

# How Allergy took me down a PEG or two.

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# Case 1

- 49 year old man
- Generalised itchiness, urticaria, lip swelling, throat tightness, and dizzy 10 minutes after taking Tesco effervescent Vitamin C tablet.
- Had breakfast before that: weetabix with milk.
- Hypotensive
- Treated with IM adrenaline , antihistamine and steroid.
- PMH: hypertension
- Med: Bendroflumethiazide, Ramipril.
- Allergy : nil.
- Ex smoker

# Case 2

- 33 year old lady
- Widespread urticaria, breathing difficulties, legs and hand swelling and throat tightness after taking paediatrics Movicol
- Treated with Iv hydrocortisone and antihistamine
- PMH: nil
- Medication: nil
- Allergy : penicillin, lavender, Diprobase (immediate swelling of hand), Diclofenac, tramadol, erythromycin ( GI upset)
- Work as a midwife.

# Case 3

- 58 year old man
- Took Gaviscon tablet for dyspepsia
- Within a few minutes described Itchy throat, generalised pruritus, then chest tightness.
- Physical examination: covered with hives
- BP: 65/33 mm Hg and HR: 135 bpm
- Treated with IV fluid and IV hydrocortisone.
- PMH: eczema.
- Med: nil
- Allergy : Betnovate cream : urticaria.

