

**XXXI** CONGRESO  
INTERNACIONAL



# **XXXI** CONGRESO INTERNACIONAL **SCAI 2025**

SOCIEDAD CHILENA DE ALERGIA E INMUNOLOGIA

# ¿Cuándo y cómo reintroducir fármacos en Exantema MP a Drogas?

Dra Paola Toche Pinaud  
Inmunología –Alergología

Alergomed- Clínica Meds



Depende.....

Familia de fármacos  
Tipo de reacción  
Estudio alérgico

# ¿Cuándo y cómo reintroducir fármacos en Exantema MP a Drogas?

- Tests de Provocacion Oral
- Alergia a **Inhibidores de Bomba de Protones**
- Hipersensibilidad a **AINEs**

# Clasificación



- Inmediatas ( < 1h )
  - IgE
  - Activ directa Mastocito
- Retardadas/No Inmediatas ( >1h)
  - Linf T
  - IgG antígeno-específico
  - Activación complemento
- Aceleradas (1-6h)
  - IgE o Linf T

Urticaria, angioedema, prurito, tos, conjuntivitis, rinitis, vómitos/diarrea, broncoespasmo, disnea y anafilaxia

Exantema MP o morbiliforme, eccema, urticaria y AE retardados (5-6 días). Nefritis, neumonía, anemia hemolítica, citopenia, hepatitis, vasculitis , enf suero CON o SIN síntomas cutáneos (>1h- semanas)  
Rx severas (SSJ, NET, DRESS )



# Test de provocación (TP)

Gold standard en Diagnóstico de Hipersensibilidad a Fármacos

Dg: Historia , tests cutáneos \*\* ( prick , IDR y parches) si negativos  TP

\*\* *Betalactam, AINEs , QT y Biol*

*Allergy. 2013;68(6):702-712.  
Contact Dermatitis. 2022;86(5):344-356.*



# Test de provocación (TP)

## INDICACIONES

- Establecer diagnóstico en historia sugerente con estudio negativo o no disponible
- Excluir hipersensibilidad a fármaco (riesgo bajo o intermedio *delabeling*)
- Dar alternativa segura de fármaco (descartar Rx cruzada misma familia)
- Varios fármacos involucrados: demostrar tolerancia a fármacos de otra clase involucrados



# Test de provocación

## CONTRAINDICACIONES

- Estudio *in vivo* o *in vitro* +
- Anafilaxia G3
- Toxicodermias
- Alt órgano específicas
- Autoinmunidad

### CONTRAINDICACIONES RELATIVAS

- Comorbilidades : asma no controlada, enf pulm crónica sev , cardiopatía isquémica sev
- Embarazo excepto alergia PNC (sífilis) , alergia anestésico local ( necesidad)

# Test de provocación



Inicio 1/10 dosis terapéutica seguida de 2/10 y luego 7/10 cada 60min

Rx inmediatas no severa : 1/10 dosis

Rx no inmediatas 1/10 dosis

Otros protocolos: 1/3 dosis total cada 60 min

Anafilaxia iniciar 1/100 o 1/1000 dosis total acumulada

ENDA : multistep challenge iniciando 1/10 de la dosis terapéutica en pacientes con rx no severa o IgE mediadas

Observación 3 a 6 h o mas....

*Expert Rev Clin Immunol. 2017;13:1017–27.  
Allergy Asthma Clin Immunol. 2007;3:114–22.  
J Allergy Clin Immunol Pract. 2018;6:1226–35.  
Allergy. 2024;79:565–579.*

# Test de provocación



Supervisión y equipamiento médico

Medio hospitalario ( riesgo intermedio y alto)

PA, FC , saturación , Piel , PEF

Suspensión ...

