

# Just Say KNOW to Drugs

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2023



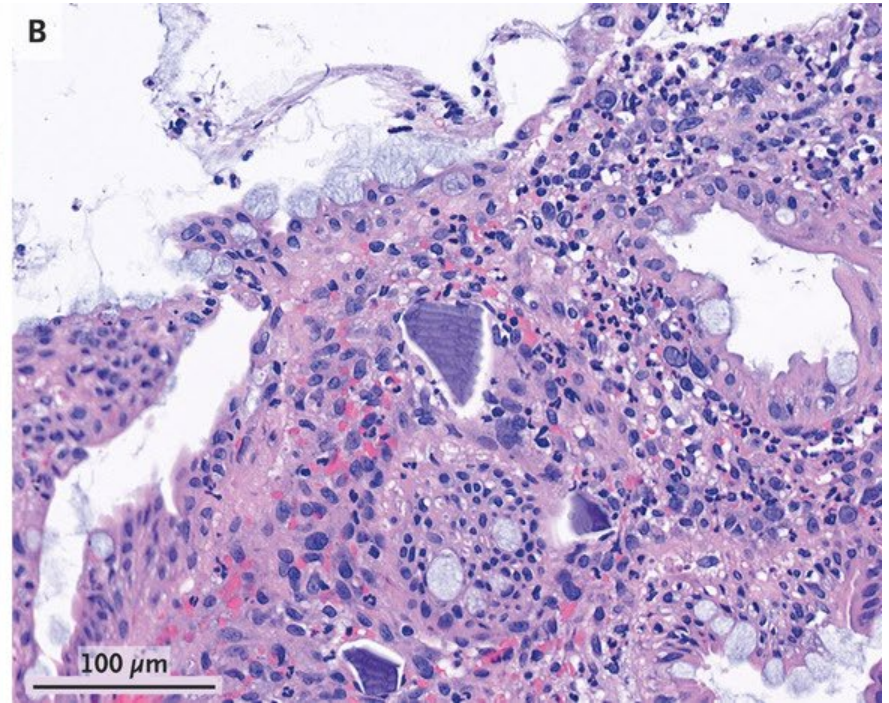
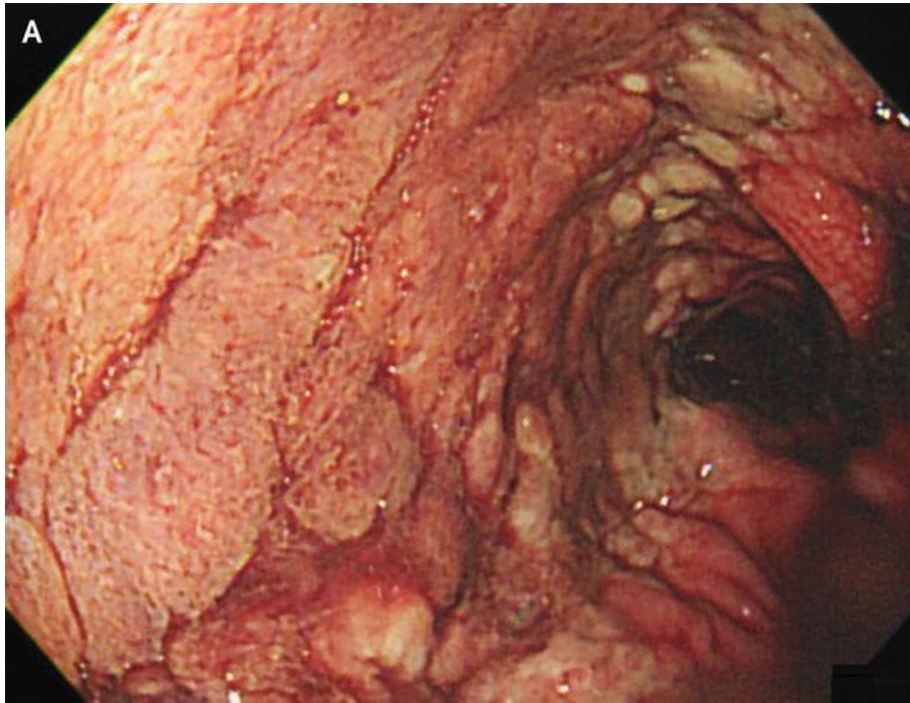
MEDICINE  
Division of Clinical Pharmacology  
& Toxicology



# Just Say Know to Drugs

- These slides are a collection of interesting, educational, often unusual but clinically important, visually illustrative, adverse events related to medications.
  - They do not represent the ‘day to day’ of the ClinPharmTox specialty, but are very helpful for the not infrequent occasion of ‘I think I’ve seen that type of problem somewhere before....’

A 58-year-old woman with AKI on CKD with hyperkalemia had sudden-onset bloody stools



What is the drug-related cause of this condition?

What is the prognosis?

# Serpentine Supravenous Hyperpigmentation

A 58-year-old woman with a history of metastatic uterine leiomyosarcoma presented to the dermatology clinic with a 1-month history of a nonpruritic rash on her arms. What is the cause? Will it resolve? How will it affect future treatment?

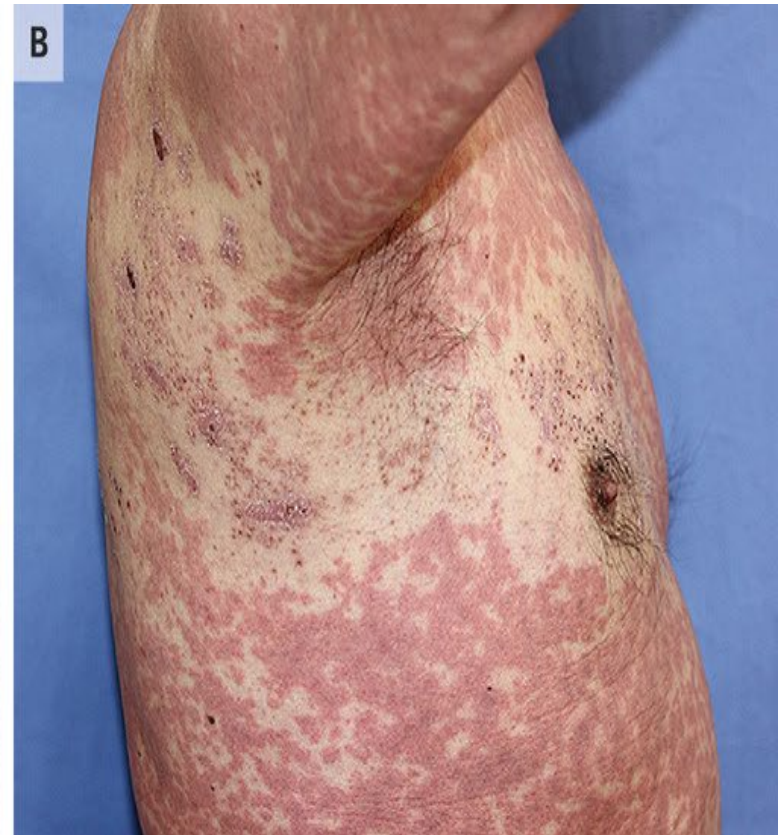


# 77 yr man with 2 day hx Rash

2 weeks prior, had an episode of zoster R chest.

Celecoxib is blamed as the cause.

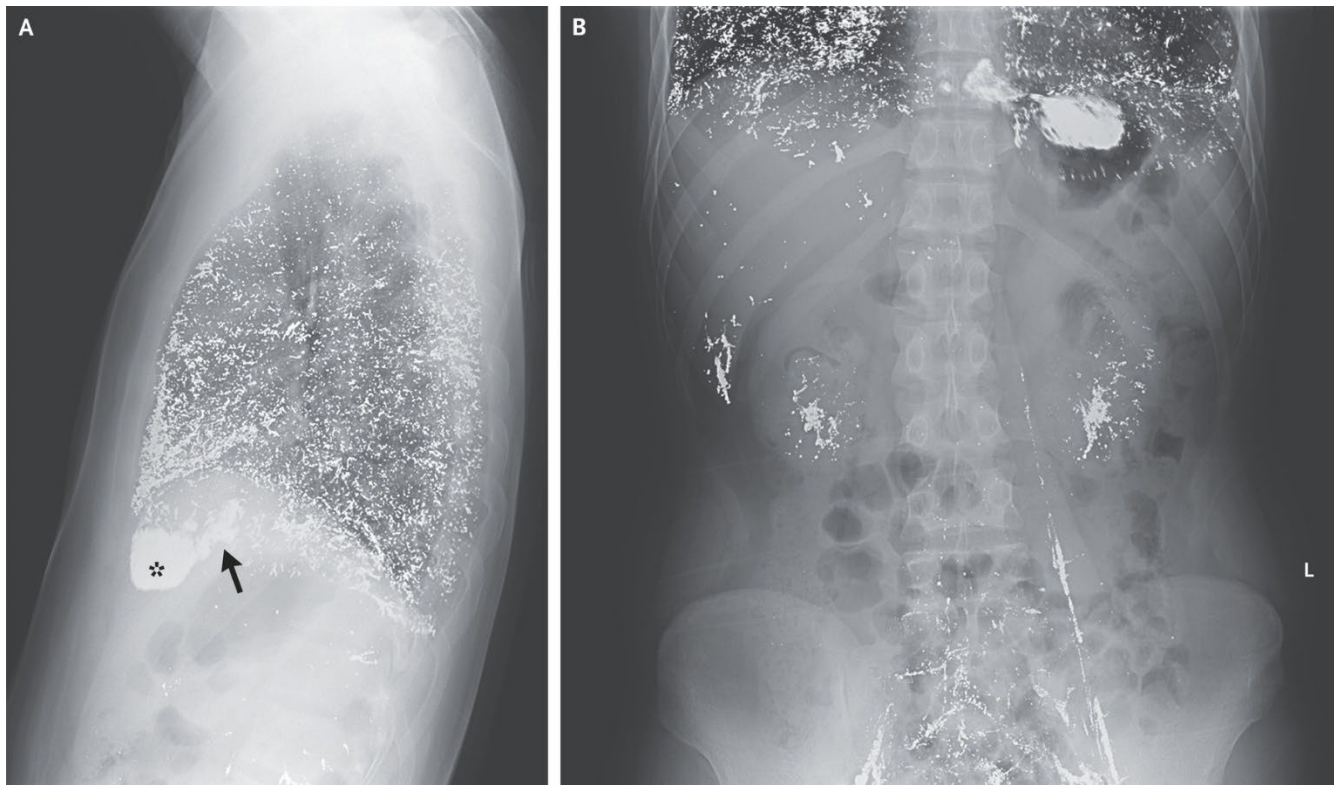
What is the picture demonstrating? Can the patient take celecoxib or other NSAIDs in future?



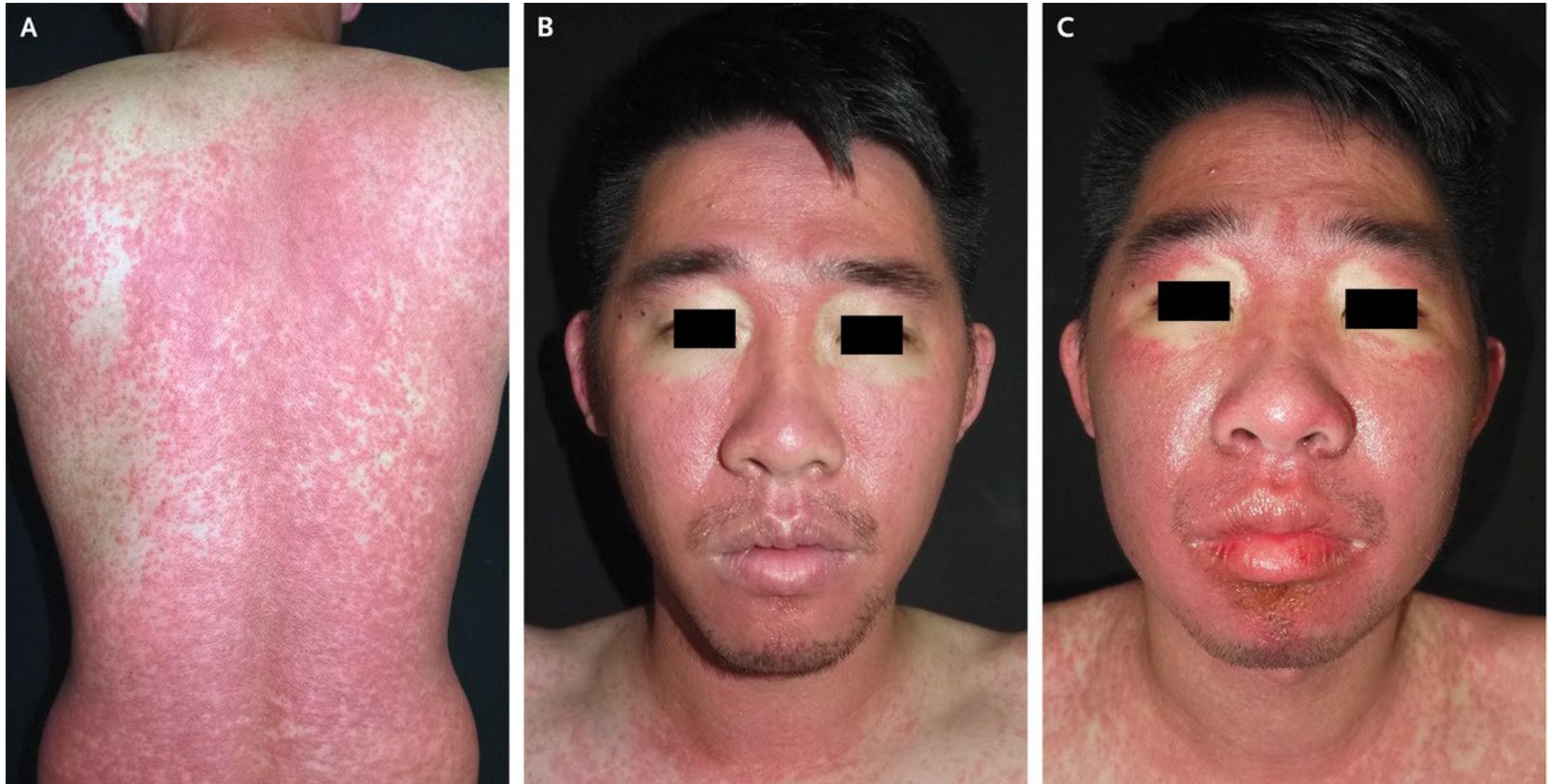
**70 yr old woman with Confusion, dyspnea and Acidosis. Background of depression and irritable bowel. What has she been taking for her IBS? Why the anion gap metabolic acidosis?**



**25 year-old man with X-ray Glitter.** Recently tried a folk remedy for tinea, now feeling nauseated and fatigued. coughing. What has he injected? What is the prognosis? What is the treatment?