# Skin prick test

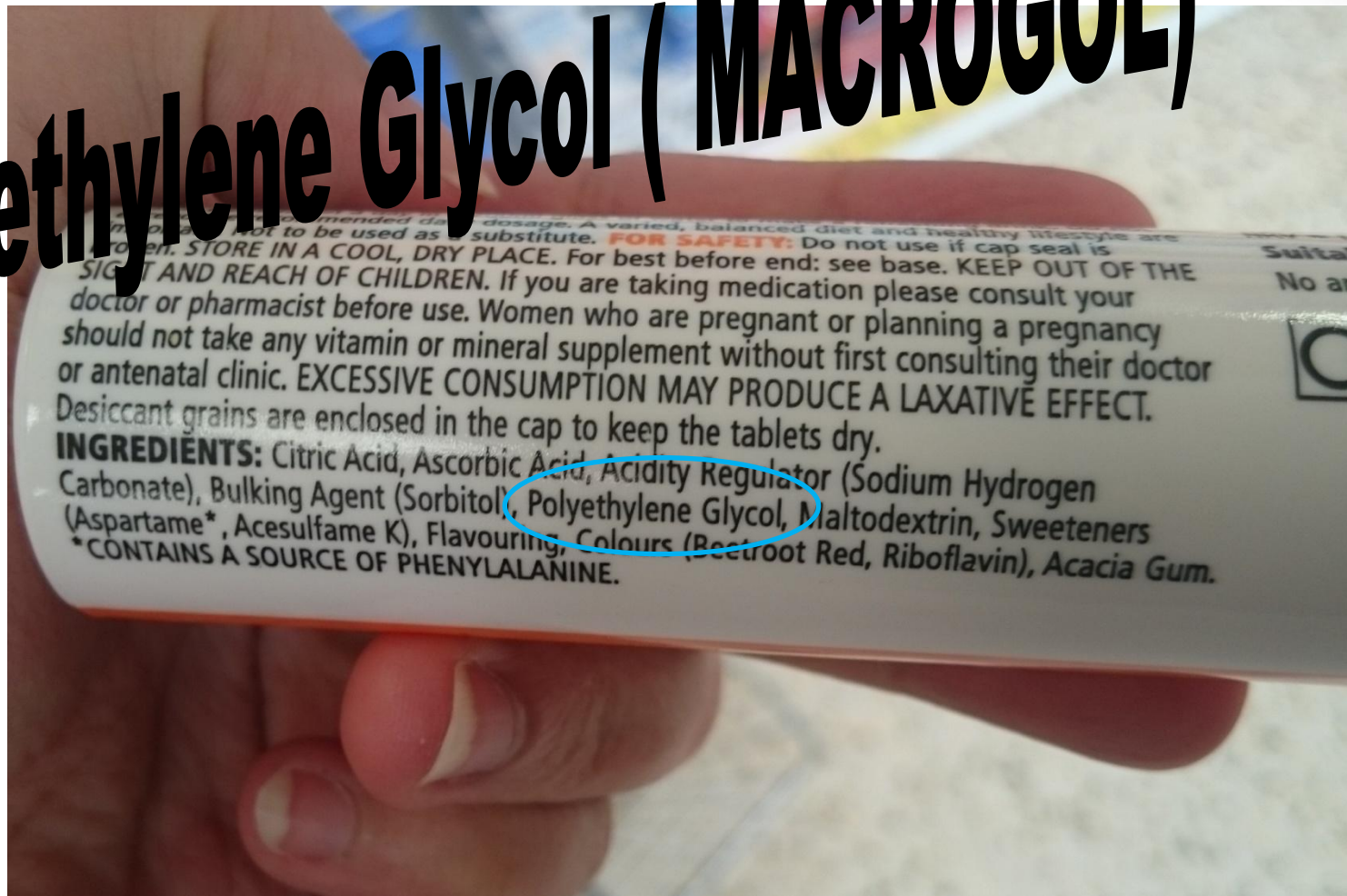






What is the common ingredient?

**Polyethylene Glycol (MACROGOL)**





50 Beutel

# MOVICOL®

Jeder 13,8 g Beutel MOVICOL® enthält folgende Bestandteile:

Macrogol 3350	13,125 g
Natriumchlorid	0,3507 g
Natriumhydrogencarbonat	0,1785 g
Kaliumchlorid	0,0466 g



PZN -7722044



Norgine B.V.,  
Hogehilweg 7,  
1101 CA Amsterdam ZO  
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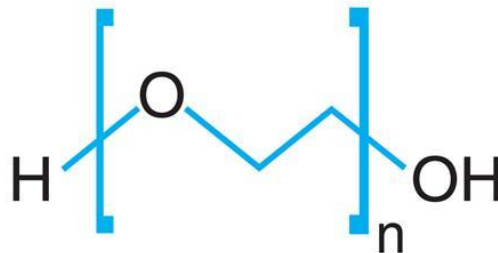
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# What is PEG?

- Polyethylene glycol
- Macrogol
- Polymers of ethylene oxide
- $\text{HO}-(\text{CH}_2-\text{CH}_2-\text{O})_n-\text{H}$
- Molecular weight varying from 6-60,000kDa
- 200-700 Da: liquid form, 1000-6000Da: solid form
- Used in numerous food, cosmetic and pharmaceutical preparations



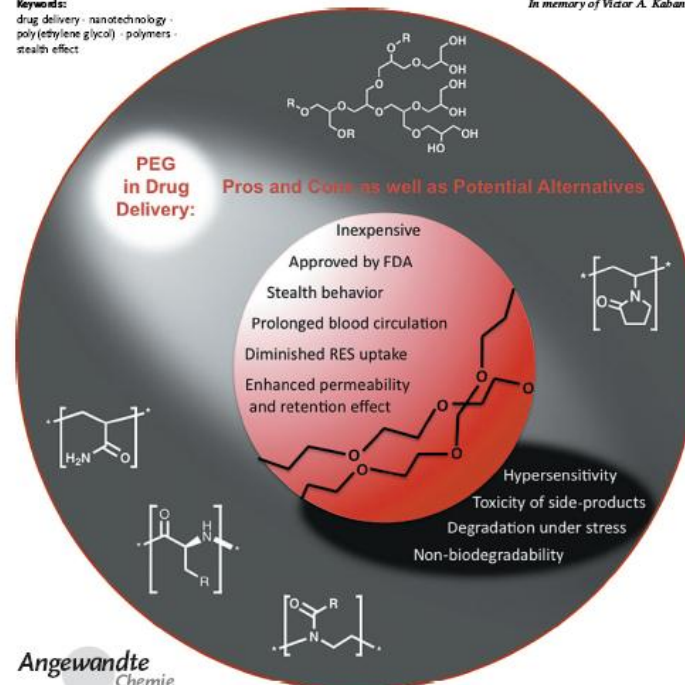
# PEG in medical use

- Often act as a solvent for substance otherwise insoluble in water.
- low toxicity with systemic absorption less than 0.5%
- Search on BNF and EMC revealed 700 medications containing PEG
- PEG3350 widely used as an osmotic laxative, bowel preparations
- Although PEG is generally considered to be safe for colonic cleansing, it can occasionally induce adverse events such as renal failure, hyponatremia, upper gastrointestinal bleeding or aspiration caused by vomiting, and even death
- Used in ANTIHISTAMINE.

