my career.