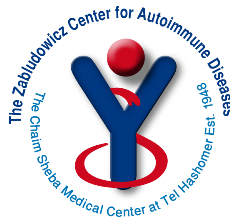
Prof. Yehuda Shoenfeld, MD, FRCP
Head, Zabludowicz Center
for Autoimmune Diseases,
Center of Excellence, Sackler
Faculty of Medicine, Tel-Aviv
University



Chaim Sheba Medical Center
Tel-Hashomer 52621, ISRAEL
Incumbent, Laura Schwarz-Kipp
Chair for Research of
Autoimmune Diseases, Tel-Aviv
University

Tel: 011-972-3-5308070 Fax: 011-972-3-5352855 Email: **yehuda.shoenfeld@sheba.health.gov.il**

February 03, 2017

To whom it may concern:

The attached questionnaire has been designed to collect information on the Autoimmune/inflammatory Syndrome Induced by Adjuvants (ASIA Syndrome), a rare condition consisting of the development of immune-mediated diseases following exposure to any substance with an adjuvant activity.
https://www.ncbi.nlm.nih.gov/pubmed/23557271

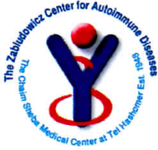
Over the last decades, exposure to certain adjuvants has been implicated in the development of defined and non-defined autoimmune diseases. Hundreds of post-exposure cases of Scleroderma, Systemic Lupus Erythematous, Undefined Connective Tissue Disease, Chronic Fatigue Syndrome and others and have been reported. To date, a unified, global approach to ASIA Syndrome does not exist and most physicians are unaware of the syndrome.

The ASIA Registry was created in 2011 by myself, Professor Yehuda Shoenfeld and Dr. Nancy Agmon-Levin of the Zabludowicz Center for Autoimmune Diseases at the Sheba Medical Center in Israel to collect data on the epidemiology, clinical and laboratory aspects of ASIA Syndrome. This registry offers the unique opportunity to systematize relevant information from worldwide clinical reports, and helps with the publishing of scientific data on the subject with the ultimate goal of promoting research, disseminating data and information, and assisting physicians with the recognition and management of the syndrome.

The scientific board of the ASIA Registry invites physicians to contribute to this effort by submitting the attached questionnaire for each patient that meets the criteria for an ASIA diagnosis to Prof. Yehuda Shoenfeld at yehuda.shoenfeld@sheba.health.gov.il or faxed to 011-972-3-535-2855.

Cases must present with at least two major, or one major and two minor criteria for an ASIA diagnosis, as described on page 2.

All information gathered is confidential and implies free and informed consent.



Please contact Carlo Perricone at carlo.perricone@gmail.com with any questions you may have.

Your time and participation in the ASIA Registry is earnestly appreciated.

Sincerely,

Prof. Y. Shoenfeld

Professor Yehuda Shoenfeld, MD, FRCP
Head, Zabludowicz Center for Autoimmune Diseases

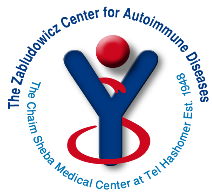
Criteria for ASIA diagnosis

Major criteria:

- Exposure to an external stimuli (infection, vaccine, silicone, or other adjuvant) prior to clinical manifestations
- Appearance of at least one of the following clinical manifestations:
  - Myalgia, myositis or muscular weakness
  - Arthralgia and/or arthritis
  - Chronic fatigue, non-restful sleep or sleep disturbances
  - Neurological manifestations (especially those associated with demyelization)
  - Cognitive alterations, loss of memory
  - Fever, dry mouth
- Removal of the initiating agent induces improvement
- Typical biopsy of the involved organs

Minor Criteria:

- Appearance of autoantibodies directed against the suspected adjuvant
- Other clinical manifestations (i.e., irritable bowl syndrome or other)
- Specific HLA (i.e., HLA DRB1, HLA DQB1)
- Initiation of an autoimmune illness (i.e., multiple sclerosis, systemic sclerosis, etc.)



