



**The Storm and
A Decathlete**

28-5-2010

Inter-hospital Geriatric Meeting


Dr TC Chan

Dr KH Luk

Queen Mary Hospital

MSF 74/M

- **Live alone**
- **ADL-I**
- **Walk unaided**
- **Non smoker non drinker**

- 
- **Past medical history**
 - **Primary biliary cirrhosis with positive anti-mitochondria antibodies follow up C hospital**
 - **Not on any regular medication**

- **Admitted C hospital for**
 - **General malaise**
 - **Weight loss of ~5kg in 1 month**
- **Physical examination unremarkable, haemodynamically stable**
- **Ix result**
 - **WBC increase**
 - **CXR right lower zone haziness**
 - **albumin 26 g/L**
 - **ALP 187 U/L**
- **Treated as sepsis with Augmentin and discharge the 2nd day**

- 
- A sunset over the ocean with a lighthouse on the left. The sky is filled with soft, colorful clouds in shades of orange, yellow, and pink. The ocean is dark blue with gentle waves. A lighthouse is visible on the left side of the image, partially obscured by the text.
- After discharge, malaise persist
 - His son was **not satisfied** with C hospital and bring the patient to Queen Mary Hospital

A background image of a sunset over the ocean. The sky is filled with soft, colorful clouds in shades of orange, yellow, and pink, with the sun low on the horizon. The ocean below is dark and textured.

- **History**

- **Malaise and weight loss of 5kg over 1 month**
- **Appetite decrease**
- **Decrease self care ability**
- **No other localizing symptom**
 - **Cough, shortness of breath, sputum production, nausea, vomiting, alternation of bowel habit, haematuria, arthralgia, myalgia, neck stiffness, blurring of vision**
- **No other systemic symptom**
 - **Fever, night sweating, chills, rigor**

A background image of a sunset over the ocean. The sky is filled with soft, colorful clouds in shades of orange, yellow, and pink, transitioning into a darker blue at the top. The ocean surface is visible in the lower half, with gentle ripples and a small wave breaking on the left side.

- **Physical examination**

- **Afebrile**
- **BP 120/80 P 72 regular**
- **SaO2 99% RA**
- **Cachexic**
- **Other P/E → generally unremarkable**
 - **Chest NAD**
 - **CVS**
 - **heart sound normal and NO murmur**
 - **Abdomen**
 - **soft, NO organomegaly, PR NO mass**
 - **CNS**
 - **Cranial nerve intact, power 5-/5 generally, NO neck stiffness, NO sensory loss**

- **CBP**

- **WBC 14.4 (x10⁹/L)**

- Neutrophil 11.7
- Lymphocyte 0.8
- Monocyte 0.8
- Eosinophil 0.3

- **Hb 10.6 g/dL**

- MCV 87.2 fL
- MCH 29.3 pg

- **Plt 527 x 10⁹/L**

- **L/RFT**

- **Na 134 mmol/L, K 3.9 mmol/L**

- **Urea 4.3 mmol/L**

- **Creatinine 58 umol/L**

- **Albumin 22 g/L**

- **Globulin 46 g/L**

- **Bili 10 umol/L**

- **ALP 187 U/L**

- **AST 10 U/L, ALT 20 U/L**

- **Clotting**

- **PT 11.4 second**

- **INR 1.0**

- **APTT 31.3 second**

A background image of a sunset over the ocean. The sun is low on the horizon, casting a warm glow across the sky with scattered clouds. The water in the foreground is dark and textured.

- **CXR**

- **Clear**

- **Urinalysis**

- **Protein 30 mg/dL**

- **Nitrites and Leucocytes esterases –ve**

- **Occult blood small, cast -ve**

- 
- A sunset over the ocean with a list item. The sky is filled with soft, colorful clouds in shades of orange, yellow, and pink. The sun is partially obscured by a cloud, creating a bright glow. The ocean is dark blue with gentle waves. The text "• Imp: Sepsis for investigation" is overlaid on the image.
- **Imp: Sepsis for investigation**

Interhospital Geriatrics Meeting

- 
- A photograph of a sunset over the ocean. The sun is low on the horizon, partially obscured by clouds, creating a warm, golden glow. The sky is filled with soft, colorful clouds in shades of orange, yellow, and pink. The ocean is dark blue with gentle ripples. The overall mood is serene and peaceful.
- **General Team Consulted Geriatrics**
 - **deconditioning**
 - **rehabilitation plan**

Interhospital Geriatrics Meeting

What will be your decision?