Antihistam y prednisona > 10mg

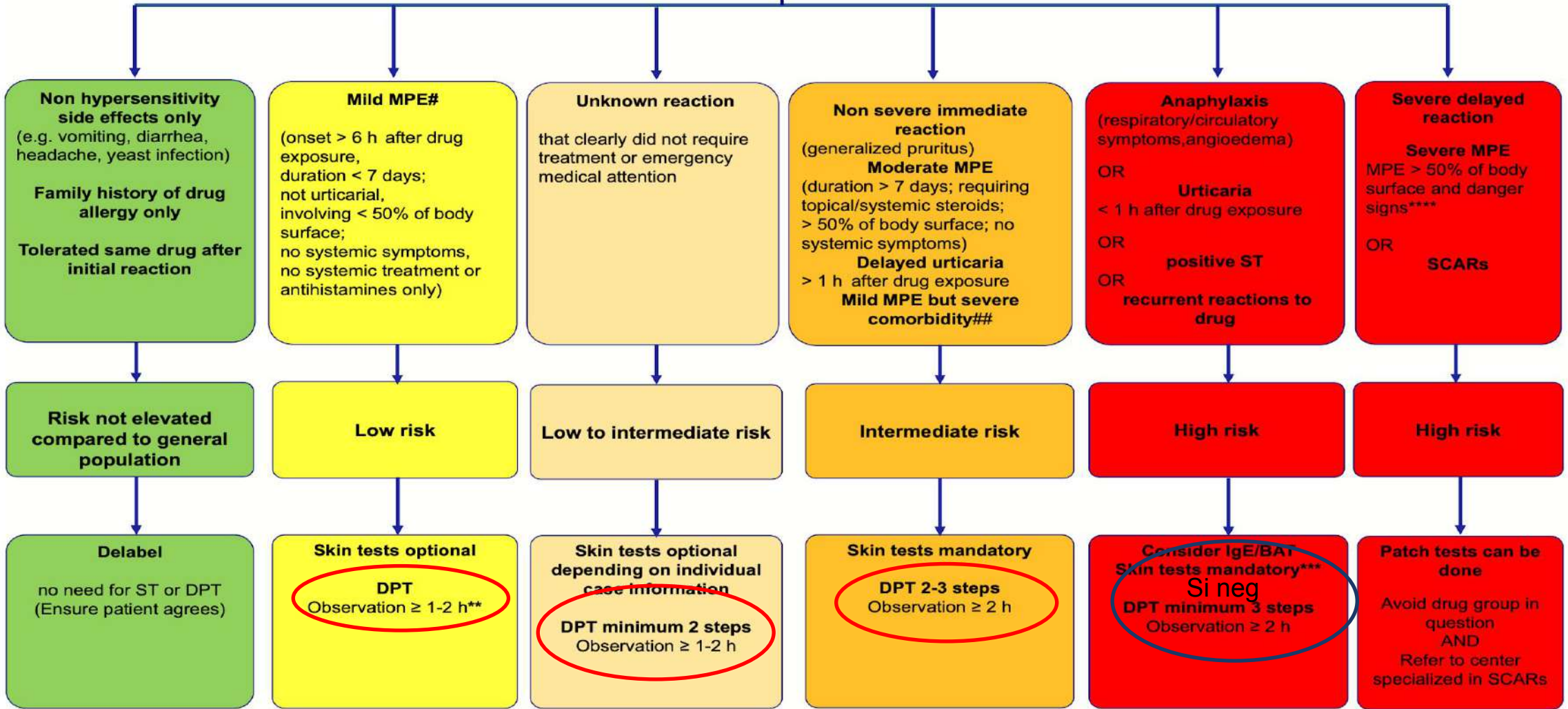
Inhib ECA NO suspender

Antidepresivos e Inmunosupresores evaluar riesgo

Betabloq ?

# TP → Estratificación

Reaction evoking drug hypersensitivity in adults and children\*



DPT NO



¿Cuándo y cómo reintroducir fármacos en Exantema MP a Drogas?

Inhibidores bomba de protón

Antiinflamatorios No esteroideos (AINEs)



# INHIBIDORES BOMBA PROTON



- Uso frecuente
- RAM~ 1-3%
- Inducción resp Th2 : alimentos , inhalantes
  
- **Hipersensibilidad inmediata** : Anafilaxia (hasta 50%), Urticaria , Rash MP
- Frecuente rx cruzada (~ 69 % a 1 , 8% a todos)
  
- Hipersensibilidad retardada : raras RMP, toxicodermias



# INHIBIDORES BOMBA PROTON

Grupos PPI anillos: benzimidazol (B) , piridina (P) y Imidazopiridina (I)

- Omeprazol Esomeprazol Pantoprazol (B)
- Lanzoprazol Rabeprazol *dexlanzaprazol* (P)
- Tenatoprazol (I)

<b>Benzimidazole group</b>				
	R1	R2	R3	R4
Omeprazole	-OCH <sub>3</sub>	-CH <sub>3</sub>	-OCH <sub>3</sub>	-CH <sub>3</sub>
Lansoprazole	-	-CH <sub>3</sub>	-OCH <sub>2</sub> CF <sub>3</sub>	-
Pantoprazole	-OCF <sub>2</sub> H <sub>3</sub>	-OCH <sub>3</sub>	-OCH <sub>3</sub>	-
Rabeprazole	-	-CH <sub>3</sub>	-O(CH <sub>2</sub> ) <sub>3</sub> -OCH <sub>3</sub>	-
Esomeprazole	-OCH <sub>3</sub>	-OCH <sub>3</sub>	-OCH <sub>3</sub>	-CH <sub>3</sub>
Dexlansoprazole	-	-CH <sub>3</sub>	-OCH <sub>2</sub> CF <sub>3</sub>	-
<b>Imidazopyridine group</b>				
R1	R2	R3	R4	
Tenatoprazole	-	-CH <sub>3</sub>	-OCH <sub>3</sub>	-CH <sub>3</sub>

# INHIBIDORES BOMBA PROTON



- Prick tests e IDR alta E baja S , Excelente VPP!