The Autoimmune / inflammatory Syndrome Induced by Adjuvants (ASIA) Research Questionnaire

---

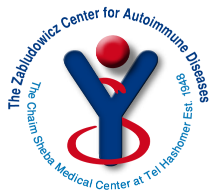
This questionnaire is to be filled out by the patient's physician and returned to Prof. Yehuda Shoenfeld at **yehuda.shoenfeld@sheba.health.gov.il** or faxed to 011-972-3-535-2855.

Please attach a list of symptoms where relevant. If needed, use page 7 to provide further details.

Full name of physician fulfilling the questionnaire: ______________________________
Specialty:____
Affiliation:____
Country:____
Contact information (including email):_____________________________________
____
____
____

1) Patient Demographics
   a) Patient code (Research office use only):_____________________________
   b) Name:____
   c) Age:____
   d) Date of birth:____
   e) Gender:____
   f) Address:____
      ____
   g) Email:____

2) Medical History
   a) Autoimmune Disease diagnosis: UCTD (_) MCTD (_) SLE (_)
      RA (_) Sjogren's Syndrome (_) Systemic Sclerosis (_)
      Autoimmune Thyroiditis (_)
      Other (specify)____
   b) Fibromyalgia (_)
   c) Chronic Fatigue Syndrome (_)
   d) Date of Autoimmune Disease diagnosis:_____________________________
   e) Duration of Autoimmune Disease:_________________________________
   f) Family history of Autoimmune Disease: (_)
   g) Previously or currently smoking: (_) If previous, quit date:______________
      Number of packs per day and number of years:______________________
   h) Allergy to metals, medications or vaccines: (_)
      If yes, specify:____
   i) Other allergies (please list):_____________________________________



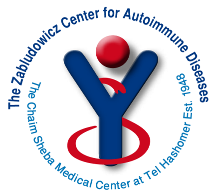
j) History of Cancer: (_)
Lymphoma (_) Type and date:____
Other (_) Type and date:____
k) Sarcoidosis: (_) Date:____

3) History of foreign material exposure prior to clinical manifestations: Mark all that apply, and provide details in item "l."
a) Piercings (_) Amount:____ Date and type:____________________________
b) Tattoos (_) Amount:____ Date and type:____________________________
c) Breast implants (_) Date and type:____________________________
____
d) Skin fillers (_) Collagen (_) Hyaluronic acid (_) Mineral oil (_)
Silicone (_) Other (_) Specify type and commercial name if available
____
____
e) Tooth amalgam (_)
f) Intrauterine device (IUD) (_) Type(s)____________________________
____
g) Contact lenses (_)
h) Cardiac valves (_) metal (_) biologic (_) Date:____________________
i) Pacemaker/icd defibrillator (_) Date:____________________________
j) Artificial joints (_) Date:________________ Type:________________
k) Metal implant (_) Date:________________ Type:________________
l) Duration of exposure____________________________________
m) Time between exposure to foreign material and onset of autoimmune disease symptoms:____________________________________
n) Local complications (_)
Local infection of foreign material (_) Date/s________________________
Rupture of silicone (_) Date/s____________________________
____
____
____
o) Have any of the above been removed or explanted? Yes (_) No(_)
If yes, which (please provide reason and dates)?____________________
____
____
____
p) In the case of removal or explant, was there an amelioration of symptoms or scaled-down therapy? Please describe:____________________________
____
____

4) Vaccinations received over the past ten years and dates received (if known)
   a) HBV (_)____
   b) HAV (_)____
   c) Seasonal Influenza (_)______________________________
   d) H1N1 (_)____
   e) HPV (_)____
   f) DPT (_)____
   g) Pneumococcal (_)___________________________________
   h) Tetanus (_)____
   i) Other (_)____
   ____
   ____
   j) Adverse effects within the first seven days after injection
   Fever (_) Type of vaccine:_____________________________
   Persistent local induration/infection (_) Type of vaccine:_______________
   Exacerbation of autoimmune disease (_) Type of vaccine:_______________
   Exacerbation of CFS/Fibromyalgia (_) Type of vaccine:________________

