

Scleroderma 101: Newly diagnosed

Dr Maggie Larche, MRCP(UK), PhD
Associate Professor,
Division of Rheumatology, McMaster University
St Joseph's Hospital

Scleroderma Conference, Calgary 2018



Objectives

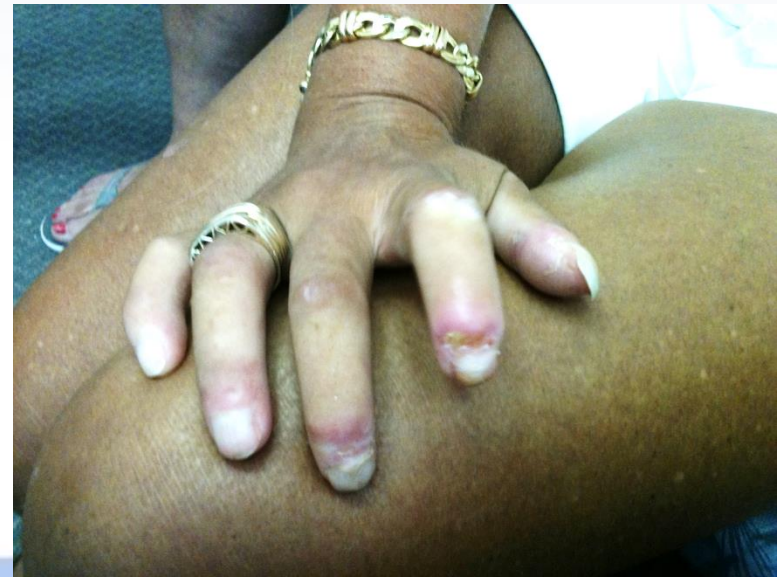
- To describe the features of scleroderma and explain the terminology
- Outline the investigations
- Consider the options in self-directed care
- Describe some of the medical treatments
- Outline some resources

Scleroderma (Systemic Sclerosis) is ...

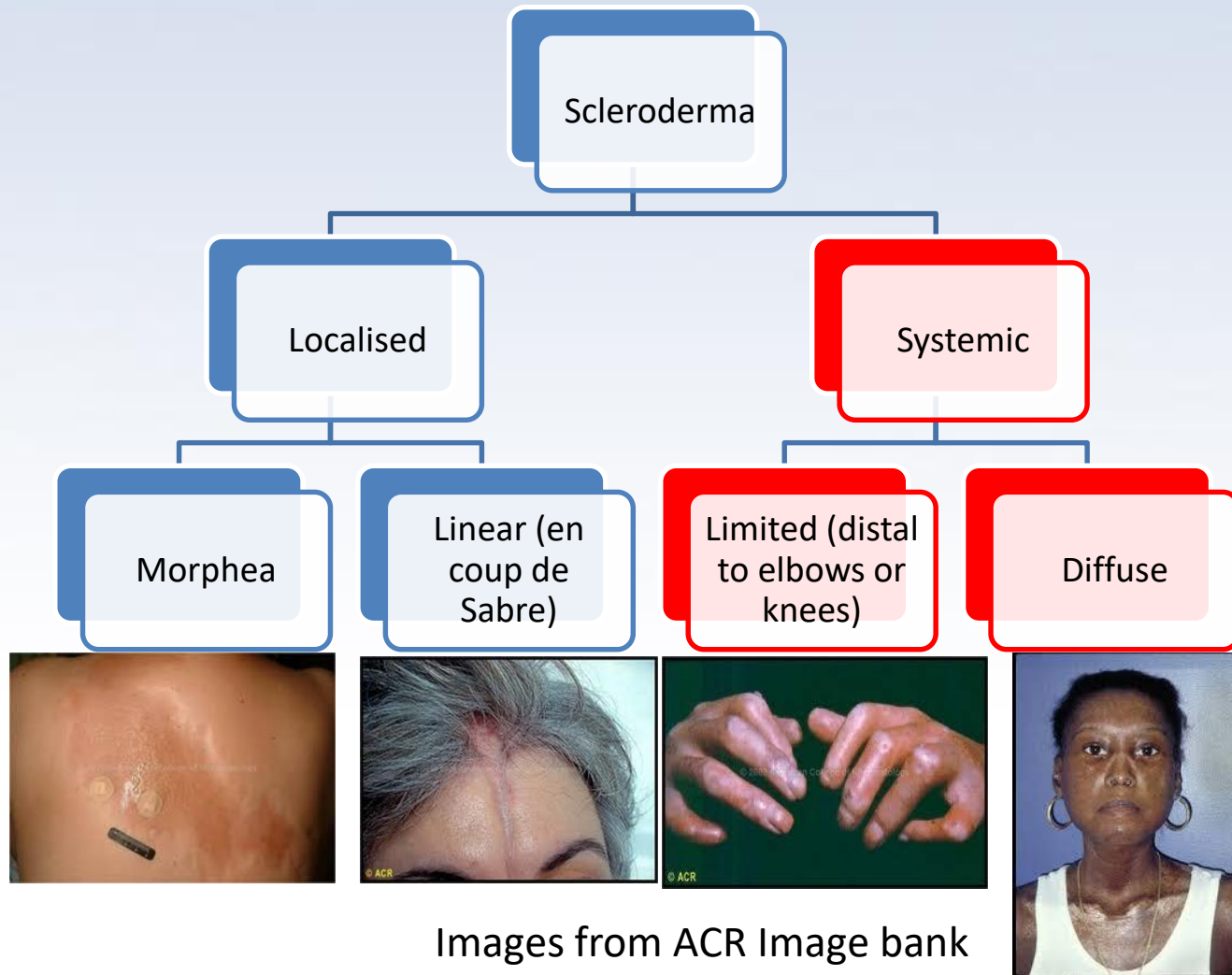
“**sclero**” (Greek meaning **hard**) + “**derma**”
(Latin meaning **skin**)

