

The American College of Allergy, Asthma, and Immunology Registry For Allergic, Asthmatic Pregnant Patients (RAAPP)

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There are few data available to assess the safety during pregnancy of agents currently used to treat asthma and allergic disorders. The American College of Allergy, Asthma, and Immunology Registry for Allergic, Asthmatic Pregnant Patients (RAAPP) was established to provide data to assess the hypothesis that the aggressive treatment of asthma and allergy in pregnant women will encourage positive outcomes for mother and baby. Currently in progress is a pilot study of 800 patients who require inhaled corticosteroids during pregnancy. The major outcome variable for the pilot study is small for gestational age, defined as a birth weight below the 10th percentile for gestational age. After evaluation of these data, the Registry will probably be opened to general enrollment of any pregnant patient with allergy and/or asthma, regardless of medication use. When completed, RAAPP will enable physicians to evaluate the safety of medications commonly used by allergists to treat allergy and asthma during pregnancy. (*J Allergy Clin Immunol* 1999;103:S364-72.)

Older studies have demonstrated that inadequate treatment of asthma during pregnancy results in poor maternal and fetal outcomes and may result in maternal or fetal death.¹ It is also recognized that there is a baseline incidence of birth defects, spontaneous miscarriage, low-birth-weight and stillborn infants unrelated to therapies used in the management of pregnancy complicated by illness or disease. For many years the Fellows and Members of the American College of Allergy, Asthma and Immunology (ACAAI) have recognized a need for data to support the hypothesis that pregnant women with asthma and other allergic disorders must be treated aggressively to ensure a positive outcome for both the mother and baby.

Patients with allergic disorders and asthma must be encouraged to avoid environmental triggers as the first line in the management of these conditions. However, most patients will require medications, immunotherapy, or both to control their symptoms. Unfortunately, there are few data, most of which are retrospective, available

Abbreviations used

ACAAI:	American College of Allergy, Asthma, and Immunology
FDA:	Food and Drug Administration
RAAPP:	Registry For Allergic, Asthmatic Pregnant Patients
SGA:	Small for gestational age

TABLE I. FDA pregnancy risk categories

Category A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of fetal harm appears to be remote.
Category B	Either animal-reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).
Category C	Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.
Category D	There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
Category X	Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

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on the safety of drugs commonly used during pregnancy to treat asthma and allergic disorders. For the newer and more effective drugs used to treat allergies and asthma, the information regarding the safety of these therapies in

ACAA&I REGISTRY for ALLERGIC and ASTHMATIC PREGNANT PATIENTS (PILOT STUDY)			
Patient's Initials:	Study ID #:	Center or Physician ID #:	
(Office use only)			

HISTORY / DEMOGRAPHICS

Date of Patient Registration: **Patient's Age:** years
(Entry into Study) month day year

EDC: **Determined by (check one):** Ultrasound ☐ Clinical estimate ☐
month day year

Race or Ethnic Origin (check one): Caucasian ☐ Hispanic ☐ Asian/Oriental ☐
Native American ☐ African American ☐ Other ☐ specify: _____

Diagnoses:

Allergic Rhinitis	no <input style="width: 20px;" type="checkbox"/>	yes <input style="width: 20px;" type="checkbox"/>	→	Age of onset:	
Asthma	no <input style="width: 20px;" type="checkbox"/>	yes <input style="width: 20px;" type="checkbox"/>	→	Age of onset:	
Other allergy	no <input style="width: 20px;" type="checkbox"/>	yes <input style="width: 20px;" type="checkbox"/>	→	specify:	_____

Drugs: no ☐ yes ☐ → If yes, please complete a medication form

Check "yes" if patient has taken any drugs (prescription drugs, oral contraceptives or OTCs) within 1 week of conception, or within 6 weeks for astemizole (Hismanal)

Alcohol Consumption: no ☐ yes ☐ →

beer:		ounces per (check one):	day <input style="width: 20px;" type="checkbox"/>	week <input style="width: 20px;" type="checkbox"/>
wine:		ounces per (check one):	day <input style="width: 20px;" type="checkbox"/>	week <input style="width: 20px;" type="checkbox"/>
liquor:		ounces per (check one):	day <input style="width: 20px;" type="checkbox"/>	week <input style="width: 20px;" type="checkbox"/>

Smoking: no ☐ yes ☐ →

↓

Passive exposure in the home? no ☐ yes ☐

Number of pack years:
(average # packs per day multiplied by # of years)

Exposure to pets: no ☐ yes ☐ →

# of cats:	# of dogs:
# of other pets:	specify: _____

FIG 1. History/demographics. EDC, Estimated date of confinement; OTCs, over-the-counter drugs.

pregnancy is even more limited. Therefore these new drugs, which may be not only more effective but have fewer adverse effects, are frequently bypassed for older treatments.