30 year-old man with Rash and Fever of 39. 4 weeks before took antibiotic for folliculitis. High eosinophils and liver enzymes. What clinical prediction rule should we use for diagnosis? What is the prognosis? What is the advice about allergy alerts for him?



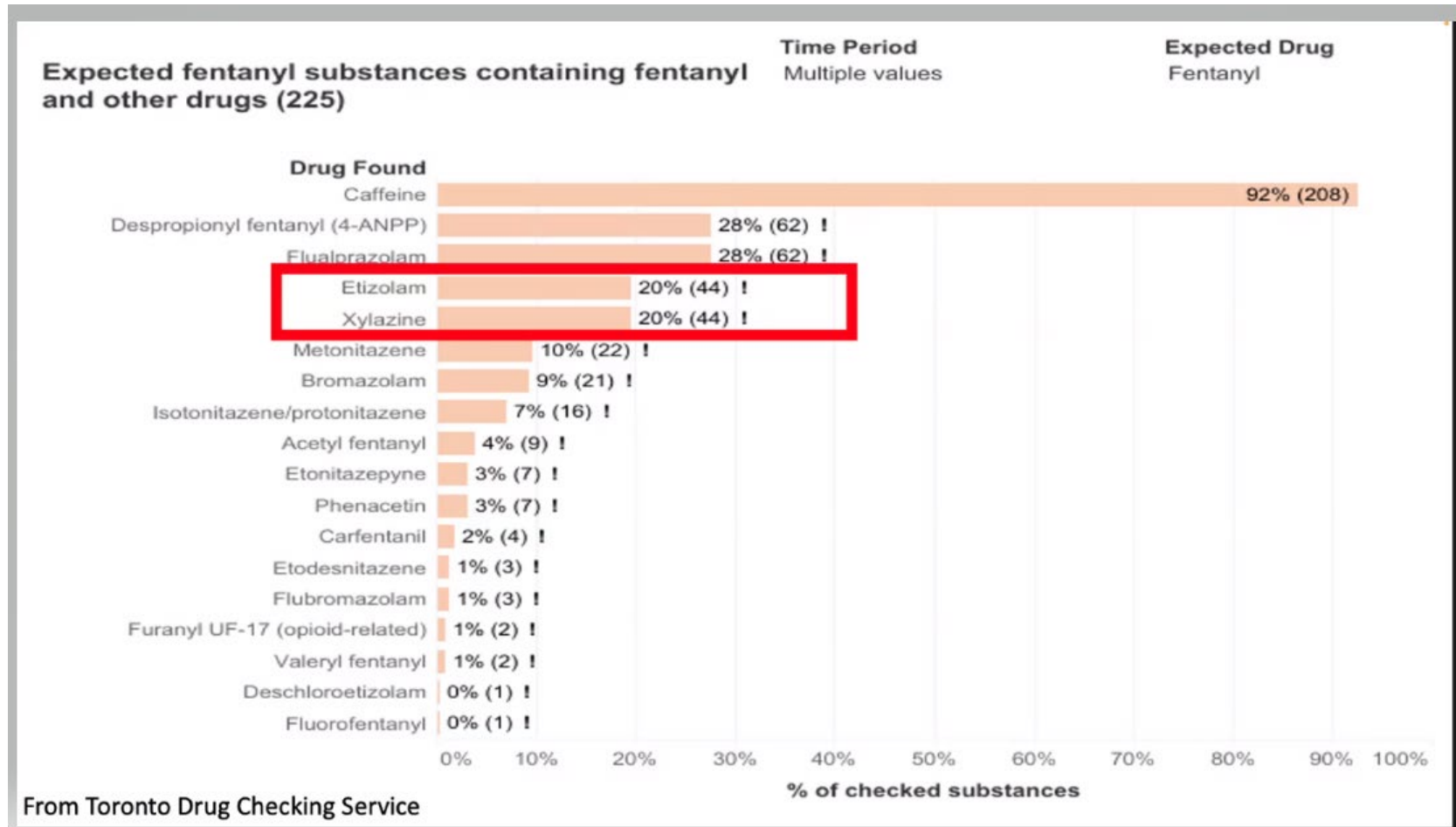
 JOURNAL of MEDICINE

Panel C is 4 days after Panel A and B

*Hung, W Chung. N Engl J Med 2022;387:167-167.*



# 24 year old male, altered LOC with hypotension



Samples from Jan to May 2022

Talk by Neil Hamilton, Tox Rounds May 20<sup>th</sup> 2022

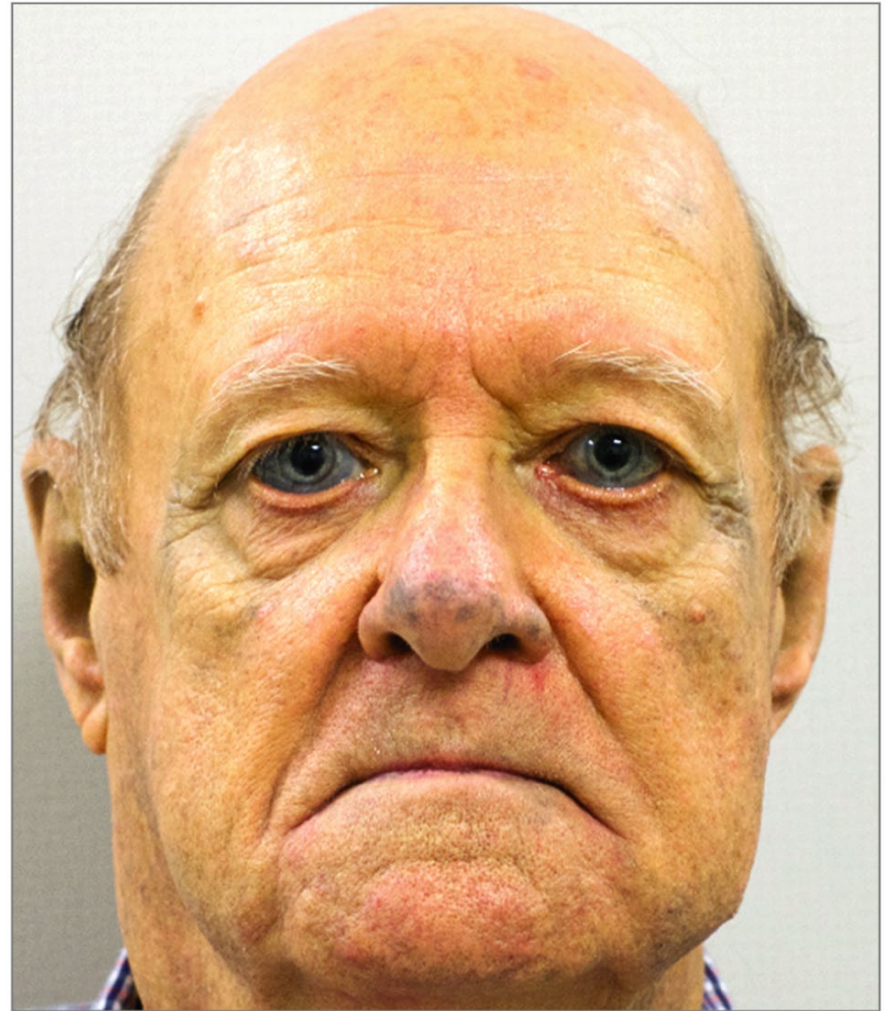
# Could this Change be Drug-induced?

What drug(s) would it be? Why would the patient's complaints have been dismissed by her doctors over the years?



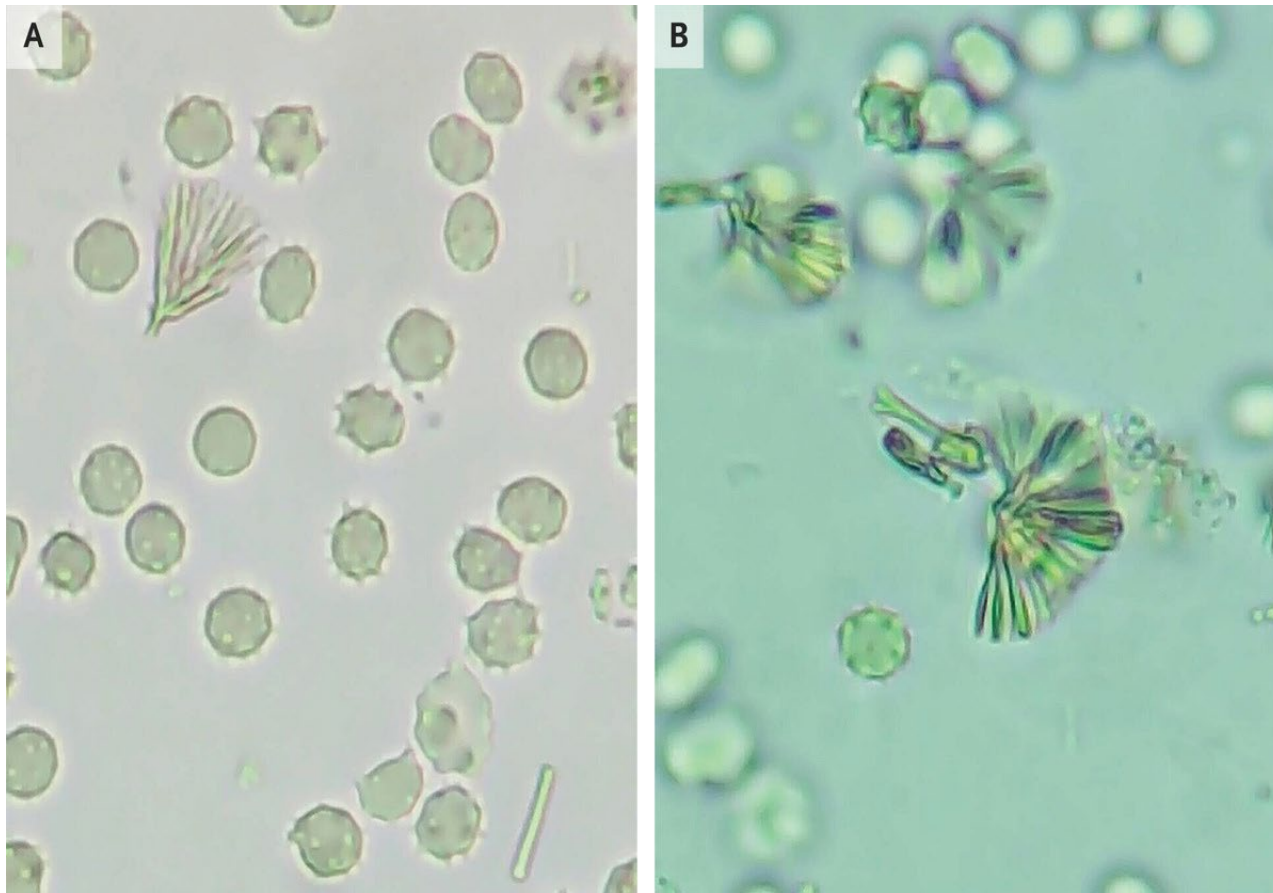
# 70 yr man with acne, 75 yr female with osteomyelitis

What is the drug cause?  
Prognosis for improvement?



# 42 yr man HIV+ with PJP now with AKI.

What drug is the likely cause and what is the mechanism shown in the slides below?



## Young boy with Aplastic Anemia on Immunosuppression.

What medication-related ADR is shown here? What medication is the likely cause? What is the treatment?



# 17 yr old talking methylphenidate



Is methylphenidate the cause? Is it ok to prescribe another stimulant for her ADHD?

**45 yr Man in ED with Malaise and Tender Ears.** What drug-related cause is in the differential? What lab test should be ordered? If drug-related what is the treatment and prognosis?