= **scleroderma** (hard skin)

- Hippocrates
- 1945 association with systemic disease



Terminology



Emotional diagnosis

Months to years of symptoms
Emotional roller-coaster



What causes it?

Did I do something wrong to get this?

How can I get rid of it?

What can I do to help myself?

I don't want to be on medications

What about the future?.....



Many aspects of scleroderma

- **Vascular system**

- Raynauds
- Healed pitting ulcers in fingertips
- Cutaneous and mucosal telangiectasia

- **Gastrointestinal system**

- GERD, GAVE
- Dysmotility
- Constipation /diarrhea

- **Respiratory system**

- ILD
- Pulmonary hypertension

- **Musculoskeletal system**

- Arthritis/myositis
- Flexion contractures
- Carpal tunnel syndrome
- Muscle weakness

- **Constitutional: Fatigue/weight loss**

- **Skin**

- Sclerodactyly
- Edema
- Digital ulcers
- Calcinosis
- Hyper or hypo-pigmentation

- **Cardiovascular system**

- Pulmonary hypertension
- Arrhythmias

- **Genitourinary system**

- Erectile dysfunction
- Dyspareunia

- **Ears, nose, and throat**

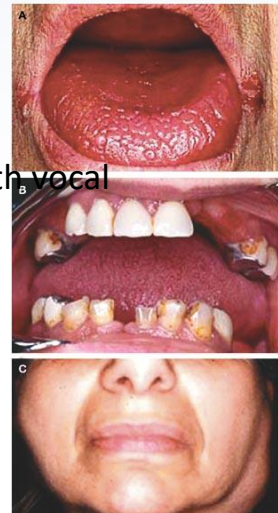
- Sicca syndrome
- Poor dentition
- Hoarseness due to acid reflux with vocal cord inflammation or fibrosis

- **Endocrine system**

- - Hypothyroidism

- **Renal system**

- Hypertension
- Renal crisis
- Chronic renal insufficiency



Many aspects of scleroderma

- **Vascular system**

- Raynauds
- Healed pitting ulcers in fingertips
- Cutaneous and mucosal telangiectasia

- **Gastrointestinal system**

- GERD, GAVE
- Dysmotility
- Constipation /diarrhea

- **Respiratory system**

- ILD
- Pulmonary hypertension

- **Musculoskeletal system**

- Arthritis/myositis
- Flexion contractures
- Carpal tunnel syndrome
- Muscle weakness

- **Constitutional: Fatigue/weight loss**

- **Skin**

- Sclerodactyly
- Edema
- Digital ulcers
- Calcinosis
- Hyper or hypo-pigmentation