- Pegylation refers to the modification of proteins by adding polyethylene glycol (PEG), leading to enhanced delivery, prolonged pharmacologic activity, and potentially reduced immunogenicity and antigenicity
- PEG-interferon alpha (Pegintron) and PEG-filgrastim (Neulasta)

**Keywords:**  
 drug delivery · nanotechnology ·  
 poly(ethylene glycol) · polymers ·  
 stealth effect

*In memory of Victor A. Kabanov*



# Examples of Common Medications containing PEG

- Anadin Original
- Bactroban Ointment
- Beechams Flu-Plus Caplets
- Benylin Four Flu Liquid
- Betadine Ointment
- Betnesol-N Eye, Ear, Nose Drops
- Buscopan Tablets
- Cellcept
- Cuprofen Ibuprofen Tablets
- Depo-Medrone
- Distaclor MR Tablets
- DULCO-LAX Perles
- Emeside Capsules
- Erythrocin
- Erythroped A
- Froben SR
- Gammagard SD I-V
- Gaviscon Advance Tablets
- Gentisone HC Ear Drops
- Imuran Tablets
- Karvol Decongestant Capsules
- Karvol Decongestant Drops
- Klaricid
- Losec
- Malarone Paediatric Tablets
- Non-Drowsy Sudafed 12 Hour Relief
- Nurofen Liquid Capsules
- Predsol-N Drops for Eye & Ear
- Rheumatac Retard 75
- Sandocal 400 & 1000
- Sando-K
- Seroxat
- Slow-K Tablets
- SUBCUVIA
- Syndol Caplets
- Syscor MR 10
- Voltarol Tablets
- Zovirax 2
- Zumenon

COMMON

# Commercial uses

- As anticaking agent, antifoaming agent, emulsifier and flavour enhancer
- E number: E1521
- Not mandatory to list PEG content in food.
- Edible salt, creamed cottage cheese, fizzy drinks, chewing gum, margarine, cocoa powder
- Toothpaste, aqueous solutions, sun block,

- Eat approximately 20-100 mg of PEG per day.
- A patient who eat chewing gum everyday and drank 500 ml of flavours drinks on occasions : regularly exposed to at least 30-50 mgs of PEG orally.

# PEG hypersensitivity

- believed to be chemically inert and thus a safe products
- But emerging reports of delayed and immediate hypersensitivity reactions to PEG containing substance.
- Sensitization through topical application, ingestion.
- 1<sup>st</sup> case report : immediate reaction to Lotrimin cream ( Fisher et al, 1977)<sub>6</sub>
- Anaphylaxis after intra-articular injection of Diprostene (Dewachter et al, 2005), citrate de betane effervescent tablets (Co-Minh et al, 2007)



**Table 1.** Seven Cases of Allergic Reaction or Anaphylaxis Associated With Polyethylene Glycol Solution Ingestion Reported Since 1990

Author (yr)	Age (yr), Sex	Presentation	Shock	Clinical outcome	Medical history	Drug history	Allergy history
Schuman et al. (1991) <sup>12</sup>	70, Male	Dyspnea, wheezing	Yes	Resolved	None		
Brullet et al. (1992) <sup>10</sup>	86, Female	Generalized urticaria	No	Resolved	Sigmoid colon cancer, atrial fibrillation	Amiodarone	
Stollman et al. (1996) <sup>9</sup>	70, Male	Tongue swelling, perioral edema, foot edema	No	Resolved	Hypertension	Captopril	
Lee et al. (2002) <sup>11</sup>	46, Male	Diffuse erythematous patch	No	Resolved	None	(-)	(-)
Assal et al. (2006) <sup>8</sup>	52, Female	Perioral edema	No	Resolved	Hypertension, coronary artery disease, aortic valve replacement		
Savitz et al. (2011) <sup>14</sup>	33, Female	Urticaria, flushing, dyspnea, arytenoid edema	No	Resolved	None		
Shah et al. (2013) <sup>13</sup>	52, Male	Flushing, urticaria, dyspnea, loss of consciousness	Yes	Resolved	UC		(-)
Current case	39, Male	Generalized skin rash, dyspnea, itching, dizziness	Yes	Resolved	None	(-)	(-)