# 53 yr woman with Appendiceal cancer: What is the cause of the trichomegaly?



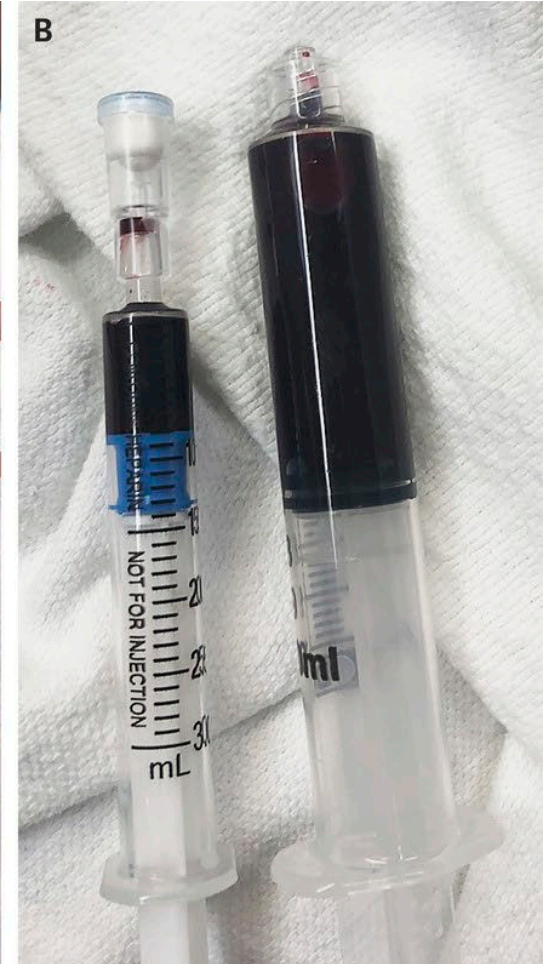


# 57 yr old woman with painful leg lesions

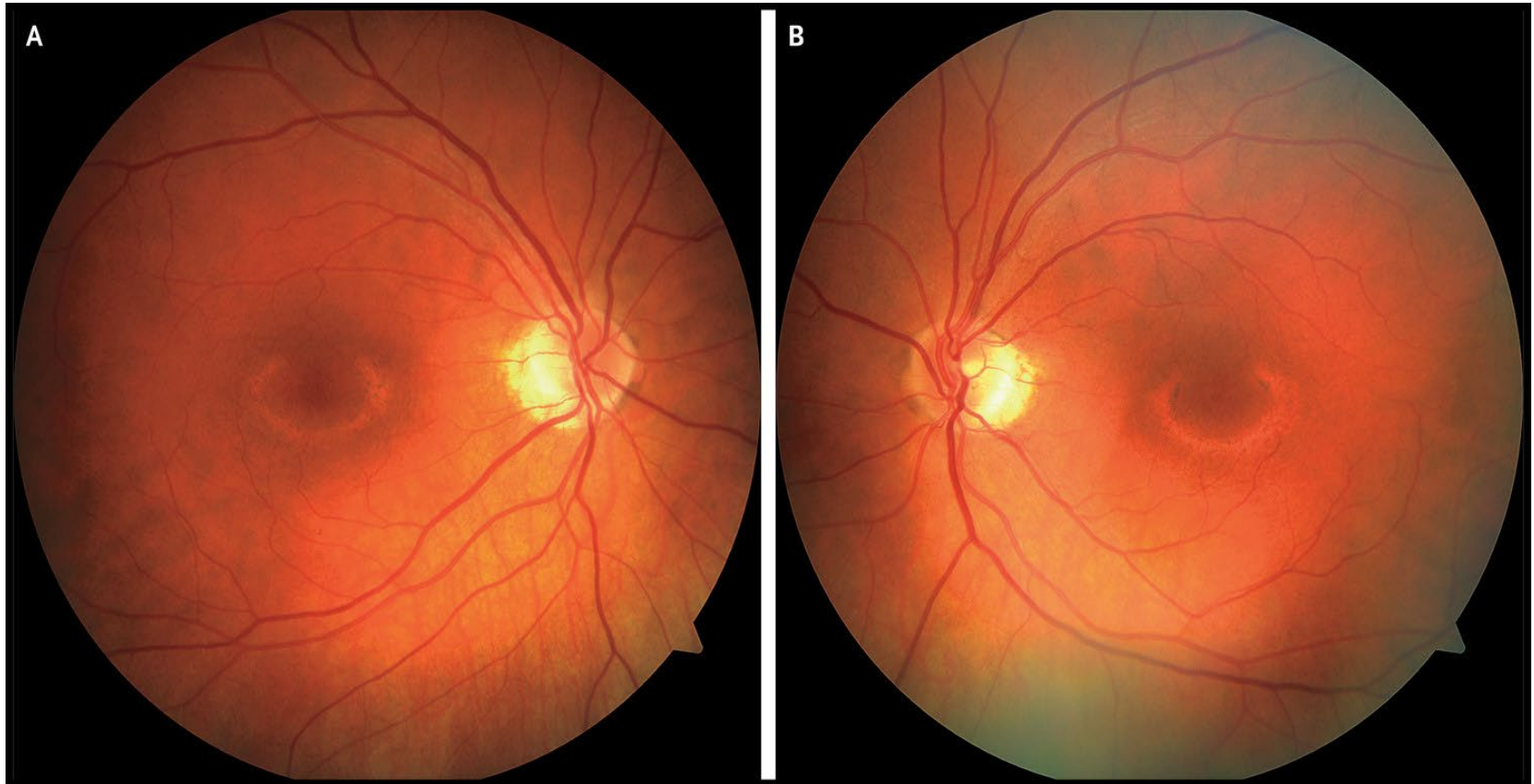


In addition to finding the diagnosis, when steroids have failed, what is the treatment?

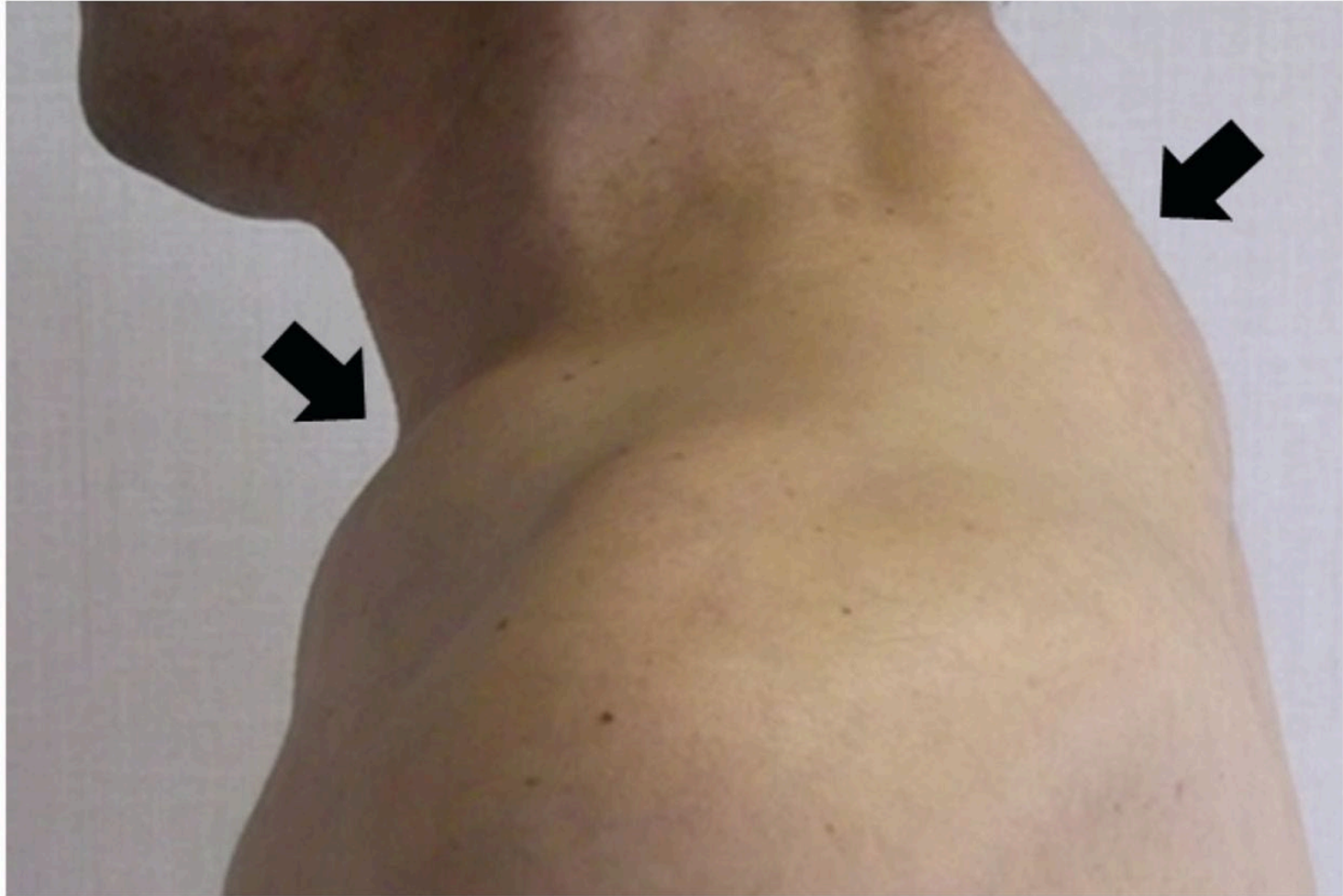
# 25 yr woman with dyspnea, cyanosis, recent toothache: What happened to explain this?



**60 yr woman with RA notices central blind spots in both eyes: What is likely cause?**



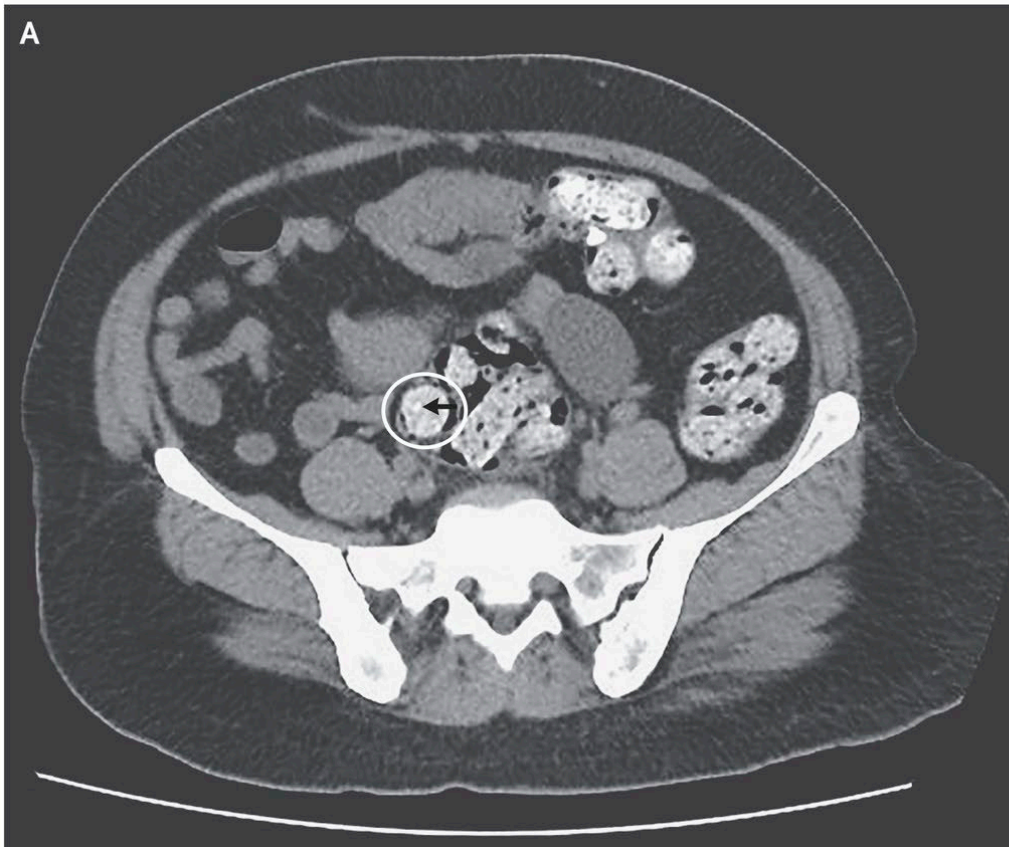
**58-year-old man with heavy alcohol use: What are the abnormalities and what is the cause?**



# Patient with inflammatory arthritis: Scleral Discoloration from What?



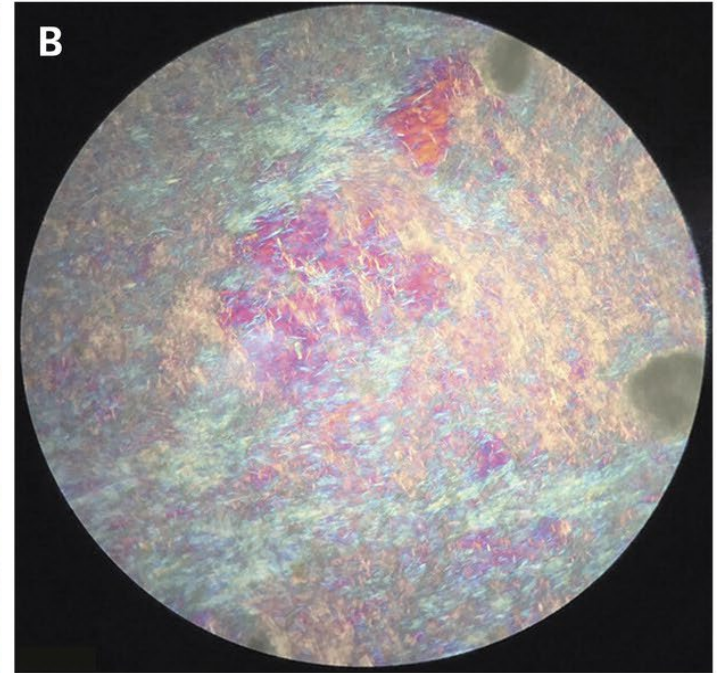
# 51 yr old body packer of opioids: Why would her lead levels be high?