- **Send to rehabilitation hospital for rehabilitation?**
- **Further investigation?**

Takeover the patient and further investigate and manage before transfer

- **Multi disciplinary assessment**
 - **Physiotherapist**
 - Premorbid walk unaided
 - Walk with frame + supervision
 - **Occupational therapist**
 - Premorbid ADL independent and live alone
 - MMSE 26/30
 - BADL still independent but feel tired easily
 - Self care ability limited

**– MORE THAN SIMPLE
DECONDITIONING**

- **ESR >140 mm/hr**
- **CRP 16.90 mg/dl**
- **Iron profile**
 - **Iron 4.7 umol/L** **Ferritin 1482 pmol/L**
 - **Serum TIBC 27 umol/L** **TRF Saturation 17%**
- **LDH 201 U/L**
- **Stool for OB**
 - **negative**

- 
- **Major abnormal finding**
 - **Increase WBC**
 - **NcNc anemia**
 - **Markedly increase inflammatory marker**
 - **Hypoalbuminemia**
 - **Significant weight loss**
 - **Markly decrease exercise tolerance**
 - **A FEBRILE**

A background image of a sunset over the ocean. The sun is low on the horizon, casting a warm glow across the sky with soft, wispy clouds. The water in the foreground is dark and textured.

- **Hypoalbuminemia**

- **Related to underlying primary biliary cirrhosis?**

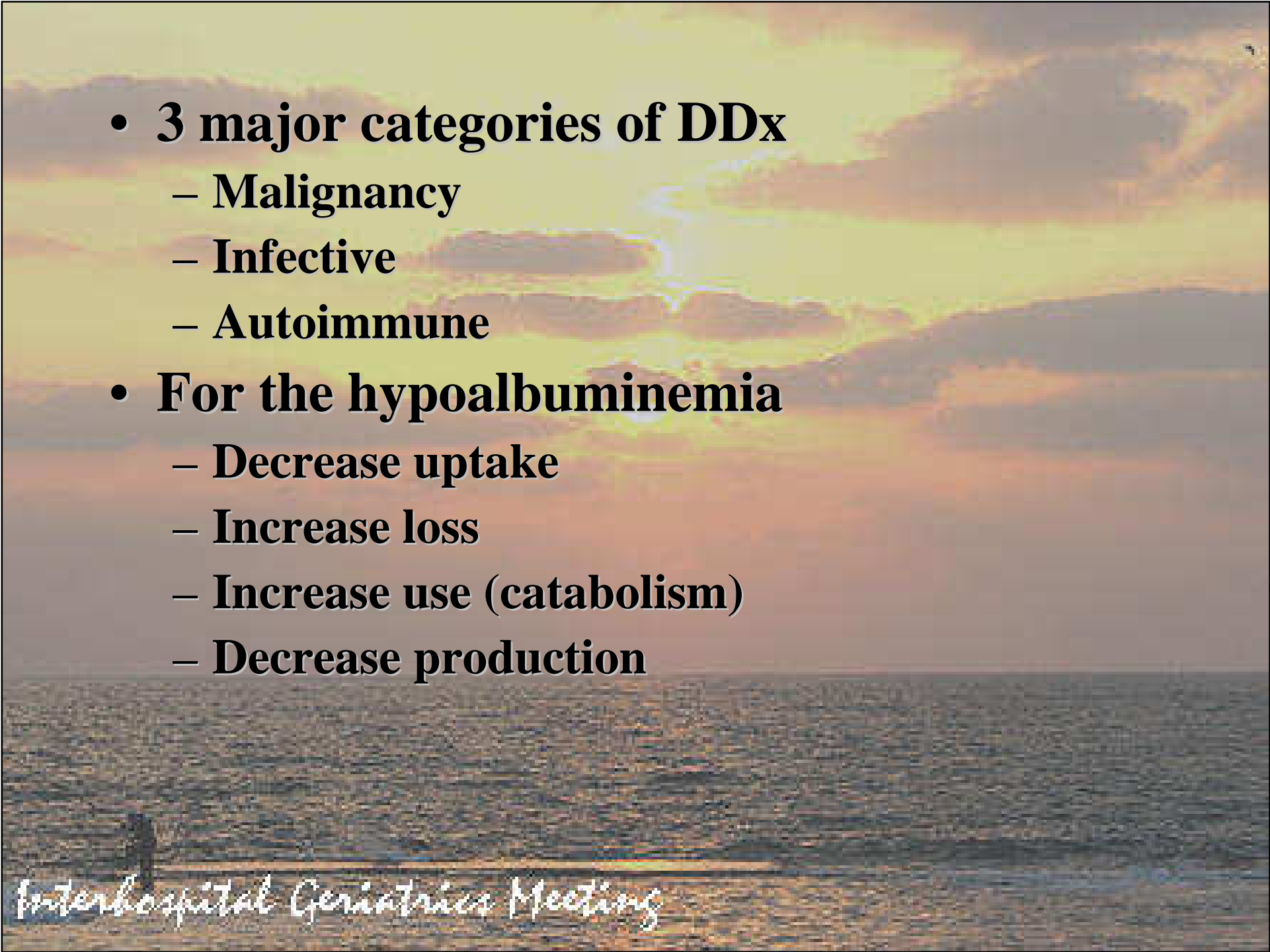
- **Unlikely**

- **No stigmata of chronic liver disease**

- **Albumin 3/12 ago normal**

- **Normal spleen size**

- **Normal clotting profile**

- 
- **3 major categories of DDx**
 - Malignancy
 - Infective
 - Autoimmune
 - **For the hypoalbuminemia**
 - Decrease uptake
 - Increase loss
 - Increase use (catabolism)
 - Decrease production

- **Malignancy and Infection**

- **Tumor marker**

- Ca 19.9, CEA, AFP negative

- **MT2**

- Not reactive

- **Bld culture, urine culture**

- no growth

- **Echocardiogram**

- no vegetation

- **Sputum, early morning urine, gastric aspirate x AFB smear**

- All negative

- **Serum and Urine electrophoresis**

- -ve

- **Weli Felix, Typhoid, Brucellosis antigen, Legionella antigen**

- All unremarkable

- **PET/CT**

- No evidence of focal occult infection or FDG-avid malignancy

A background image of a sunset over the ocean. The sun is low on the horizon, casting a warm glow across the sky with soft, wispy clouds. The water in the foreground is dark and textured.