PPIs	SPT (mg/mL)	IDT <sup>a</sup> (mg/mL)
Esomeprazole	40	4
Lansoprazole	30	1.5
Omeprazole	40	4
Pantoprazole	40	4
Rabeprazole	20	2

IDR : 1/1000, 1/100, 1/10

- BAT : útil

- Si negativos  TPO

# INHIBIDORES BOMBA PROTON



Hypersensitivity <sup>a</sup>	Cross-reactivity rate, n (%)
Any PPI	117/190, (61.6)
Omeprazole	60/69, (87.0)
Lansoprazole	28/79, (35.4)
Pantoprazole	18/26, (69.2)
Rabeprazole	1/4, (25.0)
Esomeprazole	10/12, (83.3)

	Omeprazole reaction rate n (%)	Lansoprazole reaction rate n (%)	Pantoprazole reaction rate n (%)	Rabeprazole reaction rate n (%)	Esomeprazole reaction rate n (%)
Allergy to <sup>a</sup>					
Omeprazole	—	21/34 (61.8)	50/53 (94.3)	16/17 (94.1)	20/23 (87.0)
Lansoprazole	8/43 (18.6)	—	14/57 (24.6)	7/47 (14.9)	9/48 (18.8)
Pantoprazole	13/16 (81.3)	3/11 (27.3)	—	5/9 (62.5)	9/12 (75.0)
Rabeprazole	1/3 (33.3)	0/2 (0)	0/2 (0)	—	1/2 (50.0)
Esomeprazole	6/7 (85.7)	0/3 (0)	6/9 (66.7)	1/3 (33.3)	—



# INHIBIDORES BOMBA PROTON

- **TPO** (TC-) : Riesgo bajo / intermedio : F incriminado , Riesgo alto : alternativa
- Intervalo 30/60 min
- Observación >3 h

Reference	Lobera, 2009 <sup>22</sup>	Bonadonna P, 2012 <sup>3</sup>	Kepil Ozdemir S, 2013 <sup>17</sup>	Sanchez-Morillas, 2014 <sup>23</sup>	Kepil Ozdemir S, 2016 <sup>18</sup>
Drug					
Omeprazole	5, 10, 20mg	5, 5, 10, 20mg	5, 10, 20mg	5, 10, 20mg	5, 10, 20mg
Pantoprazole	5, 10, 20mg	5, 5, 10, 20mg	5, 10, 20mg	10, 20, 40mg	5, 10, 20mg
Rabeprazole	nd	5, 5, 10, 20mg	5, 10, 20mg	5, 10, 20mg	5, 10, 20mg
Esomeprazole	nd	5, 5, 10, 20mg	5, 10, 20mg	nd	5, 10, 20mg
Lansoprazole	3.25, 7.5, 15 mg	5, 10, 15 mg	7.5, 15, 30 mg	3.25, 7.5, 15 mg	7.5, 15, 30 mg



# AINES (antiinflamatorios no esteroideos)

- Principal causa de Hipersensibilidad a fármacos :
  - 0,5- 5,7 % poblac gral.
  - 20 % en PNS y 30 % UC

- Clasificación:

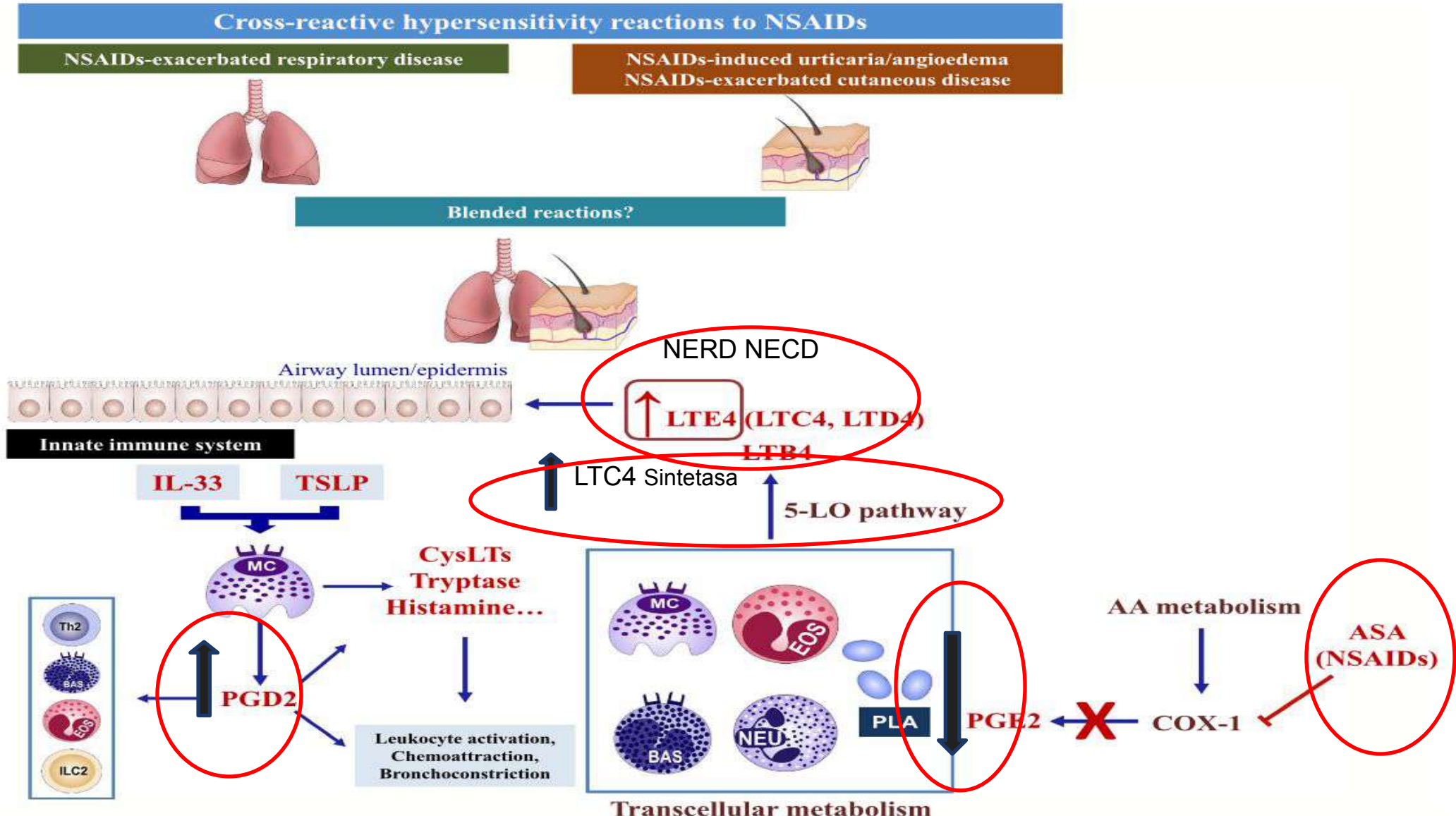
1- Reacciones de Hipersensibilidad Cruzada (> frec)

2- Reacciones de Hipersensibilidad Selectiva o Alérgica (IgE , Linfocitos T)