# What Medication is This Patient Taking?

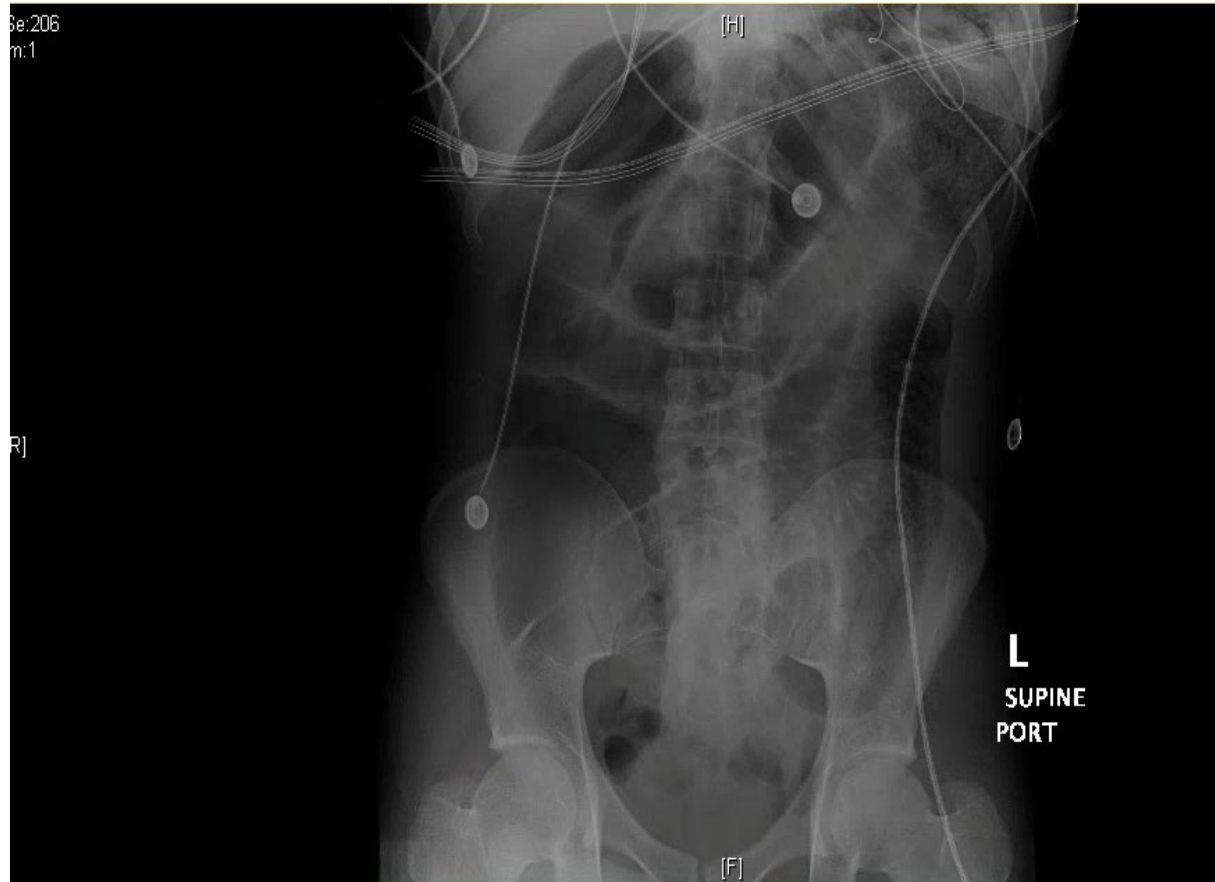


# What Medications Are Needed?





# 35 yr old MMA returning from Costa Rica, collapses at home: slide 1



# 35 yr MMA collapsed after flying home from Costa Rica: Slide 2

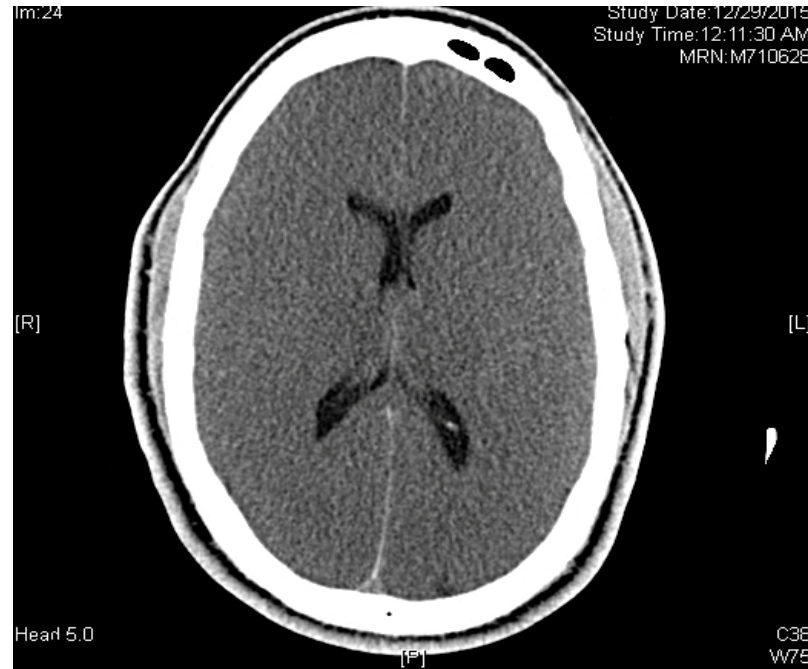
- CT Abdo:



Could drugs be a cause of his collapse?

# 35 yr MMA collapsed after flying home from Costa Rica: Slide 3

CT Head  
48 hr after  
admission:



CT reports complete loss of grey-white matter differentiation.

Urine tox now available and positive for cocaine

What is the patient's prognosis and what should happen with his life support?

21 yr old 2 days post-thyroidectomy: this occurs after she receives several doses of an antiemetic



# 11 yr old with painful skin lesions, 3 days after starting amoxicillin for URI: What is Diagnosis?

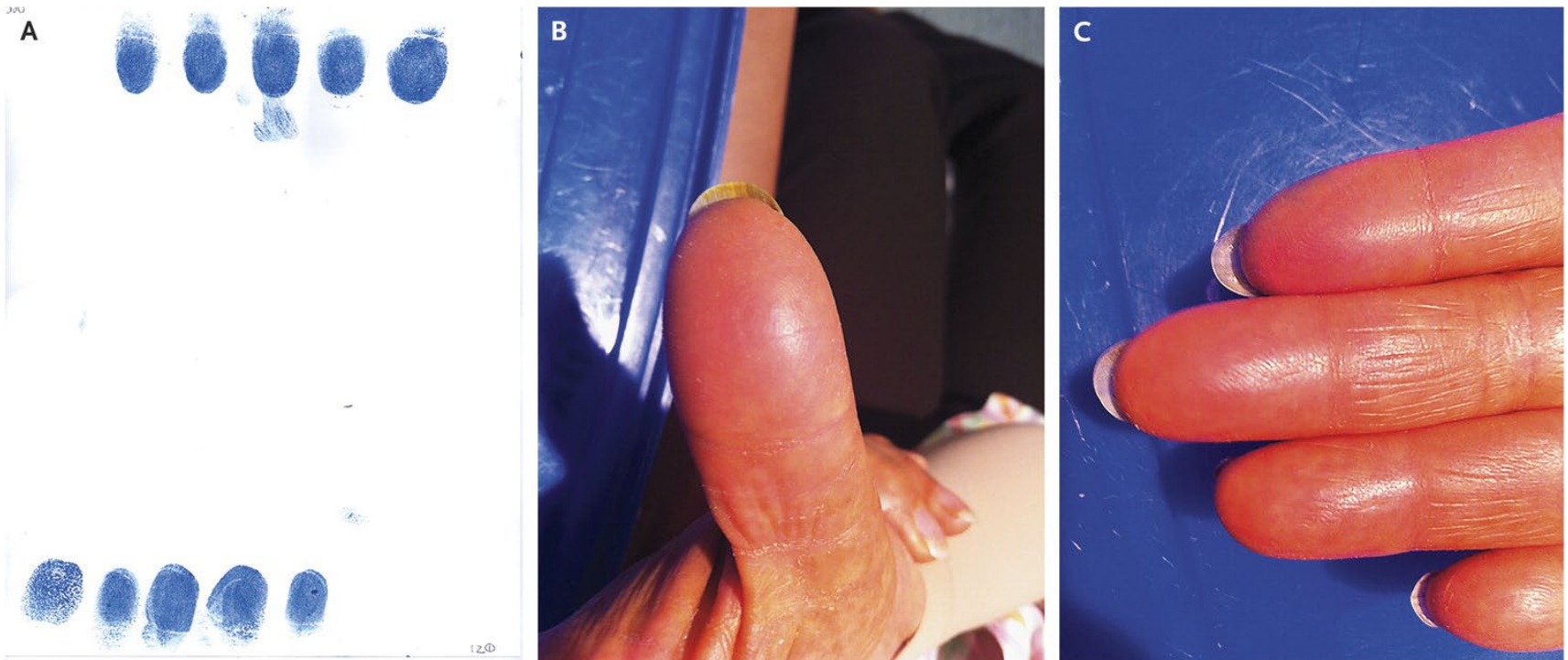


# What caused this Flagellate Hyperpigmentation?



1. Arsenic poisoning
2. Cushing's syndrome
3. Pellagra
4. Self-flagellation
5. Treatment with bleomycin

# What Causes Loss of Fingerprints?



35 yr old seen after a course of antibiotics for URI: What is this lesion and what should be the advice?



Lesion on anterior chest for 10 days now



**Which medication is most likely to be responsible for this appearance?**



1. Clarithromycin
2. Dexamethasone
3. Doxorubicin
4. Efavirenz
5. Ferrous sulfate

# Patient with Crohn's Disease Receiving Infliximab via Central Line: What happened?



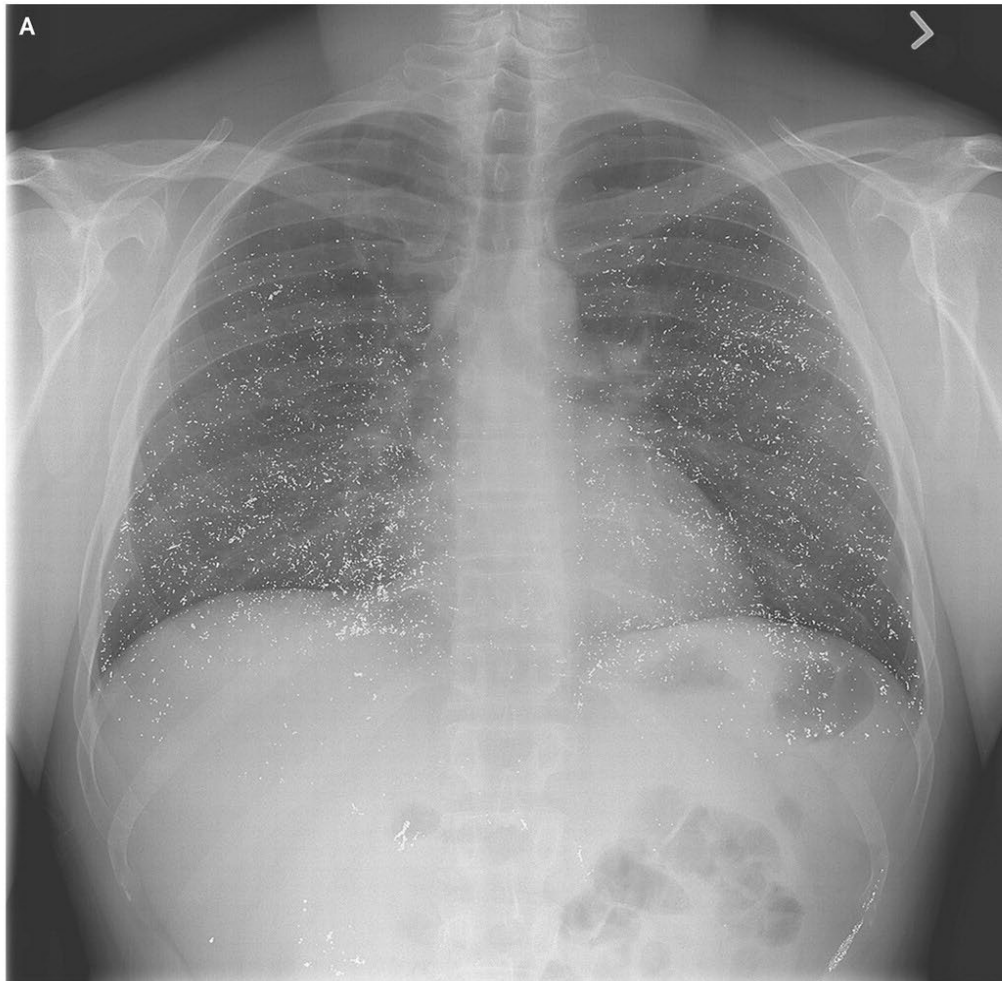
# What Causes the Hair Depigmentation Stripes?



THE NEW ENGLAND  
JOURNAL OF MEDICINE

Brzezniak C, Szabo E. *N Engl J Med* 2014;370:e27.

40 yr man with headache, dry cough, dyspnea, intention tremor, tender s/c nodules L forearm, labile mood. What is the diagnosis?



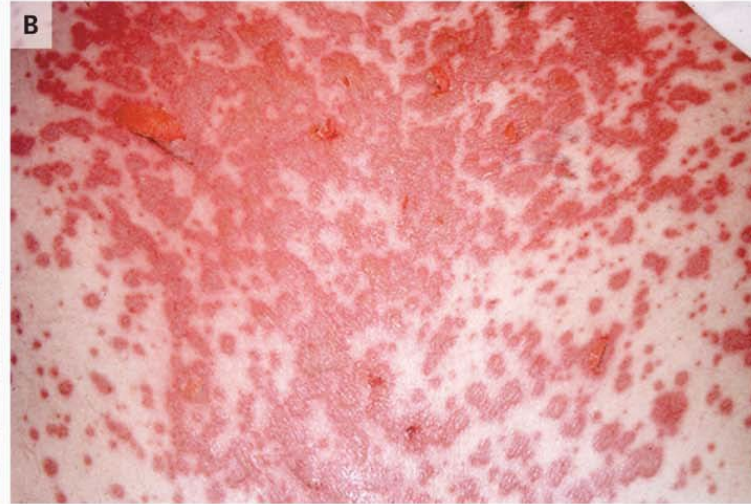
# Halitosis and Sensory Loss L lower lip, L mandible pain: What is the diagnosis? How is this medication-related?



# 50 yr Woman with Bipolar Depression with Pruritic Rash (looks like Panel A)



# Clinical Presentations of Severe Cutaneous Reactions to Drugs



**Table 1. Selected Infections and Other Conditions that Often Include an Exanthem and Characteristics that Help Differentiate Them from an Exanthematous Drug Eruption.\***

Diagnosis	Description and Distinguishing Features
Measles (rubeola)	The rash is morbilliform (meaning “measles-like”), a term often used to describe exanthematous drug eruptions, and is usually itchy. Unlike most drug eruptions, the rash seen in measles often begins on the head and neck and spreads rapidly. It usually begins a few days after the onset of fever, cough, coryza, and conjunctivitis. White spots on the buccal mucosa (Koplik’s spots) help establish the diagnosis. Typical or atypical rash may occur in previously vaccinated adults, principally those who received only older, killed vaccine or who were incompletely vaccinated.
Rubella	Symptoms are usually milder than those seen in measles, with a similar rash that usually resolves within 3 or 4 days. The rash is often accompanied by fever, adenopathy, and arthralgias.
Roseola infantum (exanthem subitum)	Young children have a high temperature for 3 to 5 days; it usually resolves around the time of onset of the rash, a pink, short-lived eruption. Human herpesvirus 6 is the most frequent cause. Adults have cervical adenopathy, with variable rash and fever that may last for months. The rash usually starts on the trunk and spreads to the face and extremities.
Erythema infectiosum (fifth disease)	In young children, fever (with characteristic “slapped cheeks”) develops 2 to 4 days before generalized rash, which begins on proximal extremities and spreads both centrally and peripherally. In adults, arthralgias, which may persist for many weeks, and fever are prominent. The rash often has a livedo pattern. Facial involvement is less prominent in adults than in children. The disease is caused by parvovirus B19.
Infectious mononucleosis	In adolescents and adults, rash is usually associated with aminopenicillin administration, with an onset within 3 days after administration (a more rapid onset than is usual for drug eruptions). Patients are unlikely to have rash with readministration of aminopenicillin after recovery.
Acute graft-versus-host disease	The rash typically occurs 2 to 4 weeks after transplantation. It may be pruritic. If generalized, the rash is often difficult to distinguish clinically from an exanthematous drug eruption.
Acute human immunodeficiency virus seroconversion	The rash has an acute onset 1 to 6 weeks after infection and is usually accompanied by fever, malaise, myalgias, arthralgias, and lymphadenopathy. It is a symmetric exanthematous rash that involves the face, palms, and soles. Oral and genital aphthous-type ulcers may occur.
Other viral exanthems	Causative agents include echoviruses, coxsackie virus, togavirus, and others.