- **Cardiovascular system**

- Pulmonary hypertension
- Arrhythmias

- **Genitourinary system**

- Erectile dysfunction
- Dyspareunia

- **Ears, nose, and throat**

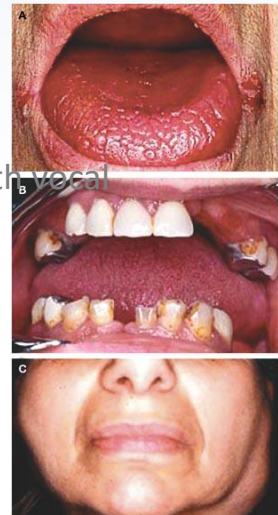
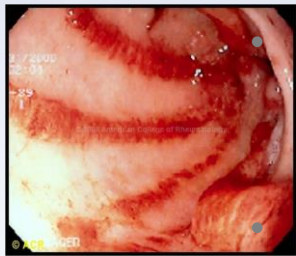
- Sicca syndrome
- Poor dentition
- Hoarseness due to acid reflux with vocal cord inflammation or fibrosis

- **Endocrine system**

- - Hypothyroidism

- **Renal system**

- Hypertension
- Renal crisis
- Chronic renal insufficiency



Many aspects of scleroderma

- **Vascular system**

- Raynauds
- Healed pitting ulcers in fingertips
- Cutaneous and mucosal telangiectasia

- **Gastrointestinal system**

- GERD, GAVE
- Dysmotility
- Constipation /diarrhea

- **Respiratory system**

- ILD
- Pulmonary hypertension

- **Musculoskeletal system**

- Arthritis/myositis
- Flexion contractures
- Carpal tunnel syndrome
- Muscle weakness

- **Constitutional: Fatigue/weight loss**

- **Skin**

- Sclerodactyly
- Edema
- Digital ulcers
- Calcinosis
- Hyper or hypo-pigmentation

- **Cardiovascular system**

- Pulmonary hypertension
- Arrhythmias

- **Genitourinary system**

- Erectile dysfunction
- Dyspareunia

- **Ears, nose, and throat**

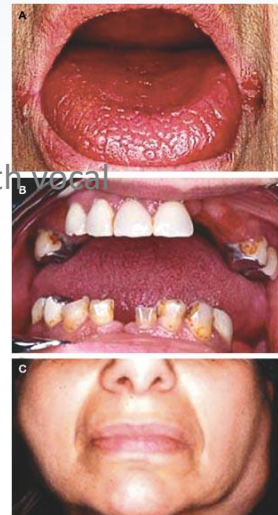
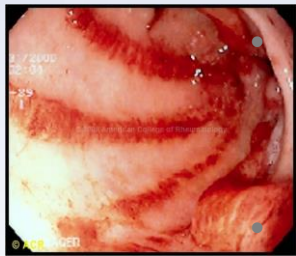
- Sjögren syndrome
- Poor dentition
- Hoarseness due to acid reflux with vocal cord inflammation or fibrosis

- **Endocrine system**

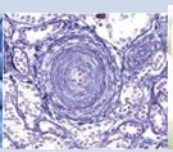
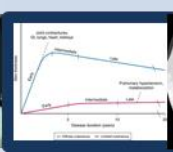
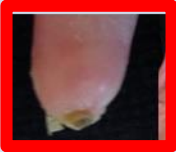
- - Hypothyroidism

- **Renal system**

- Hypertension
- Renal crisis
- Chronic renal insufficiency



Not everyone gets every symptom or complication
Outcome variable



- Vascular system

- Raynauds
- Healed pitting ulcers in fingertips

Pearl 1: clinical aspects

Gastrointestinal system

- GERD, GAVE
- Dysmotility

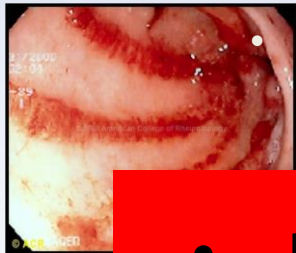
- Skin

- Sclerodactyly
- Edema
- Raynaud's phenomenon
- Hyper or hypo-pigmentation

- Cardiovascular system



- Usually presents with Raynauds, and puffy hands
- Can particularly affect lungs, heart, kidneys and skin
- May overlap with other autoimmune diseases



- - Hypothyroidism
- Renal system
 - Hypertension
 - Renal crisis
 - Chronic renal insufficiency



What is Raynaud's

- Up to 10% women. Women>men
- Occupational exposure (vibrating tools)
- Raynaud described cold extremities with a tri- or bi-phasic white, blue and or red colour changes
- Due to spasm in blood vessels
- Primary
- Or Secondary: Associated with several connective tissue diseases