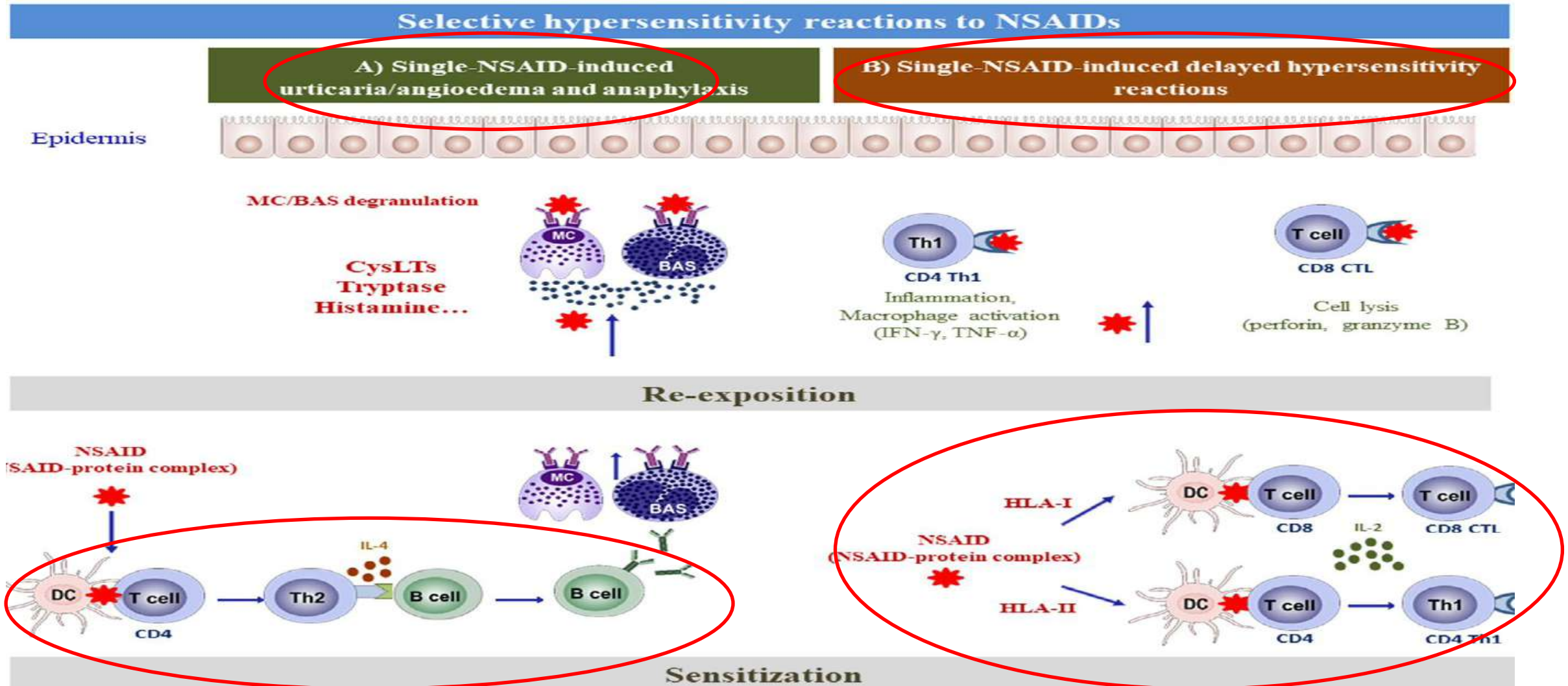
*Allergy. 2020;75:561–575.*

*Immunol Allergy Clin North Am. 2013;33(2):135-145.*

# AINEs: Mec Hipersensibilidad Cruzada



# AINEs: Mec. Hipersensibilidad Selectiva (Alérgica)





## Hipersensibilidad Cruzada (No Alérgica)

**TABLE 2** Proposed classification of NSAIDs hypersensitivity including phenotypes previously not considered by the EAACI

Hypersensitivity type	Phenotype	Latency of reaction	Underlying chronic disease	Underlying mechanism
Cross-reactive	NSAIDs-induced urticaria/angioedema (NIUA)	<24 h	No	COX-1 inhibition 60% coS acaros /TPO
	NSAIDs-exacerbated cutaneous disease (NECD)		Chronic spontaneous urticaria	
	NSAIDs-exacerbated respiratory disease (NERD)		Rhinosinusitis and/or asthma	TP inh/TPO
	Blended reactions (BRs) 25%			Probably COX-1 inhibition
	Food-dependent NSAID-induced anaphylaxis (FDNIA)		Food allergy	Unknown
Selective	Single-NSAID-induced urticaria/angioedema and anaphylaxis (SNIUAA)		No underlying chronic disease	IgE-mediated
	NSAIDs-multiple selective immediate reaction (NMSIR)			Unknown, probably IgE-mediated
	Single-NSAID-induced delayed hypersensitivity reaction (SNIDHR)	>24 h		T cell mediated



## Hipersensibilidad Selectiva (Alérgica)

**TABLE 2** Proposed classification of NSAIDs hypersensitivity including phenotypes previously not considered by the EAACI

Hypersensitivity type	Phenotype	Latency of reaction	Underlying chronic disease	Underlying mechanism
Cross-reactive	NSAIDs-induced urticaria/angioedema (NIUA)	<24 h	No	COX-1 inhibition
	NSAIDs-exacerbated cutaneous disease (NECD)		Chronic spontaneous urticaria	
	NSAIDs-exacerbated respiratory disease (NERD)		Rhinosinusitis and/or asthma	
	Blended reactions (BRs)			Probably COX-1 inhibition
	Food-dependent NSAID-induced anaphylaxis (FDNIA)		Food allergy	Unknown
Selective	Single-NSAID-induced urticaria/angioedema and anaphylaxis (SNIUAA)	>24 h	No underlying chronic disease	IgE-mediated
	NSAIDs-multiple selective immediate reaction (NMSIR)			Unknown, probably IgE-mediated
	Single-NSAID-induced delayed hypersensitivity reaction (SNIDHR)			T cell mediated