\* Other diagnostic aids may include viral culture, skin biopsy, detection of virus by means of polymerase-chain-reaction assay, and serologic tests for antibodies (especially IgM antibody in acute infections).



**Table 2. Features of Selected Severe Cutaneous Adverse Reactions to Drugs.**

Feature	Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)	Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis (SJS–TEN)	Acute Generalized Exanthematous Pustulosis (AGEP)
Clinical features			
Rash	Widespread rash (involving >50% of body-surface area), often exanthematous, and very inflamed; may have other morphologic features, including erythroderma; facial edema and erythema; exanthematous eruption may become purpuric, especially on lower legs	Severe, acute blistering; initially, rash may be macular erythema or exanthematous eruption and trunk lesions predominate; individual lesions may include “spots” and flat, atypical target lesions but not true target lesions characteristic of erythema multiforme, which is not usually drug-related; Nikolsky’s sign (ready removal of the epidermis with slight tangential pressure); diagnosis depends on extent of epidermal necrosis according to body-surface area: 10 to 30% in SJS–TEN versus less than 10% in SJS and more than 30% in TEN	Rapid evolution (over a period of hours) of sterile, nonfollicular pustules on erythematous swollen skin; accentuation of rash in body folds; facial edema
Mucosal involvement	Mucosal involvement infrequent	Mucous membranes nearly always involved with blisters and erosions	Mucosal involvement rare
Onset of rash	Onset of rash often >14 days after first dose of drug, especially in the case of antiepileptic agents; for most other drugs, onset 4 to 21 days after first dose	Onset 4 to 21 days after first dose of drug	Initial onset (<3 days) after first dose of an antibiotic but slower onset with other drugs
Other features	Temperature >38.5°C, malaise, lymphadenopathy, involvement of at least one internal organ: liver (in >80% of cases), kidney, muscle, lung, heart, pancreas	Temperature >38.5°C, malaise, sore throat, dysphagia, dysuria, or photophobia initially	Temperature >38.5°C
Laboratory findings	Eosinophilia ( $\geq 700 \times 10^6$ per liter or $\geq 10\%$ if white-cell count $< 4000 \times 10^6$ per liter) and lymphocytosis or lymphopenia, atypical lymphocytes, thrombocytopenia; simultaneous activation of latent or new infection with human herpesvirus 6 common (not a routine test)	Epidermal necrosis on skin biopsy, with full-thickness loss of epidermis	Leukocytosis with neutrophilia (absolute count, $> 7000 \times 10^6$ per liter)
Relation to medication	By definition, all cases drug-related	80% of cases drug-related	50% of cases drug-related
Differential diagnosis	Systemic lupus erythematosus, mycoplasma infection, viral hepatitis, infectious mononucleosis, other infections	Autoimmune blistering diseases: pemphigus and pemphigoid, acute phototoxicity, staphylococcal scalded skin syndrome	Psoriasis (shares many features with pustular psoriasis)

# Reticulated White Striae on the Lower Lip: What is the drug-related cause?

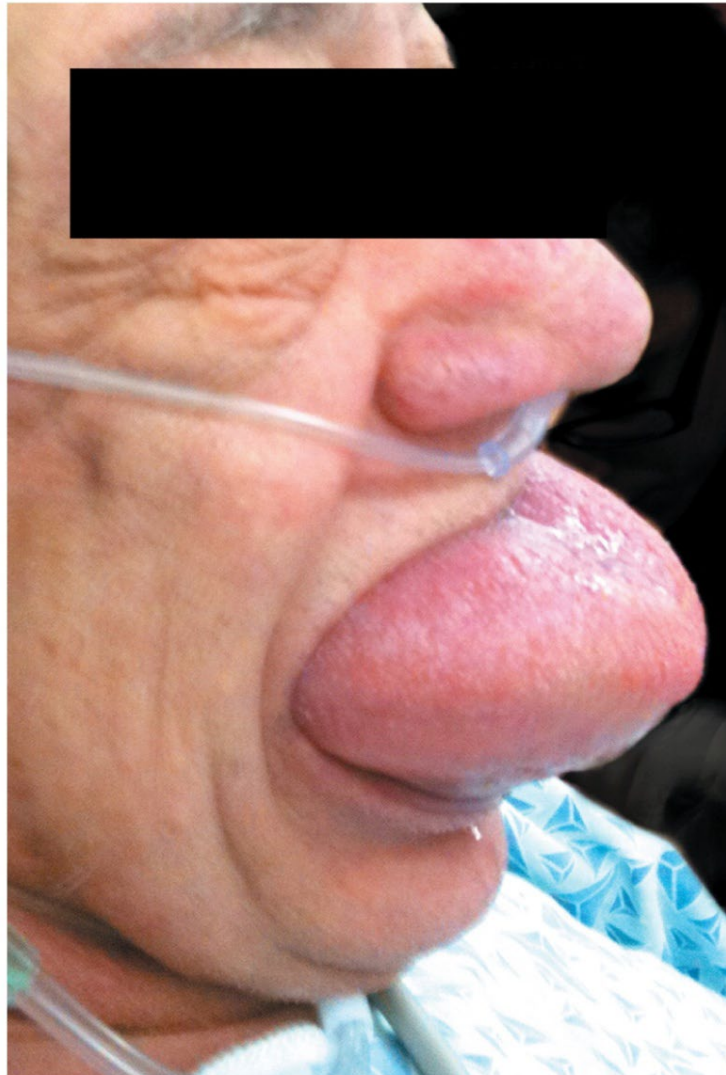


What is the advice to the patient?

Shackelton, J. B. et al. JAMA 2011;306:2267-2268

71-year man with 5 hr worsening swelling as shown:  
What is the likely diagnosis and medication culprit?

Vitals are  
normal.  
No new  
medication



# 35-year old man with 10-day history of 5 cm lesion



# 54 year woman with polysubstance drug use disorder comes with 2 days painful rash



What is the likely medication-related diagnosis? What is the treatment?

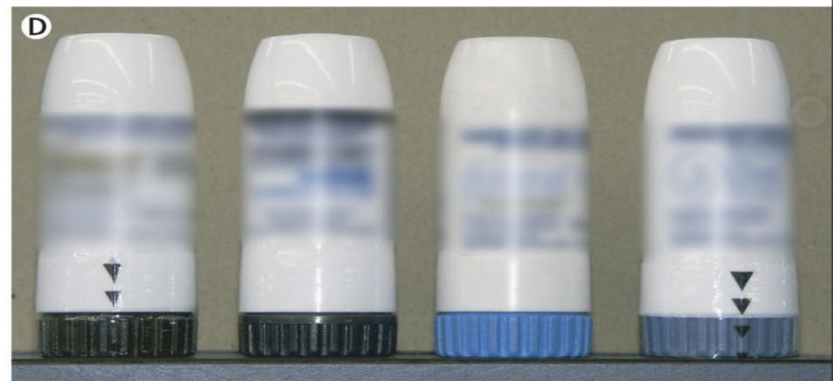
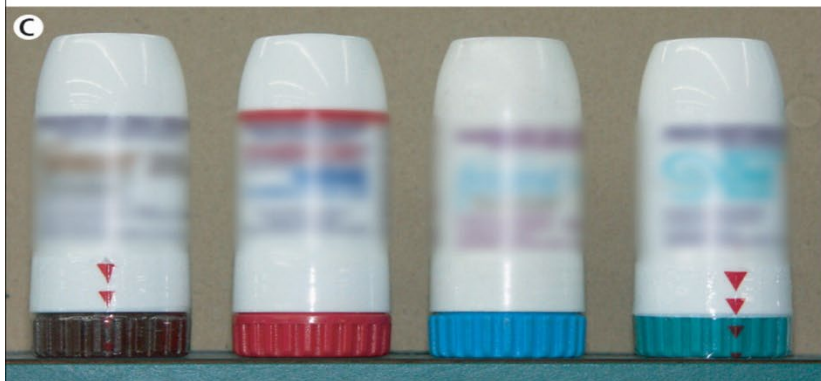
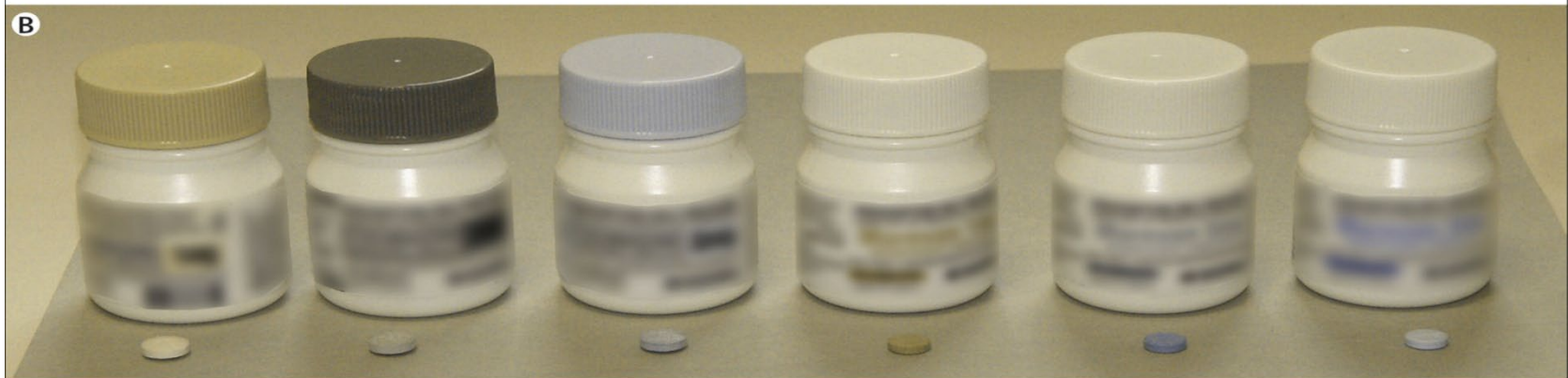
N Engl J Med 2011;364:e52

# Post-MI Thrombolysis Complication: Sore Tongue



What is the diagnosis?  
What is the treatment?

# Caution: coloured medication and the colour blind



## A 77-year-old man 4 weeks after sorafenib for metastatic RCC: Painful swelling of R elbow



What is the diagnosis?

What tests should be done?

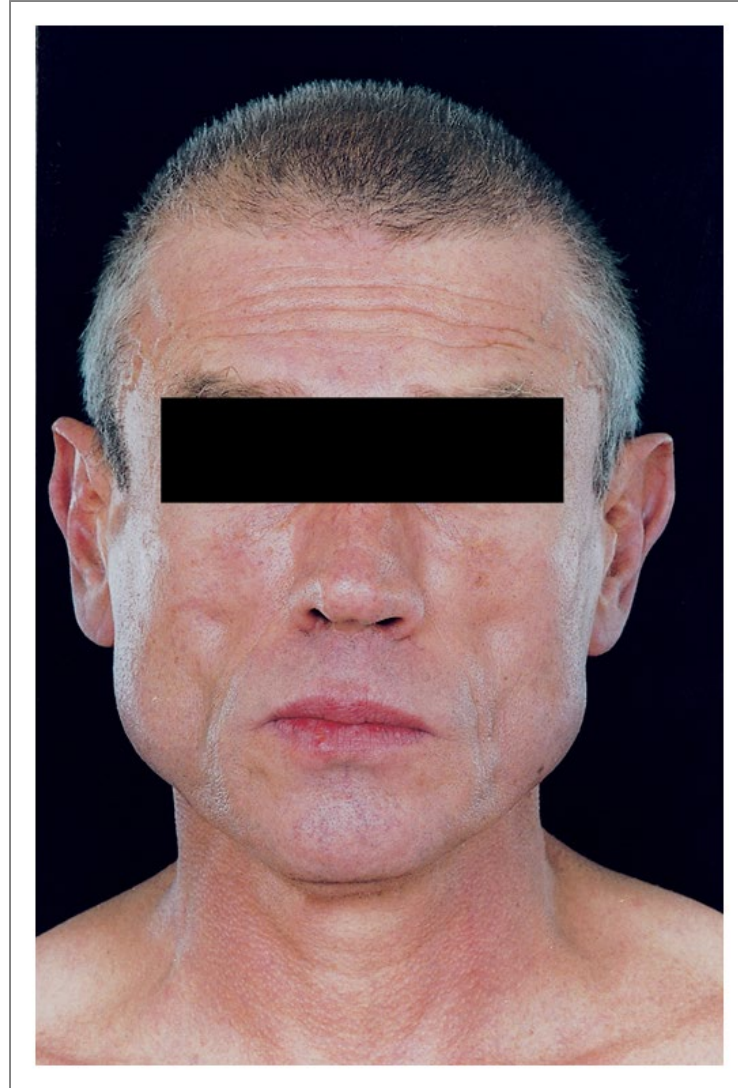
What treatments should be started?



**What nebulized medication is most likely to have caused this patient's anisocoria?**



**What family of medication is this patient taking?**



N Engl J Med 1998; 339:1296

# 21-year old Bodybuilder: Panel A to C occur over 6 months

What are the medication-related complications shown here?  
What additional complications are there likely to be?