Raynaud's



Criteria

1. Are your fingers unusually sensitive to cold?
2. Do they change colour?
3. Do they change to white, blue or both?

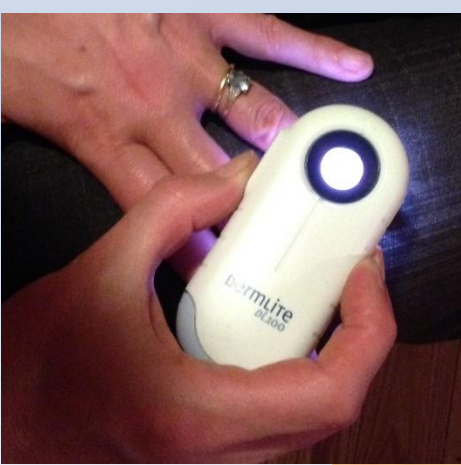
Primary Raynaud's

- Not associated with any other CT disease
- Often begins in adolescence
- Good history and examination are required
- Bloodwork not (usually) necessary
- No associated tissue injury
- Ulcer or digital pits are warning signs

Secondary Raynaud's

- Associated with a connective tissue diseases
 - Scleroderma and SLE
 - (also RA, MCTD, Sjogrens)
 - Thromboangiitis obliterans (Buerger's disease) Smokers young men
 - Other: acrocyanosis, Takayasu's arteritis, anti phospholipid syndrome, cryoglobulinemia, thoracic outlet syndrome
-
- 20% rheumatoid arthritis
 - 30% lupus
 - 30% Sjogren's syndrome
 - 30-40% polymyositis
 - 40% mixed connective tissue disease
 - 90% scleroderma

Nail Fold Capillaries



Blood tests

Complete blood count	Anemia/leucopenia/thrombocytopenia
ESR/CRP	Elevated or normal
Renal function	Elevated or normal
Urinalysis	Look for active urinary sediment
Antinuclear Abs (ANA)	May be positive
Possibly other tests	dsDNA, complement, cryoglobulins, CK, APLA

Red flag symptoms or signs in Raynauds

- Sudden and late onset
- Weight loss, fevers
- Thickened skin
- Digital ulcers
- Rashes
- Calcium deposits
- Arthritis
- Dry eyes/mouth
- Mouth ulcers
- High Blood pressure
- Shortness of breath
- Muscle weakness
- Swallowing difficulties
- Gut disturbances





Pearl 2: Raynauds Red flags

- Older age
 - Male
- Digital ulcers
- Other features of autoimmune diseases

New criteria aid early diagnosis

- Puffy fingers
- Raynaud's phenomenon
- Dilated nail fold capillaries
- (ANA)



2013 ACR/EULAR SSc guidelines

Item	Sub-item	Weight
Skin thickening of fingers of both hands extending proximal to MCP joints (sufficient criterion)		9
Skin thickening of fingers (<i>only count higher score</i>)	Puffy fingers	2
	Sclerodactyly of fingers (distal to MCP joints but proximal to PIP joints)	3
Fingertip lesions (<i>only count higher score</i>)	Digital tip ulcers	2
	Fingertip pitting scars	3
Telangiectasia		2

2013 ACR/EULAR SSc guidelines

Item	Sub-item	Weight
Abnormal nailfold capillaries		2
Pulmonary arterial hypertension and/or interstitial lung disease <i>(maximum score is 2)</i>	Pulmonary arterial hypertension	2
	Interstitial Lung Disease	2
Raynaud's phenomenon		3
SSc-related autoantibodies <i>(Maximum score is 3)</i>	Anti-centromere	3
	Anti-topoisomerase I	
	Anti-RNA polymerase	

Total score = Sum of maximum score in each category

Total Score ≥ 9 Classified as Definite SSc; Maximum Score is 19

Early diagnosis allows improved monitoring and treatment of complications

- Diffuse disease – more likely to get ILD, PAH, renal disease
- Intensive monitoring necessary – ECHO, PFTs, renal function, BP
- Improved treatments available



Pearl 3: early diagnosis

- New criteria make it easier to diagnose SSc early
- Consider in patients with Raynaud's, puffy hands and dilated nailfold capillaries



Part 1: Take Home Messages

- Consider SSc in:
 - new onset Raynauds
 - Raynauds in older patient
 - Puffy fingers
 - Digital ulcers
- Monitor for:
 - pulm fibrosis with annual PFTs (6 monthly if less than 5 yrs)
 - PAH with annual ECHO refer for RHCath if pressures ≥ 40 and dyspnoeic
 - BP and creatinine carefully esp in diffuse disease
- Beware of steroid dose in SSc – $\geq 15\text{mg}$ may precipitate Scleroderma Renal Crisis (SRC)
- Multisystem disease: Talk to colleagues...