LEE Sh et al, Intestinal research 2015;13 91):90-94

?loss of mucosal integrity promote systemic absorption of PEG

# Diagnosis

- Skin prick test
- Intradermal test
- One case report of oral challenge to identify reaction threshold dose



Figure 1.—Hives after oral challenge ES.

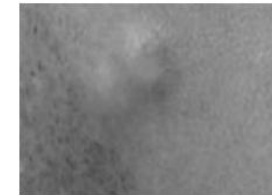
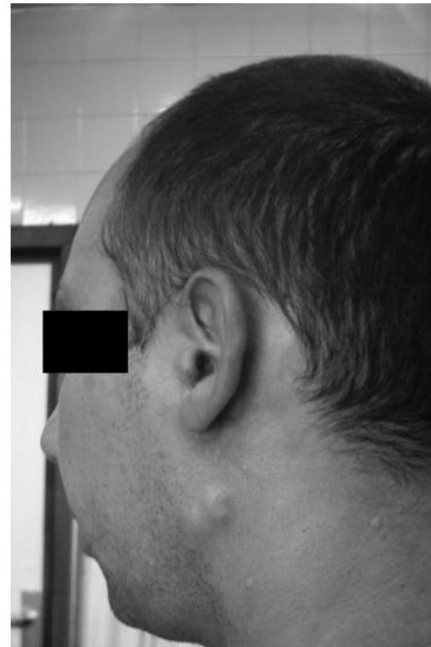


Figure 2.—Nodules after intradermic test with PEG-4000.

# Management

- Avoidance
- Due to lack of standardized nomenclature and clear product labelling, avoidance is made difficult.
- Important to investigate patient with anaphylaxis and educate the patients about risk reduction and anaphylaxis treatment.
- Increased use of PEG in household and pharmaceutical product (often as a hidden allergen), increase in the incidence of PEG allergy may be expected.

# References

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# Hypersensitivity to Polyethylene Glycols

- Journal of Clinical Pharmacology 2013
- Shah, Adkinson, Ishmael et al



# In brief

- Polymers of ethylene oxide used extensively in the cosmetic and pharmaceutical industry as surfactants, dispersing agents, bases for ointments and excipients in a wide variety of substances and medications
- Ranging in MW between 200 and 20 000g/mol they are characterised by different physical properties (ie viscosity) and different products may contain PEG polymers of different lengths
- PEG with a MW of 3350g/mol is widely used as an osmotic laxative
- PEG polymers can also be linked to proteins and other molecules to decrease toxicity and increase half life

- PEGs are believed to be chemically inert and thus 'safe products'
- Emerging reports suggest unrecognised allergenic potential



# Case Report

- 52 yr old caucasian male with history of Ulcerative Colitis
- Immediate allergic reaction to 3g of PEG 3350
- Previous non PEG enemas
  
- Immediate local reaction to sunscreen
- Swelling of lips after PEG containing toothpaste
- Metronidazole with PEG cause systemic reaction
- Self administration of adrenaline pen following naproxen (PEG)
- No symptoms unassociated with PEG



# Mechanism

- Naturally occurring PEG antibodies found in 'normal' people
- VIT results in antibodies which then disappear
- In some patients integrity of the gut may be an issue
- The overall scope of reactions to PEG is unknown
- ? Multiple drug allergy population

# Key Learning Point

- PEG may cause both delayed and immediate reactions
- SPT useful but ? IDT
- Patch testing possible

Consider the possibility of  
**PEG Allergy**

Especially in the context of multiple allergies

Do we now have a PEG to hang  
things on?