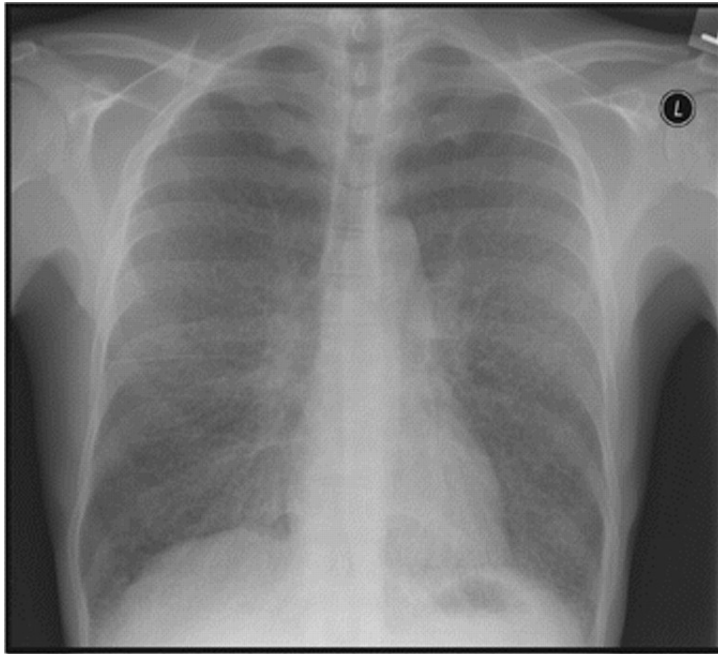


# A 25-year-old bodybuilder: What happened?

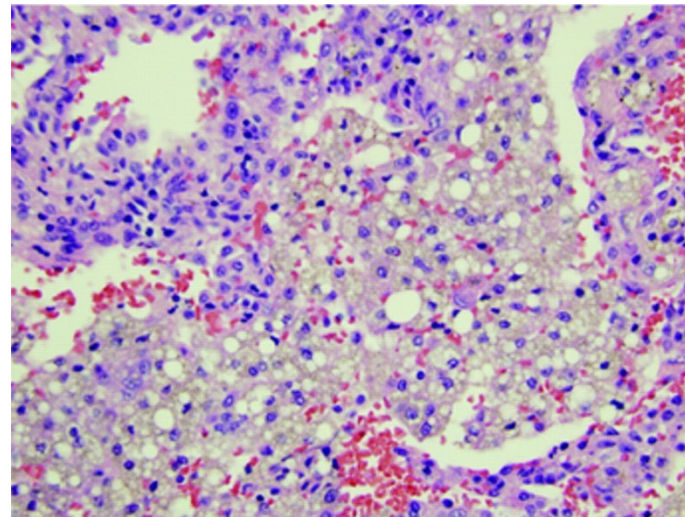
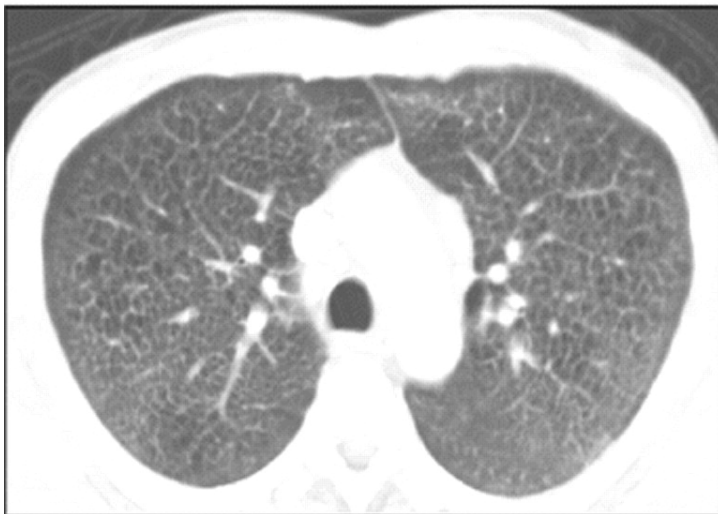


Gautschi O and Zellweger R.  
N Engl J Med 2006;355:713

# 42 yr Man with 6 mo worsening dyspnea: Crack Cocaine User



How could this be drug-related?  
What is the prognosis for improvement?

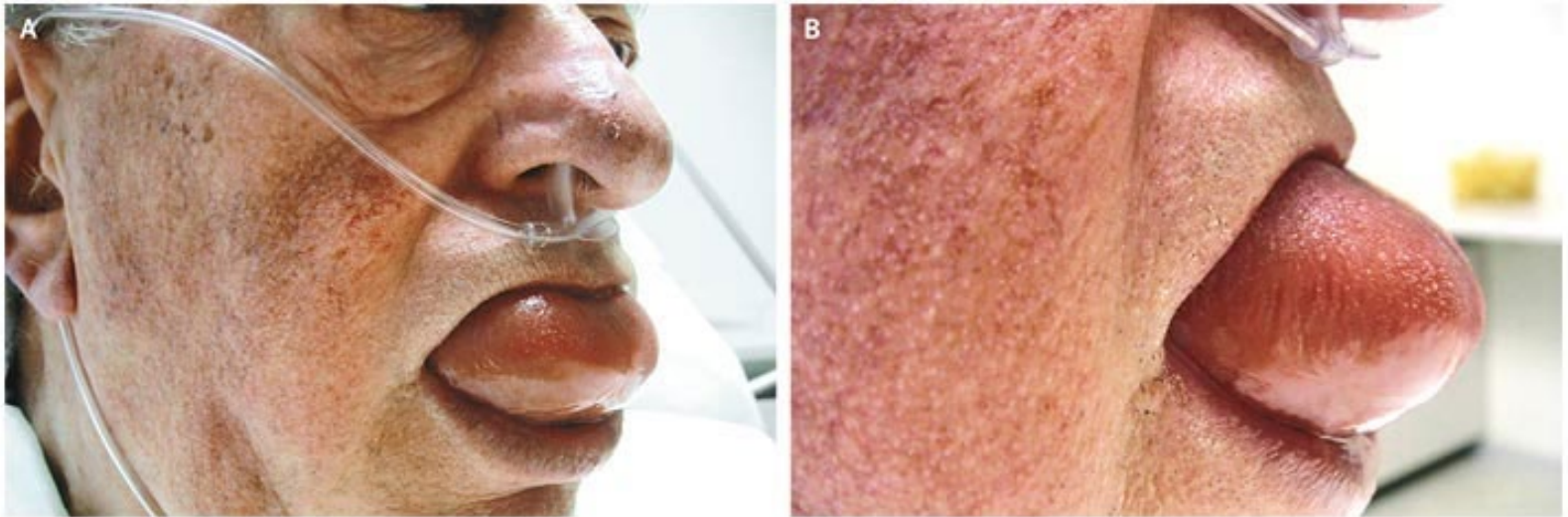




**Treatment with what antibiotic is most likely to have resulted in this patient's skin changes?**

- 1. Rifampin**
- 2. Chloramphenicol**
- 3. Nitrofurantoin**
- 4. Minocycline**
- 5. Trimethoprim**

**A 75-year-old man presented to the emergency department with diffuse swelling of his tongue that had begun a few hours earlier**



PMH: hypertension

What is likely cause? What is the treatment?

# 28 year woman with Weight Gain over 6 months

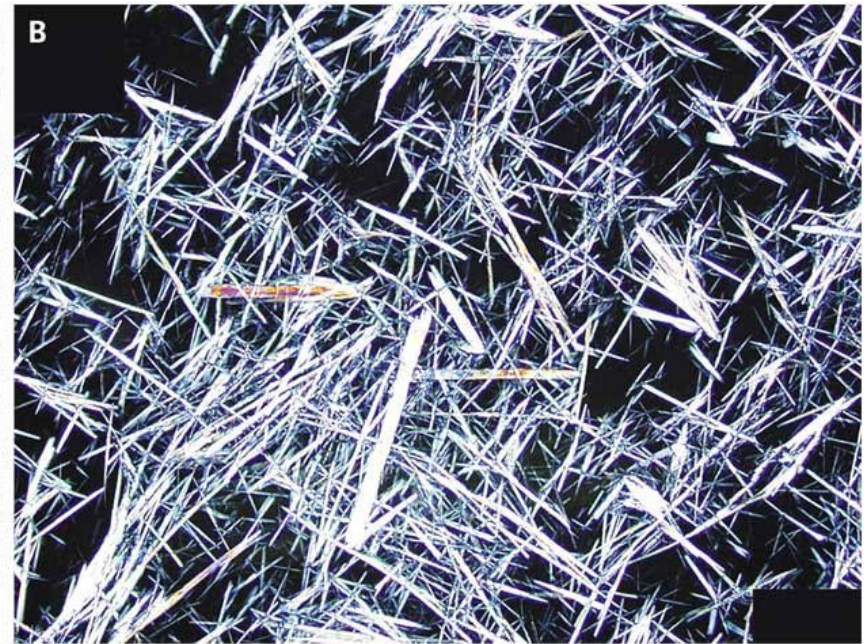


What self-induced cause could this be?



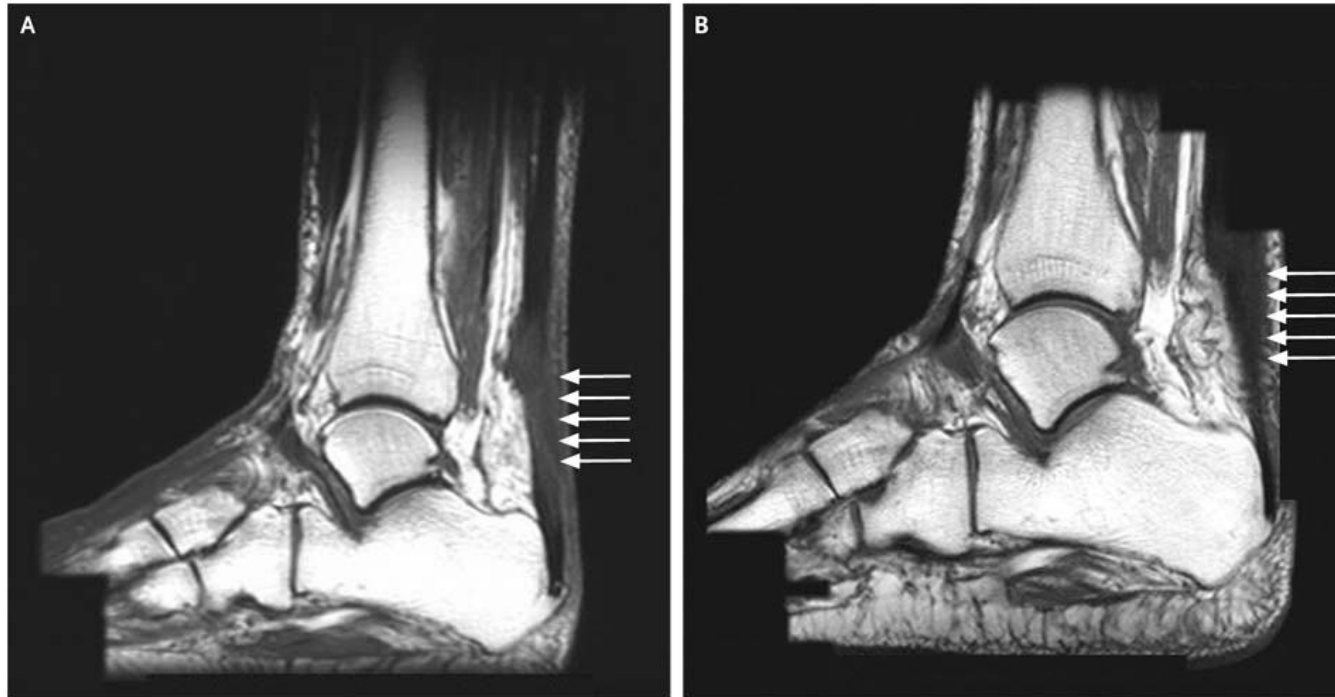
**A 60-year-old man infected with the human immunodeficiency virus (HIV) (CD4 count of 450 per cubic millimeter and HIV viral load of <50 copies per milliliter) who had HIV-associated dementia was admitted to our hospital because of an altered mental status, a temperature of 101{degrees}F (38.3{degrees}C), and seizure-like activity. Treatment was started.**

**Within hours, his urine was cloudy and these pictures are seen under microscope**



What is the drug cause?  
What is the treatment?

81 yr old with sudden pain and swelling at heel after 1 week antibiotic for bronchitis



What is the diagnosis?

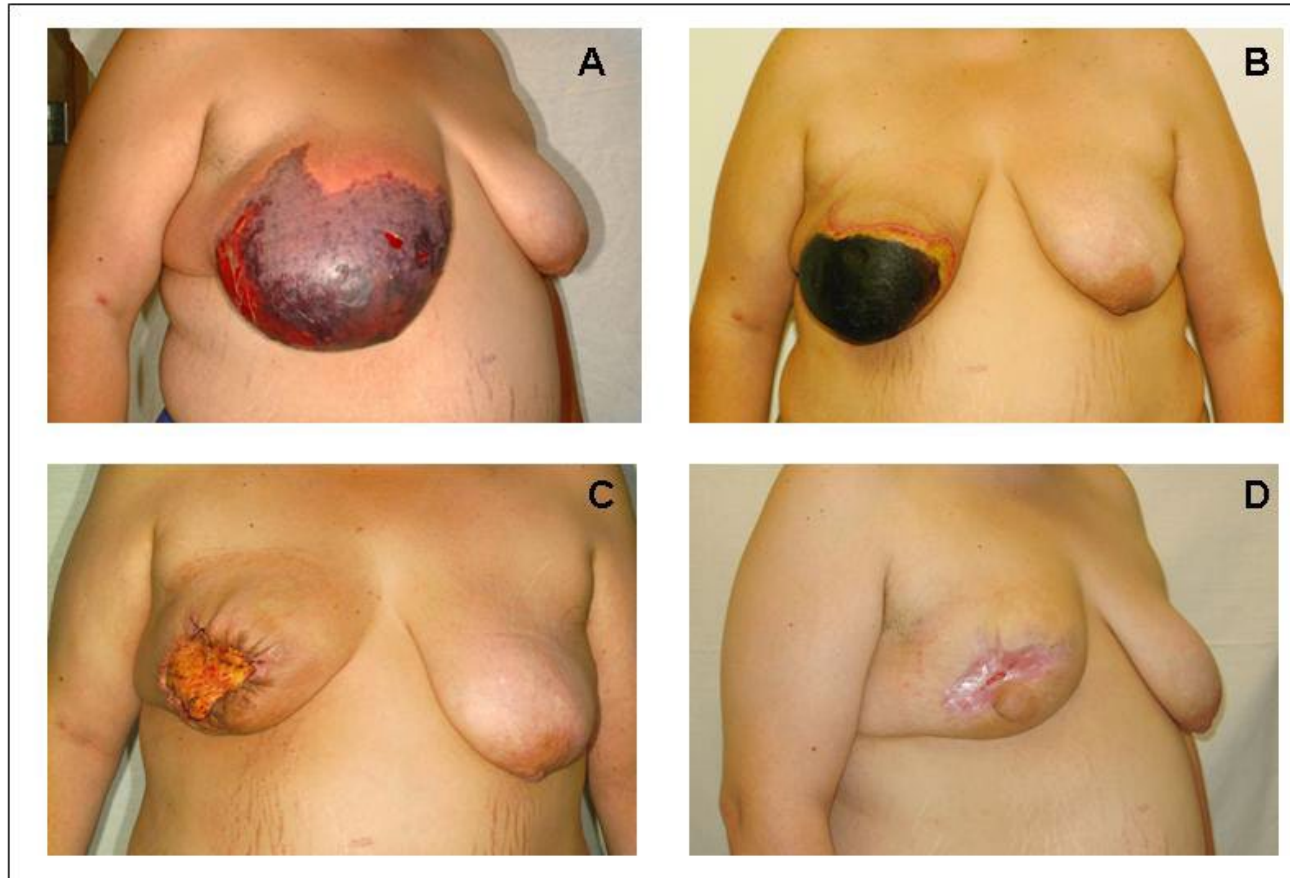
What is the likely medication cause?