Management of specific aspects of SSc

- Raynauds
- Gastro-intestinal
- Pulmonary fibrosis
- Pulmonary hypertension
- Renal crisis

Raynauds: Management

Conservative measures

- Smoking cessation and avoiding the cold
- Emollients
- Avoid drugs such as
 - Beta blockers
 - Clonidine
 - Cyclosporin
 - Cocaine
- Heated gloves, socks



First line medications

- Calcium Channel blockers
 - Amlodipine 10-20mg daily
- Nitrate patches
 - 0.2mcg daily
- Angiotensin Receptor blockers
 - Losartan 50-100mg od



2nd line treatments

- Prostacyclins (IVI – CCU monitoring)
 - Alprostadil
 - Iloprost
- PDE5 inhibitors:
 - Sildenafil 100mg od
 - Tadalafil 40mg od
- SSRIs - Prozac
- Sympathectomy – digital vs axillary

Raynauds: Management

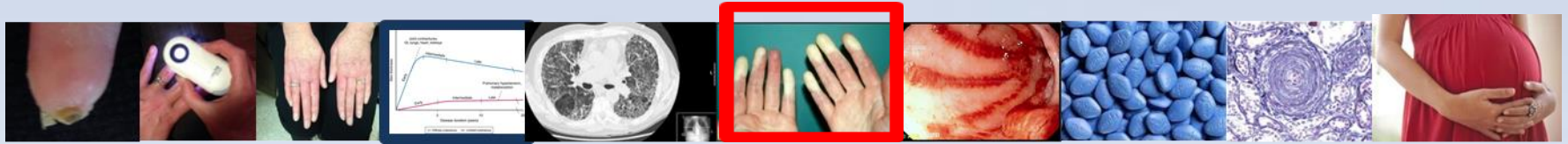
Conservative

- Smoking cessation
- Avoid cold exposure
- Emotional stress management
- Avoid vasoconstrictors
 - Cocaine
 - Amphetamines
 - Sympathomimetics
- Heated gloves, socks



toring)

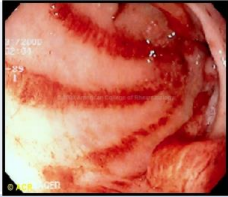
- PDE5 inhibitors:
 - Sildenafil 100mg od
 - Tadalafil 40mg od
- SSRIs - Prozac
- Sympathectomy – digital vs axillary

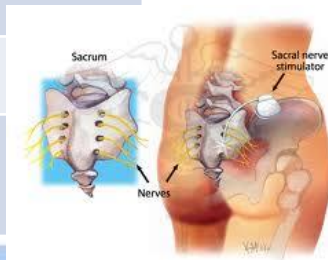


Pearl 4: Specific treatments for Raynauds prevent damage

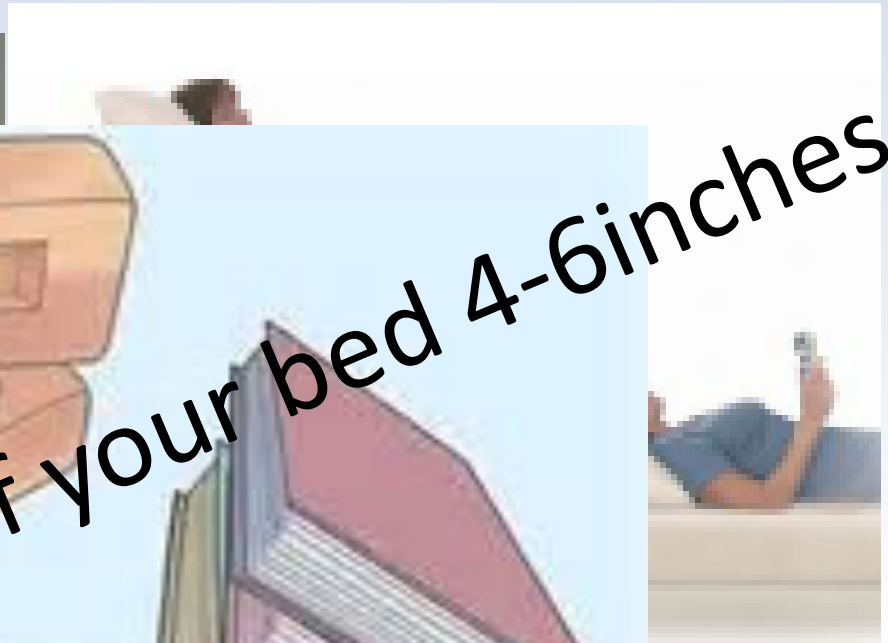
- Amlodipine 10mg od
- Losartan 100mg od
- Prozac +/-Pentoxifylline
- Nitrodur patches 0.2-0.4mcg/day
- Sildenafil/Tadalafil
- IV prostacyclins