# AINEs

- TP

- Confirma diagnóstico
- Descartar Rx cruzadas
- Dar alternativas

- Condiciones

- Se puede mantener antiH1 y antiIgE en UC
- Anti LT en asma





**Table 4** Provocation test to NSAID in children

	Drug	Dose (mg/kg)	Subsequent doses	Interval between doses (h)	Maximum dose (mg/kg)	Mean reaction time (h)
Kidon MI, 2007 [91]	ASA	2,5	Same dose	1	10	1–4
	Ibuprofen	2,5	Same dose	1	10	2–4
	Paracetamol	5	Same dose	1	20	2–4
Kidon M, 2018 [27]		1/10–1/4 of the maximum dose	Incremental doses	1	- Paracetamol 15–20 mg/kg/dose, -Ibuprofen 10 mg/kg/dose,	2–4 Additional doses of the drug can be necessary

ASA in mg	References
10-17-44-117-312	Bavbek S, <i>Allergol Immunopathol (Madr)</i> 2012;40(4):225-230
125-375	Asero R, <i>Int Arch Allergy Immunol</i> 2007; 144: 226-230
50-100-150-250	Doña I, <i>Clin Exp Allergy</i> 2011; (41) 86–95. Ariza A, <i>Cytometry A</i> 2014;85(5):400-7
1st day: 5-30-100. 2nd day: 150-300	Doña I, <i>Clin Exp Allergy</i> 2011; (41) 86–95
1st day: 5, 50,100. 2nd day: 250-500	Viola M, <i>Clin Exp Allergy</i> 2011;41(1):96-103
1st day: 50,100. 2nd day: 250-500	Viola M, <i>Clin Exp Allergy</i> 2011;41(1):96-103
1st day: 50-100. 2nd day: 250-500	Quiralte J, <i>J Allergy Clin Immunol</i> 1996; 98:678-685
1st day: 5, 50,100. 2nd day: 250-500	Quiralte J, <i>J Allergy Clin Immunol</i> 1996; 98:678-685
250-500	Sánchez-Borges M, <i>Ann Allergy Asthma Immunol</i> 2000;84:101–106. De Paramo BJ, <i>Ann Allergy Asthma Immunol</i> 2000;85:508–511
1-5-20-50-100-200-500	Messaad D, <i>Ann Intern Med.</i> 2004;140:1001-1006.
1st day: 50-150. 2nd day: 250-500	Doña I, <i>Allergy.</i> 2019 Jun;74(6):1135-1144
1 <sup>st</sup> day: 30-45 or 60 (at the discretion of the physician on the basis of the severity of the reported reaction)- 60 ó 180. 2nd day: 100-150-325-650	Woessner KM, <i>Annals Allergy Asthma Immunol</i> 2004; 93:339-344
40.5 or 81 or 162 mg (at the allergist's discretion)-325 mg	Li L, <i>J Allergy Clin Immunol Pract</i> 2022;10:1286-92

Paracetamol	References
1-10-50-250-500-1000	Messaad D, <i>Ann Intern Med.</i> 2004;140:1001-1006.
1/100 of the therapeutic dose, 1/10, and the remaining dose (maximum dose: 1000)	Viola M, <i>Clin Exp Allergy</i> 2011;41(1):96-103
1st day: 1/100 of the therapeutic dose. 2nd day: 1/10 of the therapeutic dose. 3rd day: full dose (1000)	Viola M, <i>Clin Exp Allergy</i> 2011;41(1):96-103
100-250-500	Quiralte J, <i>J Allergy Clin Immunol</i> 1996; 98:678-685
5-50-100-350	Doña I, <i>Clin Exp Allergy</i> 2011; (41) 86–95
50-100-350-500	Doña I, <i>Clin Exp Allergy</i> 2011; (41) 86–95. Ariza A, <i>Cytometry A</i> 2014;85(5):400-7
500-1000	Sánchez-Borges M, <i>Ann Allergy Asthma Immunol</i> 2000;84:101–106
¼ or 1/10 (at the allergist's discretion)-the remaining of the target dose	Li L, <i>J Allergy Clin Immunol Pract</i> 2022;10:1286-92