50 yr old with abdominal tenderness, fever, vaginal bleeding, necrosis of upper vaginal wall



As per laparotomy picture on R, what was the cause?

# Young women 5 days after Pulmonary Embolism diagnosis (Panel A) then later



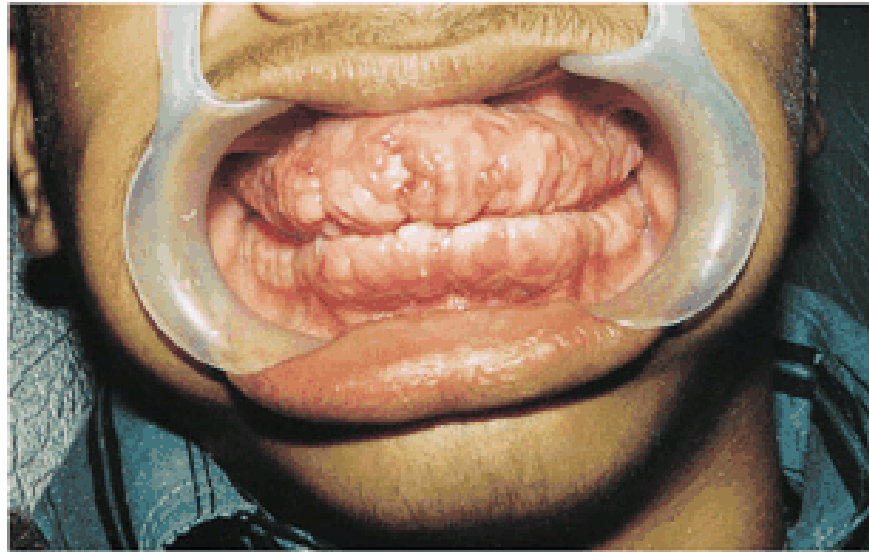
© Stephan Moll, M.D.

These are pictures of a classic complication of which drug?

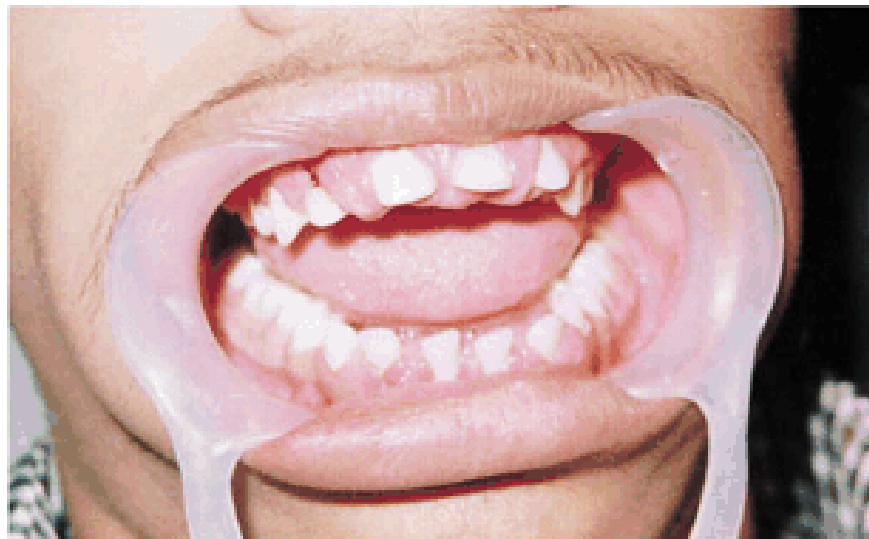
*Moll S: Br J Haematol 2004;126:628.*

# 17 yr old male with seizure disorder

What drug-related complication is this likely to be?  
What is the treatment?



A



B

# 22 yr old with epilepsy: Presents with rash, fever, rash



What is the likely diagnosis?  
What would you consider in the differential?  
What is the treatment?

# Young man with swelling, pain, fluctuance: What is the key history?



# 79 yr old before-and-after: What is the diagnosis and why is it drug-related?



A



B



## 79 yr old on antibiotic for rosacea over 5 years.

What is the medication-related cause?  
Will this discolouration go away?



# 61 yr old with ICD X years

What is the medication cause of his skin?  
What is the treatment?  
What is the prognosis?



# 56 yr old woman with skin discolouration since age 14

- Prescribed unknown 'alternative' nose drops at age 11
- Picture with her daughter on R
- What is the likely cause? How to prove it?



# 16 yr old with skin discolouration: 2 yr after using dietary supplement

Picture with his mother. What is in the supplement that could cause this?



# 43 yr old with Classic Complication of Alcohol Abuse

What are the findings in this picture?  
What would you look for in addition on physical exam?  
What is the treatment?



# 79 yr old electrician

What is the picture showing?

How functional are his hands likely to be?

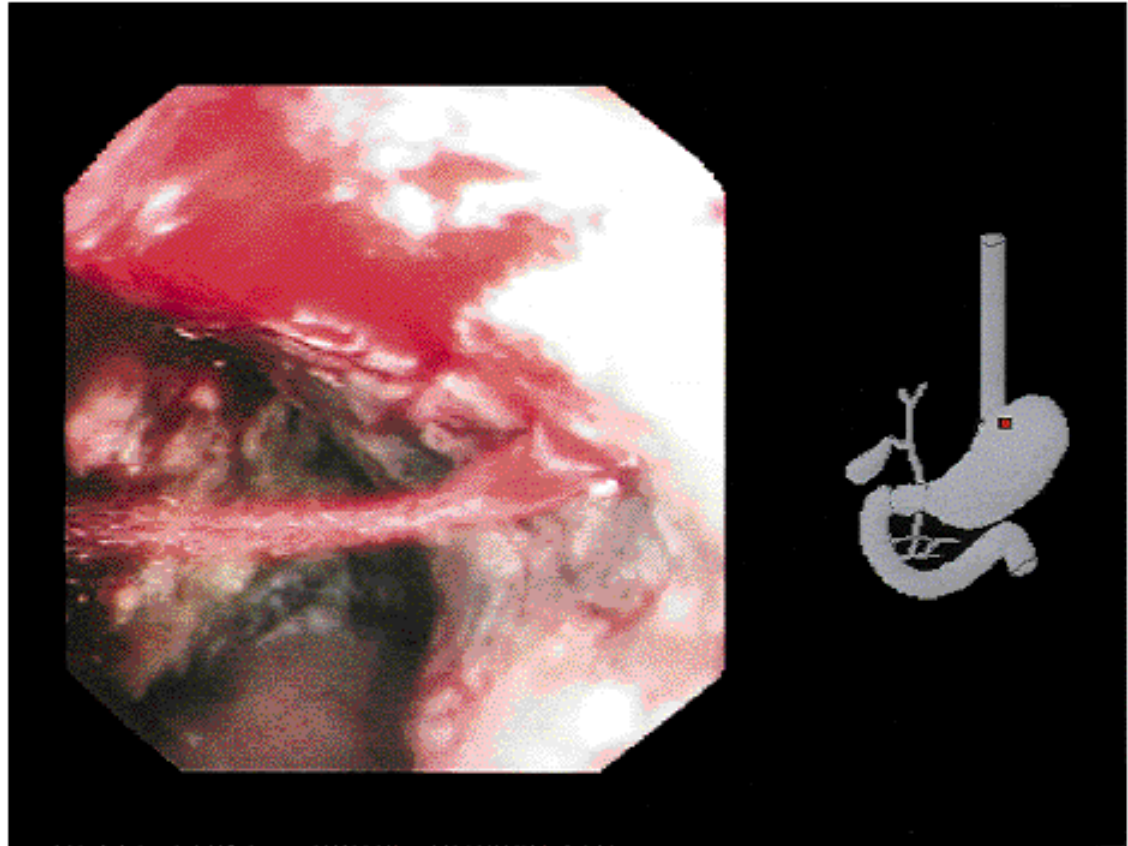
What drug is this often related to?

What is the treatment?



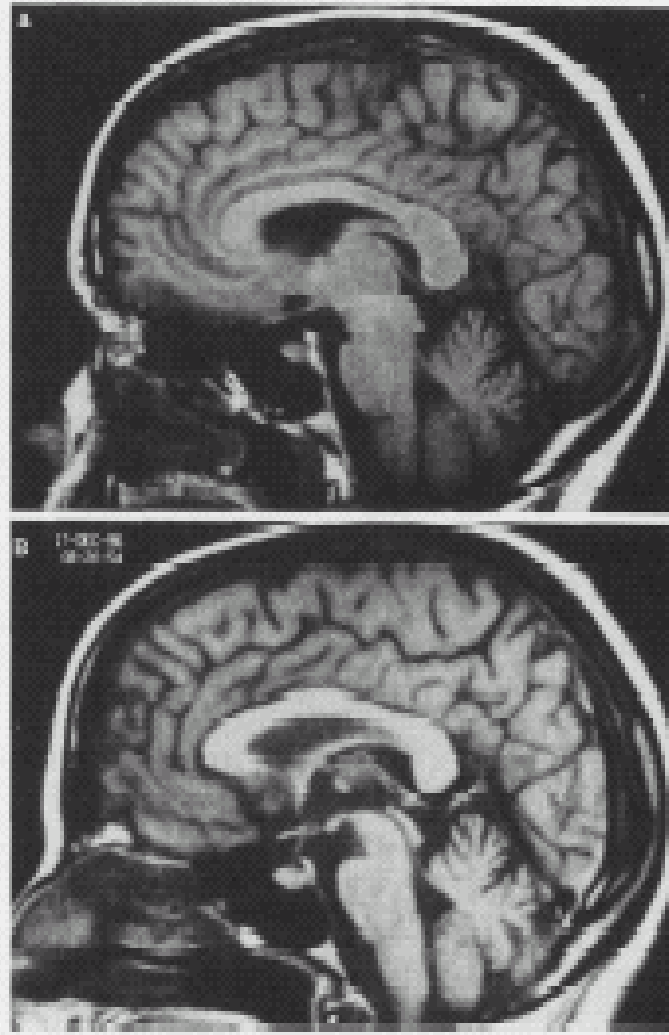
# 67 yr old woman with black stools and anemia: Endoscopy

What are the top 3-4 medication-related causes of this complication?  
What is the treatment?  
What is the prognosis for re-bleeding?



# 31 yr old with hyperemesis gravidarum: Begins to have nystagmus and confusion

What is the CT diagnosis?  
Why is this a medical emergency?  
What drug is essential to give asap?

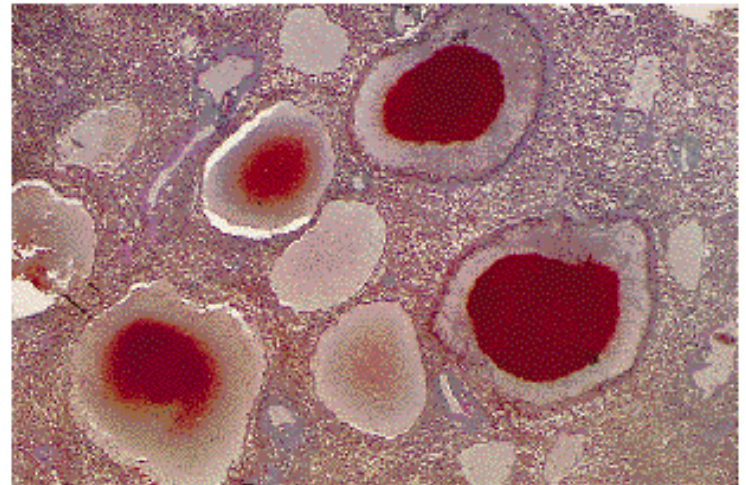




# 69 yr woman on androgens for aplastic anemia: Autopsy



What is post-mortem diagnosis based on liver pictures here?  
Why is this drug-related?



# 68 yr old man with AF, post-MI, post-CABG: develops painful toe discolouration on Rehab ward

What is the medication that this is likely due to?

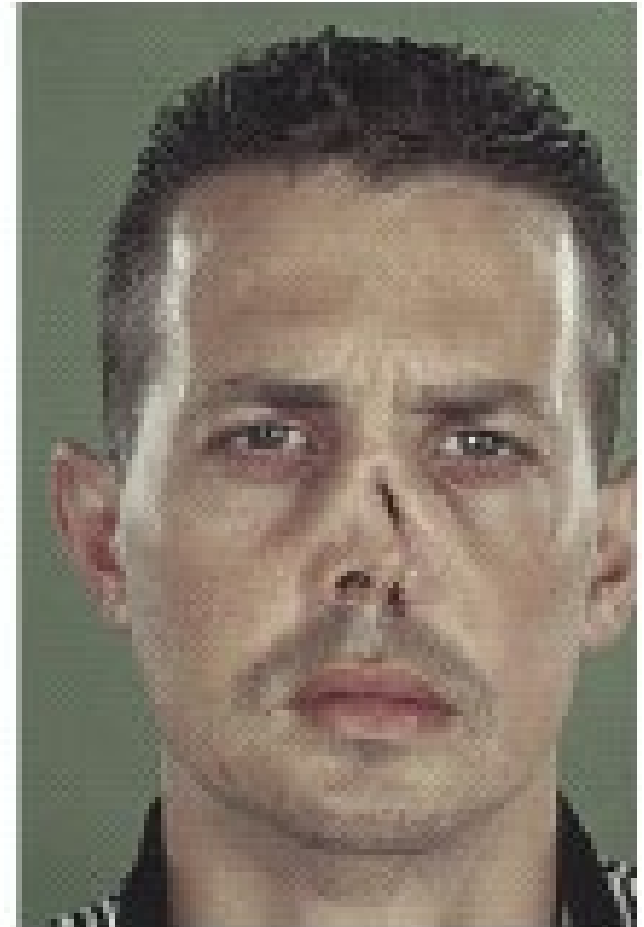
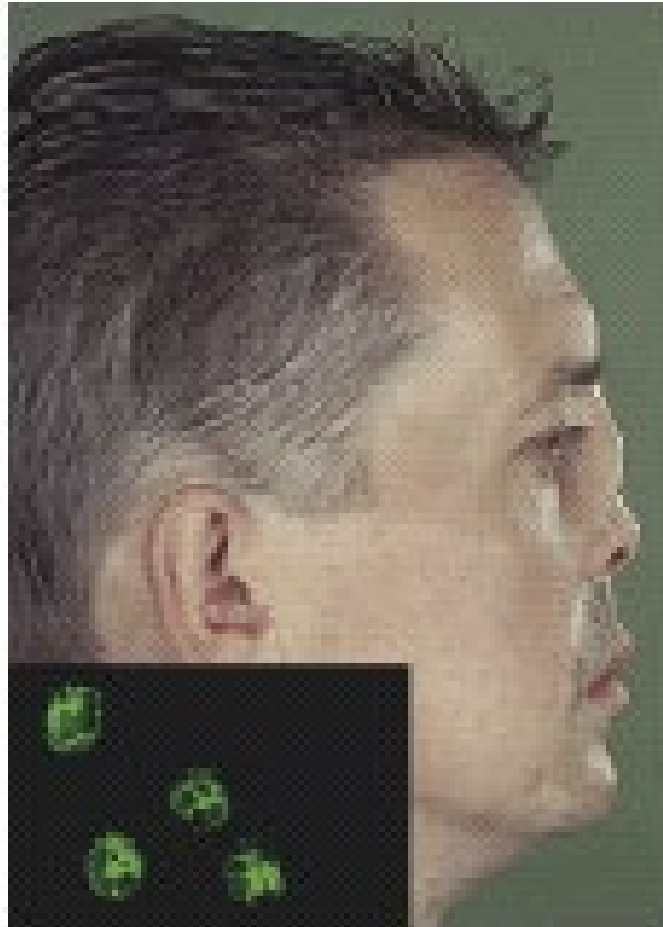
What is the prognosis for improvement?