Treatment of GI manifestations

Feature	Treatment
GERD	Conservative measures PPI – high doses
GAVE (Watermelon stomach) 	Laser photocoagulation Transfusions
Gastroparesis, Dysmotility Pseudoobstruction	Domperidone 20mg tid Prucalopride 2mg od Octreotide 25-50mcg bid 1G liquid Erythromycin q3 days Pyridostigmine or Neostigmine 1g slow iv
Bacterial overgrowth	Cyclical antibiotics Rifaximin 200mg tid for 3 days
Constipation	Prucalopride 2mg od Laxatives
Diarrhoea	Codeine or loperamide
Incontinence	Low dose loperamide Sacral nerve stimulator



Self-help: GERD or reflux



Raise the head of your bed 4-6 inches



STOP SMOKING

It is Never TOO Late to Stop!

The Healing Time Line

A realistic look at how long it takes for your body to recover after your last puff



● Twenty minutes after quitting, your blood pressure decreases.

● Eight hours: The amount of carbon monoxide in your blood drops back to normal while oxygen increases to normal.

You can do it.

We're here to help.



Ten years: Your risk of all smoking-related cancers such as lung, mouth, and throat decreases by up to 50 percent.

● Fifteen years: Your risk of heart disease and smoking-related death is now similar to that of someone who never smoked.



Finger ulcers

- Keep warm
- Keep moisturised
- Good dressings
- Antibiotics if infection
- Medications



Finger ulcers

First line medications

- Calcium Channel blockers
 - Amlodipine 10-20mg daily
- Nitrate patches
 - 0.2mcg daily
- Angiotensin Receptor blockers
 - Losartan 50-100mg od



2nd line treatments

- Prostacyclins (IVI – CCU monitoring)
 - Alprostadil
 - Iloprost
- PDE5 inhibitors:
 - Sildenafil 100mg od
 - Tadalafil 40mg od
- SSRIs - Prozac
- Sympathectomy – digital vs axillary



Renal crisis risk factors

- Diffuse SSc
- Male gender
- Steroids >15mg daily – (used for arthritis, myositis, pulmonary fibrosis). 1.5% increased risk for each mg of prednisone/day
- (Calcium channel blockers protective)

DeMarco PJ et al 2002 Arthritis Rheum
Steen VD et al 1998 Arthritis Rheum
Montanelli et al 2013 Clin Exp Rheum

Self-help: kidney involvement

- KNOW YOUR BLOOD PRESSURE
- Call for help if BP rises $>30\text{mmHg}$ higher than normal
- If non-specialist doctor, explain at risk of scleroderma renal crisis
- Get bloodwork and urine testing done



Self-help: kidney involvement

- KNOW YOUR BLOOD PRESSURE
- Call for help if BP rises ≥ 30 mmHg higher than normal
- If non-specialist doctor, explain at risk of scleroderma renal crisis
- Get bloodwork and urine testing done