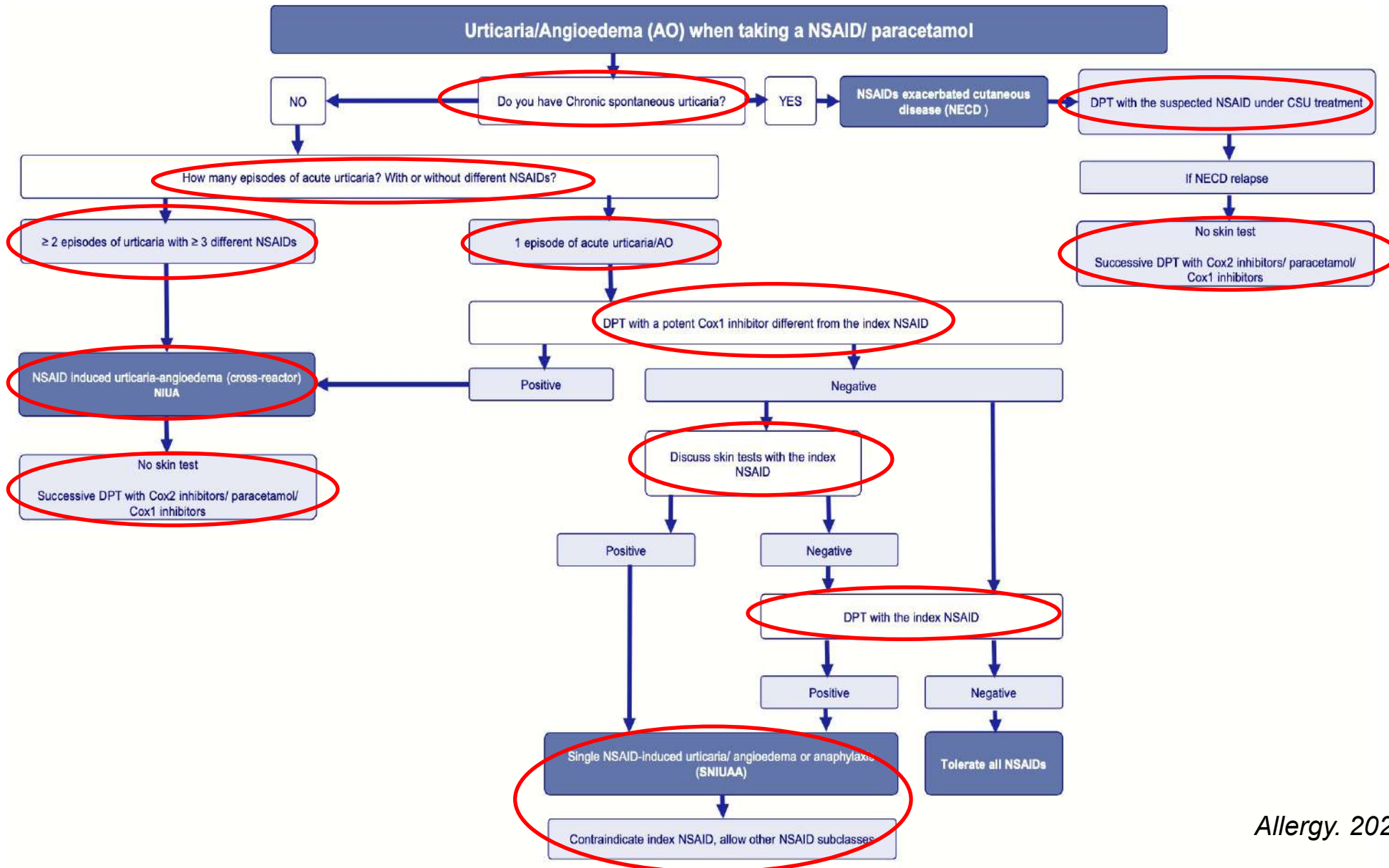


**TABLE 1** Classification of NSAIDs according to their chemical group

Chemical group	Drug
Salicylic acid derivatives	Acetylsalicylic acid (aspirin), sulphosalazine
Indole and indene acetic acids	Indomethacin, etodolac, sulindac
Hetero-aryl acetic acids	Diclofenac, ketorolac, tolmetin
Aryl-propionic acids	Ibuprofen, ketoprofen, flurbiprofen, naproxen, fenoprofen
Anthranilic acids (fenamates)	Mefenamic acid, meclofenamic acid
Enolic acids (oxicams)	Piroxicam, tenoxicam, meloxicam
Alkanones	Nabumetone
Diarylheterocycles (selective COX-2 inhibitors, coxibs)	Celecoxib, rofecoxib, etoricoxib
Pyrazolone derivatives <sup>a</sup>	Antipyrine, dipyron, propyphenazone
Para-aminophenol derivatives	Acetaminophen (paracetamol) <sup>b</sup>
Sulphonanilide derivatives	Nimesulide



# AINE





# EVOLUCIÓN NIUA

60% de los pac toleran ASA 6 años después... otros necesitan > dosis para gatillar síntomas

- Atopia > tiempo de persistencia de NIUA

## SEGUIMIENTO

6 años atópicos , 4-5 año no atópicos

Rx > 1h

Urticaria aislada

**Nuevo TPO**



# ¿Cuándo y cómo reintroducir fármacos en MP Exantema a Drogas?

- **Estratificación riesgo**
- Estudio (Tests cutáneos /in vitro)
- **Tests de Provocación oral**

¡Gracias!