What is the treatment?



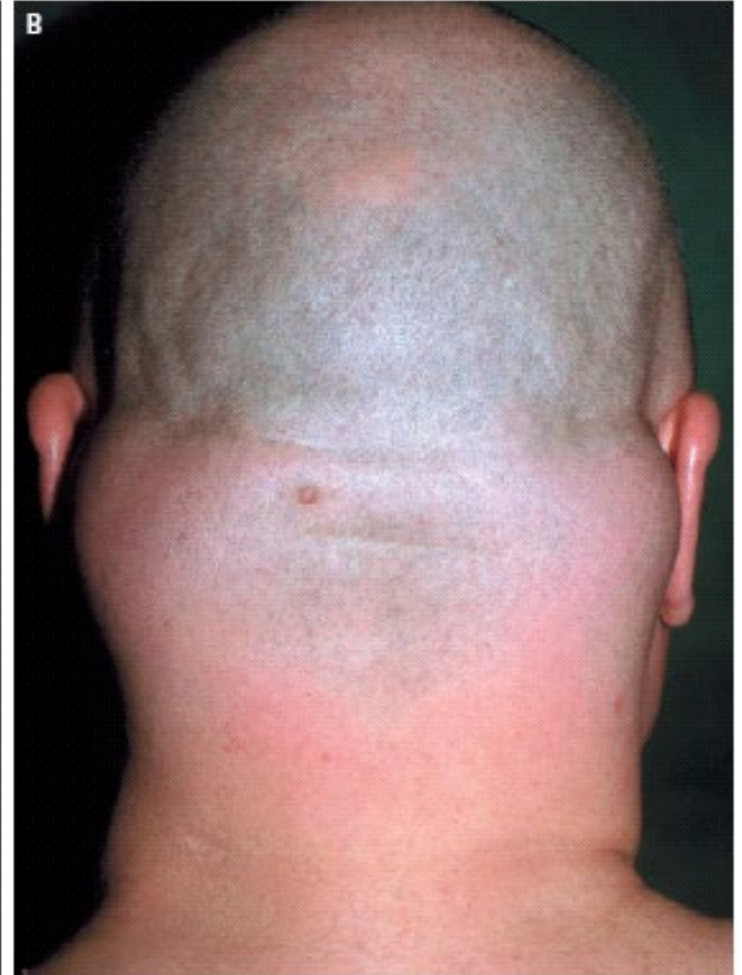
# 30 yr man for re-evaluation re ? Wegener's granulomatosis

What test was used to clarify his diagnosis?  
What drug was the cause?  
What is the prognosis for improvement?



# 51 yr old who is HIV +: What is the cause of this appearance?

Does this medication complication occur with current favoured regimens?



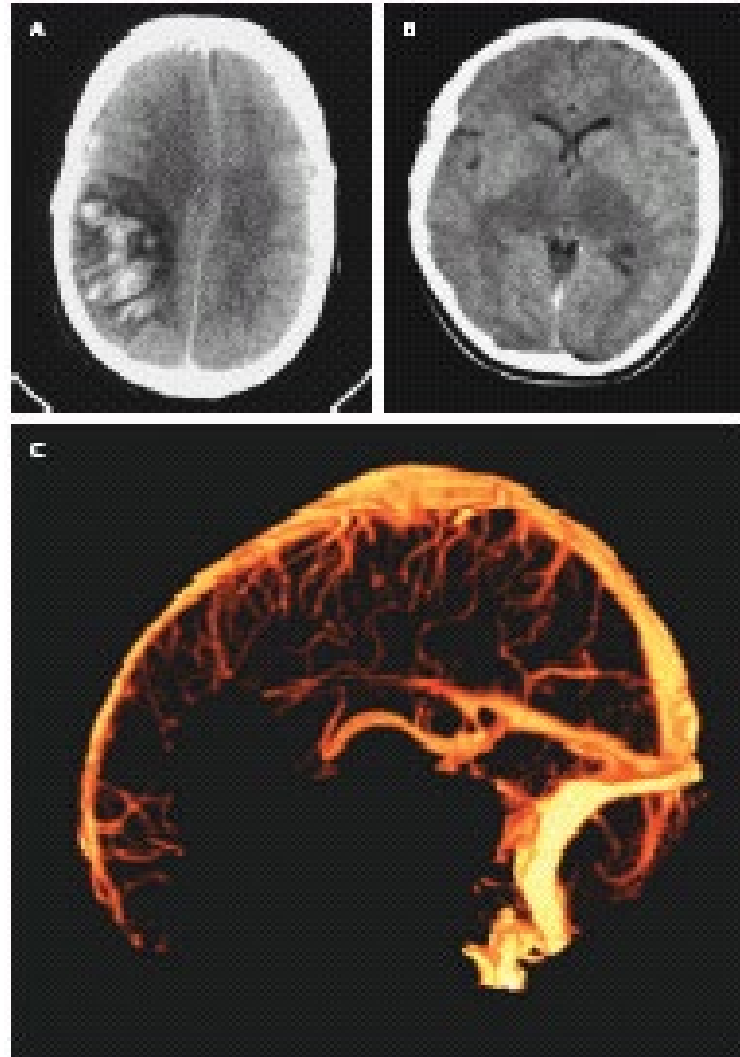
# What Medication Family is this classically associated with?

What is the name of this sign?  
What is the pathophysiology?



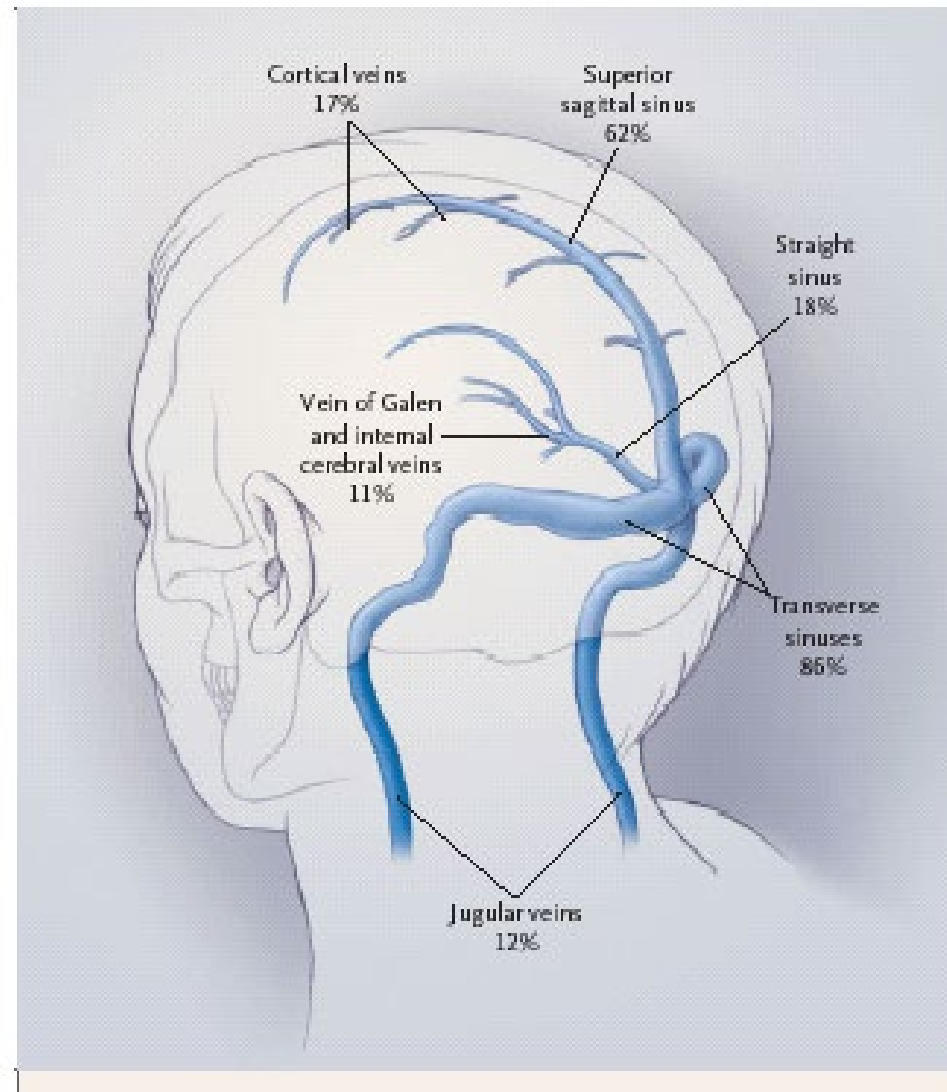
# Young woman taking oral contraceptives: Slide 1:CT and CT venogram

What is the complication that this is showing?  
What disability is she likely to demonstrate?  
What is the treatment?  
What is your advice to the patient regarding contraception?



# Young woman taking OCP: Slide 2

Demonstrates frequency of this complication



# 54 yr old with multiple myeloma and hypercalcemia

Suffered severe bilateral jaw pain for 1 month.  
Receiving ongoing treatments for hypercalcemia without reassessment. What is the likely cause? What is the treatment?





# 68 yr old woman with erosive mucositis

She reports difficulty swallowing and is on treatment for osteoporosis

What is the likely cause?

What is the treatment?



Kubegni P and Fimiani M: N Engl J Med 2006;355:e25

# 37 yr man with Crohn's disease seen for vomiting, bloating

What is this picture showing (abdo X-ray)?

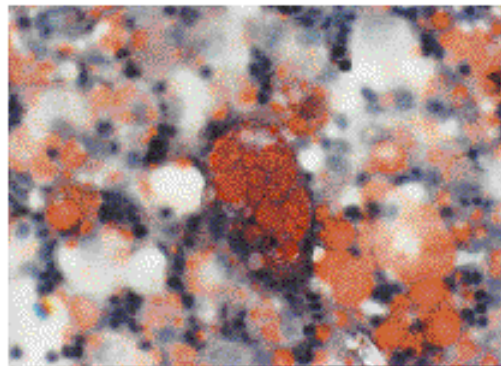
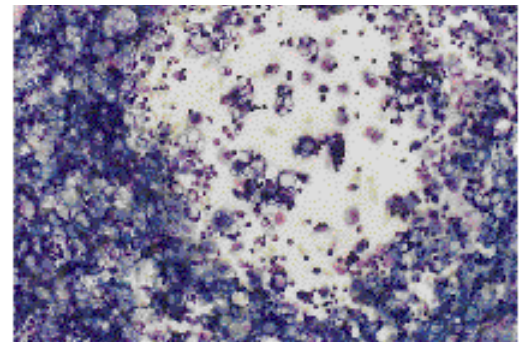
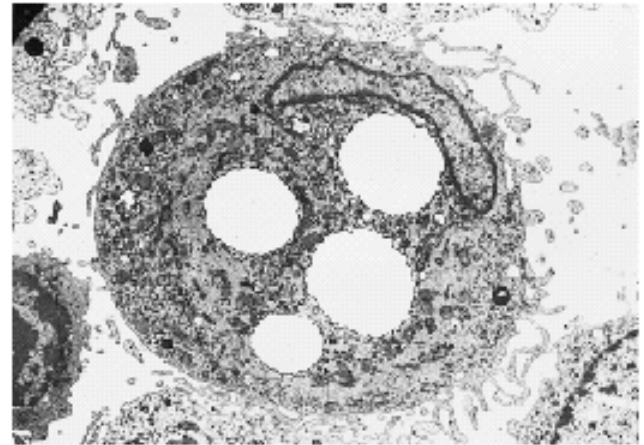
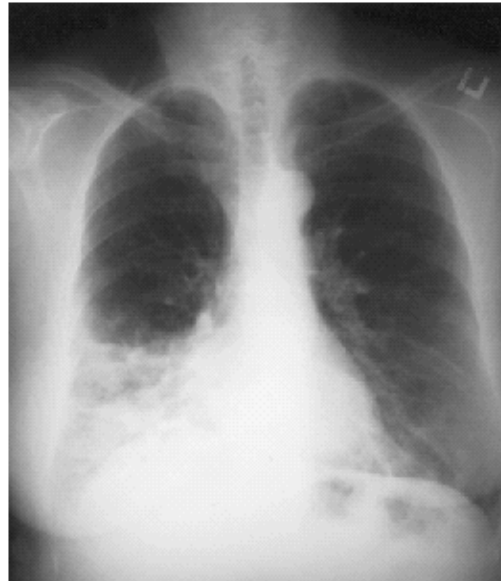
How is this related to his Crohn's disease?

How should it be treated?



# 68 yr old using mineral oil at bedtime

What is the diagnosis?  
What is the pathophysiology?  
She has progressive dyspnea; what is the prognosis?



# 33 yr old with hemophilia and HIV+ presents with severe R flank pain

What was the medication-related diagnosis?  
What was the culprit medication?  
How is this avoided in future?