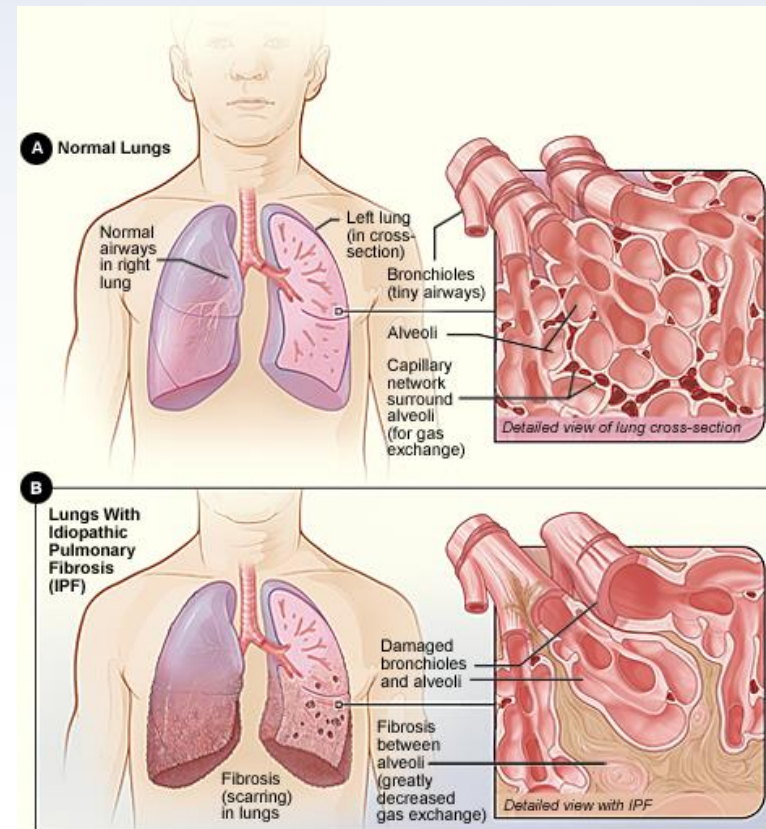


Pearl 7: Scleroderma Renal Crisis – high index of suspicion; treat intensely

- Monitor BP and creatinine
- Careful with dose of oral steroids <15mg daily
- ACE-I – Captopril 12.5mg tid increasing aggressively

Shortness of breath

- Can be a symptom of 2 complications of scleroderma
 - Pulmonary fibrosis
 - Pulmonary hypertension



Testing for pulmonary fibrosis and pulmonary hypertension

- ECG and ECHO every 6-12months



- Lung function tests every 6-12months



Treatment of Pulmonary fibrosis

- Simple measures like reducing GERD
- Medications to suppress immune system – shown to help with inflammation in lung
 - Cyclophosphamide
 - MMF
 - Azathioprine
 - Rituximab

Treatment of Pulmonary fibrosis

Bottom Lines:

- Several drugs helpful in SSc-ILD
 - Cyclophosphamide
 - Mycophenolate
 - Rituximab
- Stem cell transplantation showing promise

- Rituximab – Improves GG appearance (Daoussis D et al Clin Exp Rheum 2013)
- ASTIS trial ARD 2012 Suppl Abs LB0002

Pulmonary Hypertension: treatment

- Improved survival in PAH
- Supportive therapies:
 - Oxygen (if resting pO₂ under 60mmHg)
 - Loop diuretics
 - Digoxin
 - (anticoagulation)
- Calcium channel blockers (after dynamic testing)
- IV epoprostenol
- Endothelin receptor antagonists – Bosentan, Ambrisentan-improved exercise capacity and functional status
- PDE5 inhibition- Sildenafil, tadalafil – improved exercise capacity

Each patient is different

- Different symptoms
- Different combination of medicines
- Some may have few or no medicines

- Support groups
- Educational events
- Fund-raising
- Raising awareness
- Research



GET INVOLVED



Get involved in research

- Databases
 - Bloodwork
 - Questionnaires
 - New treatment options
-
- Research is our hope...



Resources

- Hamilton Scleroderma Group –
www.hamiltonscleroderma.org
- Scleroderma Society of Canada (/Ontario)
www.scleroderma.ca
- Scleroderma Foundation
www.scleroderma.org

Conclusions

- Everyone is different
- Supportive management and self-help
 - Quit Smoking
 - Keep hands and feet warm and moisturised
 - Raise the head of your bed 4 inches
 - Know your Blood Pressure
- Specific treatments – should be under a specialist
- New hope...



Scleroderma ``Team approach``

Hamilton Scleroderma Group

www.hamiltonscleroderma.org/



Thanks

- Scleroderma Society of Ontario and Canada
- Multidisciplinary colleagues at Hamilton Scleroderma Group – Andrea Gardner– the patient's quarterback!
- Questions: mlarche@mcmaster.ca