<b>OMEPRAZOLE</b>	<b>Time interval</b>	<b>References</b>
5, 5, 10	30	Bonadonna et al.
5, 10, 20	30	Ozdemir et al. 2016
5, 10, 20	60	Sanchez-Morillas et al., Lobera et al.
<b>PANTOPRAZOLE</b>	<b>Time interval</b>	<b>References</b>
5, 5, 10, 20	30	Bonadonna et al.
5, 10, 20	30	Ozdemir et al. 2016
10, 20, 40	60	Sanchez-Morillas et al.
5, 10, 20	60	Lobera et al.
<b>ESOMEPRAZOLE</b>	<b>Time interval</b>	<b>References</b>
5, 5, 10, 20	30	Bonadonna et al.
5, 10, 20	30	Ozdemir et al. 2016
<b>RABEPRAZOLE</b>	<b>Time interval</b>	<b>References</b>
5, 5, 10, 20	30	Bonadonna et al.
5, 10, 20	30	Ozdemir et al. 2016
5, 10, 20	60	Sanchez-Morillas et al.
<b>LANSOPRAZOLE</b>	<b>Time interval</b>	<b>References</b>
5, 10, 15	30	Bonadonna et al.
7.5, 15, 30	30	Ozdemir et al. 2016
3.25, 7.5, 15	60	Sanchez-Morillas et al., Lobera et al.



# Clasificación

- Inmediatas ( < 1h )
  - IgE
  - Activación directa Mastocito

Urticaria, angioedema, tos, conjuntivitis, rinitis, vómitos/diarrea, broncoespasmo, disnea y anafilaxia

- Retardadas/No Inmediatas ( >1h )
  - IgG antígeno-específico
  - Activación complemento
  - Resp Linf T

- Aceleradas (1-6h)
  - IgE o Linf T

Exantema MP o morbiliforme, eccema, urticaria y AE retardados (5-6 días)  
Nefritis, neumonía, anemia hemolítica, citopenia, hepatitis, vasculitis , enf suero CON o SIN  
síntomas cutáneos (>1h- semanas)  
Rx severas (SSJ, NET, EM )

# Test de provocación Fármacos

**Table 1** Precautions, indications and contraindications of DPT

---

Contraindications

- SCAR, Serum Sickness-Like Reactions, internal organ or system involvement.
- Availability of alternative drugs, the drug will be probably not used in the future.
- Suggestive clinical history, positive allergy tests.
- Active disease such as uncontrolled asthma, urticaria, intercurrent infections, severe allergic rhinitis. Conditions that may affect treatment of allergic reactions, such as cardiovascular disease, treatment with  $\beta$ -blockers.

Precautions

- The risk/benefit balance must be discussed with patient and caregivers in children with anaphylaxis.

Indications

- Mild reactions.
  - Suggestive clinical history with negative or unavailable allergy tests.
  - Clinical history not suggestive and/or non-specific symptoms.
  - To exclude cross-reactivity with related drugs in subjects with known drug reaction.
-

# Test de Provocación

Inicio 1/10 dosis terapéutica seguida de 2/10 y luego 7/10 cada 60min

Otros protocolos: 1/3 dosis total cada 60 min

Anafilaxia iniciar 1/100 o 1/1000 dosis total acumulada

ENDA : multistep challenge iniciando 1/10 de la dosis terapéutica en pacientes con rx severa o IgE mediadas

Observación 3 a 6 h o mas....

# Test de Provocación

**Table 4** Provocation test to NSAID in children

	Drug	Dose (mg/kg)	Subsequent doses	Interval between doses (h)	Maximum dose (mg/kg)	Mean reaction time (h)
Kidon MI, 2007 [91]	ASA	2,5	Same dose	1	10	1–4
	Ibuprofen	2,5	Same dose	<b>X 3</b> 1	10	2–4
	Paracetamol	5	Same dose	1	20	2–4
Kidon M, 2018 [27]		1/10–1/4 of the maximum dose	Incremental doses	1	- Paracetamol 15–20 mg/kg/dose, -Ibuprofen 10 mg/kg/dose, -ASA 15–20 mg/kg/dose	2–4 Additional doses of the drug can be necessary on the following days at home

# Test de Provocación

**TPO +** AINE involucrado

TPO ASA (para definir mecanismo)

- Si positivo TPO ASA : mec no inmune CI AINES

- Si negativo TPO ASA : mec inmune TPO otro AINE no relacionado

# Test de Provocación

Paciente con anteced de rx urticarial a los 75 minutos post ingesta de ibuprofeno (sin anteced previo)