For an expectant mother, it is not reassuring to be told that her fetus is going to be exposed to drugs that have not been studied and proven to be safe in clinical trials in pregnant women, and therefore cannot be deemed safe.

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HISTORY / OUTCOME OF PRIOR PREGNANCIES

	Pregnancy # →	1st	2nd	3rd	4th	5th
	CODES (9 = unknown)					
Gestational Age at Delivery	(weeks)					
Birthweight	(grams)					
Abortion	0 = none 1 = elective 2 = spontaneous					
Maternal Asthma	0 = none 1 = better 2 = worse 3 = same as before pregnancy					
Other Allergic Disorders	0 = no 1 = yes - specify below					
Congenital Malformations	0 = no 1 = yes - specify below					
Other Fetal Complications	0 = no 1 = yes - specify below					

For each "Yes" response above, please describe and note pregnancy #:

Other Allergic Disorders: _____

Congenital Malformations: _____

Other Fetal Complications: _____

FIG 2. History/outcome of prior pregnancies.

The Food and Drug Administration (FDA) has attempted to provide guidance for physicians who are selecting drugs for use in pregnant women with a letter-based classification system: A, B, C, D, or X (Table I). In this system drugs listed as Pregnancy Category A are deemed safest, and those listed as Pregnancy Category X are

deemed unsafe and contraindicated. These categories are based primarily on data from animal studies. At present, there are no Category A drugs available for use in treating pregnant patients with asthma or allergies. With the knowledge that inadequately controlled asthma may be detrimental to mother and fetus alike, the most effective

CLINICAL FOLLOW-UP

*** Please complete

a Medication form

 → for the initial pregnancy visit
→ when medications have changed since the last visit

an ER/Hospitalization form

 → for each emergency room visit or hospitalization since last visit

FIG 3. Clinical follow-up.

Most traditional methods for studying drugs, such as randomized trials, may be inappropriate during pregnan-

FIRST VISIT (SUBMIT WITH PAGES 1 and 2 after initial study visit)

ACAA&I REGISTRY for ALLERGIC and ASTHMATIC PREGNANT PATIENTS (PILOT STUDY)

Patient's Initials: Study ID #: Center or Physician ID #:
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MEDICATIONS

#	Medication	#	Medication	#	Medication	#	Medication	#	Medication
1	acrivastine	11	budesonide	21	epinephrine	31	loratadine	41	prednisone
2	albuterol	12	chlorpheniramine	22	flunisolide	32	metaproterenol	42	promethazine
3	aminophylline	13	cetirizine	23	fluticasone	33	methylprednisolone	43	pseudoephedrine
4	antazoline	14	clemastine	24	quaifenesin	34	naphazoline	44	pyrilamine
5	astemizole	15	codeine	25	hydrocortisone	35	nedocromil	45	salmeterol
6	atropine	16	cromolyn	26	hydroxyzine	36	oxymetazoline	46	tetrahydrozoline
7	azelastine	17	dexamethasone	27	ipratropium	37	pheniramine	47	terbutaline
8	beclomethasone	18	dexchlorpheniramine	28	isoetharine	38	phenylpropanolamine	48	terfenadine
9	bitolterol	19	dextromethorphan	29	ketorolac	39	pirbuterol	49	theophylline
10	brompheniramine	20	diphenhydramine	30	iodoxamide	40	prednisolone	50	triamcinolone
88	other(s), specify:							51	tripolidine

Inhaled Corticosteroids

Med #	# Puffs / Day	Start Date 00 / 00 / 00 = before conception 99 / 99 / 99 = unknown	Stop Date 00 / 00 / 00 = continuing 99 / 99 / 99 = unknown

Other Medications

Med #	Delivery 1 = Nasal 4 = Injected 2 = Oral 5 = Inhaled 3 = Ophthalmic	Dosage Frequency 1 = < OD 4 = TID 2 = OD 5 = QID 3 = BID 6 = > QID	Start Date 00 / 00 / 00 = before conception 99 / 99 / 99 = unknown	Stop Date 00 / 00 / 00 = continuing 99 / 99 / 99 = unknown

FIG 4. Medications. OD, once a day; BID, twice a day; TID, 3 times a day; QID, 4 times a day.

cy for reasons that have been discussed by other participants during this workshop. A "Registry for Allergic and Asthmatic Pregnant Patients (RAAPP)" has been initiated by the ACAAI and funded by an unrestricted grant

from Rhône Poulenc Rorer. Such a study will collect prospective data for all medications prescribed for those patients enrolled in the study.