5) Genetic testing and mutations
   a) MTHFR: (_) Factor V Leiden (_) Factor II/Prothrombin G20210A (_)
   Other related to Thrombophilia (_) Specify:__________________________
   ____
   b) BRCA: (_) Other related to cancer (_) Specify:________________________
   ____
   c) Other: (_) Specify:__________________________________

6) Clinical manifestations
   a) Date of onset of symptoms:_____________________________
   b) Date of diagnosis:__________________________________
   c) Fever (_)
   d) General weakness (_)
   e) Weight loss (_)
   f) Weight gain (_)
   g) Myalgia (_)
   h) Myositis (_)
   i) CPK level:_________ Maximal CPK titer_________U/L
   j) Arthralgia (_)
   k) Arthritis (_)
   l) Pruritus (_)
   m) Chronic rash (_)
   n) Lymphadenopathy (_)
   o) Chronic fatigue (_)



---

p) Chronic pain (_)
q) Sleep disturbances (_)
r) Cognitive impairment (_)
 Please specify:____
s) Memory disturbances (brain fog) (_)
t) Irritable Bowel Syndrome (IBS) (_)
u) Postural hypotension (_)
v) Postural tachycardia (_)
w) Recurrent non-infectious cystitis (_)
x) Neurological manifestations (_)
 Please specify:____
y) Pathology on CT or MRI: Yes (_) No (_)
 Please specify:____
z) Other: Please attach a separate sheet listing additional clinical manifestations.

7) Were any of the following serological markers positive in patient sera?
 a) ANA (_)
 b) Anti-dsDNA (_)
 c) Rheumatoid Factor (_)
 d) Anti RNP (_)
 e) Anti SS-A / Ro (_)
 f) Anti SS-B/La (_)
 g) Anti SCL-70 (_)
 h) Anti Sm
 i) Anti Centromere (_)
 j) Anti-TPO (_)
 k) Anti-TTG (_)
 l) Anti-citrulline antibodies (anti-CCP/ACPA) (_)
 m) Anti ASCA (_)
 n) low C3 (_)
 o) low C4 (_)
 p) Lupus anticoag. (_)
 q) Anticardiolipin (_)
 r) Anti-beta2-glycoprotein 1 (_)
 s) c-ANCA (_)
 t) p-ANCA (_)

u) Other (_) Please specify:____

v) Has HLA determination been done? Yes (_) No (_)
If yes, please specify and list genotype:______________________________

8) Removal or explant of foreign material

a) If a foreign material has been removed (see item 3n), was a clinical improvement experienced? Yes (_) No (_)
If yes, please provide details:____________________________________

b) Was the explanted material sent to pathology? Yes (_) No (_)
If yes, please provide brief report details:___________________________

9) Biopsies related to autoimmune disease

a) Were any biopsies performed? Yes (_) No (_)
If yes, please specify:____
Biopsy results:____

10) Current treatments

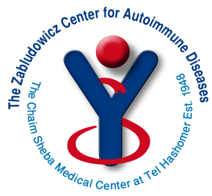
a) Analgesics (_)
b) Antihypertensive (_)
c) Sleep medications (_)
d) Oral contraceptives (_)
e) Aspirin (_)
f) NSAIDS (_)
g) Hydroxychloroquine (_)
h) Azathioprine (_)
i) Methotrexate (_)
j) Other (_) Please specify:____

11) Has the patient ever received any of the following?

a) IVIG (_)
b) Rituximab (_)
c) anti TNF (_)
d) Corticosteroids (_)
e) Other biologic therapy (_) Please specify:____
____
____

12) Has the patient's case been published? Yes (_) No (_) If yes, please provide:

a) Journal:____
b) Number and Vol:____
c) First page:____
d) Title:____
e) PMID:____
f) DOI:____



Please add information about any complementary diagnostic exams and/or additional symptoms you may find relevant (include dates).