Initially, a pilot study will be conducted by the approx-

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EMERGENCY ROOM VISIT / HOSPITALIZATION

ER Visit: ☐ Hospitalization: ☐ Gestational Age: wks Trimester:
(99 = unknown)

Date of Admission or ER Visit: If hospitalized, Discharge Date:
month day year month day year

Chief Complaint: _____

Pulmonary Function before treatment (999 = unknown)

Peak Flow: liters / min Arterial Blood Gasses

Predicted FEV₁: % pH: units pO₂: mmHg

Pulse Oximetry: % pCO₂: mmHg O₂ sat: %

Treatment	no	yes	med #	# Medication	# Medication	# Medication
Inhaled beta agonist	☐	☐	→	2 albuterol	32 metaproterenol	99 unknown
				28 Isoetharine	47 terbutaline	
				88 other, specify:		
Inhaled anticholinergic	☐	☐	→	6 atropine	27 ipratropium	99 unknown
Injected beta agonist	☐	☐	→	21 epinephrine	47 terbutaline	99 unknown
IV aminophylline	☐	☐				
IV corticosteroid	☐	☐	→	25 hydrocortisone	33 methylprednisolone	99 unknown
				88 other, specify:		
Other treatment	☐	☐	→	specify: _____		

Obstetrical Complications

	no	yes	uncertain		no	yes	uncertain
Hyperemesis gravidarum	☐	☐	☐	Hyperglycemia	☐	☐	☐
Preeclampsia	☐	☐	☐	Uterine bleeding	☐	☐	☐
Uterine contractions	☐	☐	☐	Abruption	☐	☐	☐
Fetal distress	☐	☐	☐	Placenta Previa	☐	☐	☐
Other complication(s)	☐	☐	→ specify: _____				

	no	threatened	incomplete	complete
Abortion	☐	☐	☐	☐

FIG 5. Emergency room visit/hospitalization.

imately 3500 fellows and members of the ACAAI. In the first phase, 800 patients who require inhaled corticosteroids in their treatment and who are in their first or second trimester of pregnancy will be enrolled. The major

outcome variable will be small for gestational age (SGA). SGA may be defined as a birth weight below the 10th percentile for gestational age. Thus the incidence of SGA in a population demographically equivalent to the reference

ing inhaled corticosteroids. However, data will be collected and analyzed for all drugs used during the study. Examples of the case report forms being used in the initial pilot study are included (Figs 1-7).

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Labor and Delivery (continued)

Obstetrical Intervention

	no	yes	
Epidural anesthesia	☐	☐	
Pitocin augmentation	☐	☐	
Operative delivery forceps	☐	☐	
Vacuum extraction	☐	☐	
C-section	☐	☐	
Induction	☐	☐	→ specify drug: _____
Other intervention	☐	☐	→ specify: _____

Neonatal Status

Multiple birth? no yes
☐ ☐ → If yes, please complete this page for each newborn

Birthweight: gms
 or
 lbs oz

5 min. Apgar:

Neonatal Complications

	no	yes	
Transient tachypnea	☐	☐	
RDS	☐	☐	
Congenital malformation(s)	☐	☐	→ specify: _____
Other complication(s)	☐	☐	→ specify: _____

FIG 7. Labor and delivery/pregnancy outcome (continued).

After completion of a pilot study, it is the intention to open the registry for much wider physician participation. These might include obstetricians (many of whom treat medical complications of pregnancy themselves), pulmonologists, family physicians, internists, and other allergists who are not members of the ACAAI. Furthermore, any pregnant patient with allergic disorders or asthma will be eligible for enrollment in the second phase, even if no treatment is necessary during the pregnancy. In

this manner, data will be collected for the multitude of classical and nonsedating antihistamines, decongestants, nasal corticosteroids, noncorticosteroid anti-inflammatory agents such as cromolyn and nedocromil, bronchodilators, and leukotriene inhibitors or antagonists.

When completed, RAAPP will be the largest prospective study to date evaluating the safety of drugs used to treat asthma and allergic disorders during pregnancy. The

study will not only offer investigators the opportunity to analyze data on traditional drugs but will also enable them to evaluate the safety of newer medications that are being taken at the time of conception and during the early weeks of pregnancy, often before a woman realizes that she has conceived.

In 1993, The Working Group on Asthma and Pregnancy of the National Asthma Education Program, chaired by Allan T. Luskin, MD, provided "Guidelines for the Management of Asthma During Pregnancy."² These guidelines are a major step in improving care of the pregnant woman with asthma and her fetus. The proposed

registry will provide the next step by accumulating data, hopefully reassuring, on the efficacy and safety of medications for the treatment of this serious and frequent medical complication of pregnancy.

REFERENCES

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