- **Autoimmune**

- **Anti-ds DNA**

- **5 IU/ml**

- **C3**

- **133 mg/dl**

- **C4**

- **36 mg/dl**

- **Anti-mitochondria**

- **positive**

- **RF**

- **270 IU/ml**

- **Anti CCP**

- **<16 units**

- **Anti ENA**

- **Negative**




- **Autoimmune**

- **ANA**

- **Cytoplasmic staining, titre cannot be interpreted**

- **ANCA**

- *Perinuclear ANCA by immunofluorescence*
- *MPO ANCA titre 196 RU/ml*

- 
- **Active finding**
 - **Increase WBC**
 - **Anemia**
 - **Marked hypo albumin**
 - **Increase inflammatory marker**
 - **Positive p-ANCA / MPO-ANCA**
 - **Conclusion: Active ANCA +ve vasculitis**

A photograph of a sunset over a body of water. The sky is filled with dark, heavy clouds, with a bright orange and yellow glow from the setting sun breaking through near the horizon. In the foreground, the water is dark and reflects the light from the sky. In the middle ground, a pier or breakwater extends into the water, with several vertical posts. In the far distance, a line of wind turbines is visible against the horizon.

ANCA +ve Vasculitis

Do you agree?

- **ANCA +ve vasculitis**
 - **Small vessel vasculitis**
 - **WG (Wegener's granulomatosis)**
 - **MPA (Microscopic polyangiitis)**
 - **Churg Strauss syndrome**
 - **Drug related vasculitis**

- **NO TCM, OTC intake**
- **Chest**
 - CXR unremarkable
 - PET CT show old TB scar
- **Renal**
 - 24 hour urine for protein: 0.3g
- **Nerve**
 - NCV: no vasculitic change
- **Detail clinical examination of skin**
 - unremarkable

- **Other occult infection / occult malignancy which cannot be detected by PET/CT**
- **Active ANCA +ve vasculitis without major organ involvement but with significant catabolism**
 - **Direction**
 - **Empirical immunosuppressant?**

Interhospital Geriatrics Meeting

- 
- **DDx 1**
 - **PET/CT limitation**
 - Major Malignancy / infection that may not be able to be detected...

Tell you later...

Interhospital Geriatrics Meeting

- **DDx 2**
- **ANCA: high sensitivity and specificity**
- **All international guideline suggest**
 - **histological proof is essential before starting immunosuppressant**
 - **Should not dependent solely on autoimmune marker for guiding subsequent diagnosis**

- 
- **Luckily, one more important information!**

Interhospital Geriatrics Meeting

- **For the hypoalbuminemia**
 - **Decrease uptake**
 - **Malnutrition**
 - **Increase loss**
 - **Renal loss 0.3g protein / 24 hours**
 - **Increase use (catabolism)**
 - **Active inflammation**
 - **Decrease production**
 - **PBC (should not be significant)**

Interhospital Geriatrics Meeting

- **Additional information**
 - **Stool for alpha-1-antitrypsin for calculation of alpha-1-antitrypsin clearance**
 - **Increased**
 - **A sensitive test for PLE**
 - **Chromium-labeled albumin scan**
 - **Protein losing enteropathy over ascending colon or level proximal to ascending colon**
 - **A specific test for PLE**
 - **Protein losing enteropathy**

- **Active ANCA +ve vasculitis + isolated protein losing enteropathy (no other major organ involvement)**
 - NO case report in pubmed
- **Infective/malignant cause of protein losing enteropathy which cannot be detected in PET/CT**
 - **TB ileitis (especially in this locality and evidence of old TB scar)**
 - **Stromal tumor**
 - **Colonoscopy arranged**

- **Investigation, investigation and investigation...**
 - **Patient was weaker and weaker... progressive weight loss, extreme poor appetite**
 - **Functional status: walk with frame → chairbound → nearly bedbound...**
 - **Any definitive plan?**

Interhospital Geriatrics Meeting

- Patient become more and more miserable...
- Daily multi disciplinary support
 - PT, OT, MSW, clinical psychologist
 - Geriatrician
- “多謝晒你哋!”

Interhospital Geriatrics Meeting

- **Rheumatologist**
 - Send the patient to rehabilitation hospital for rehabilitation
 - The possibility of vasculitis is LOW
- **Geriatrician**
 - Save the patient who have an excellent premorbid...

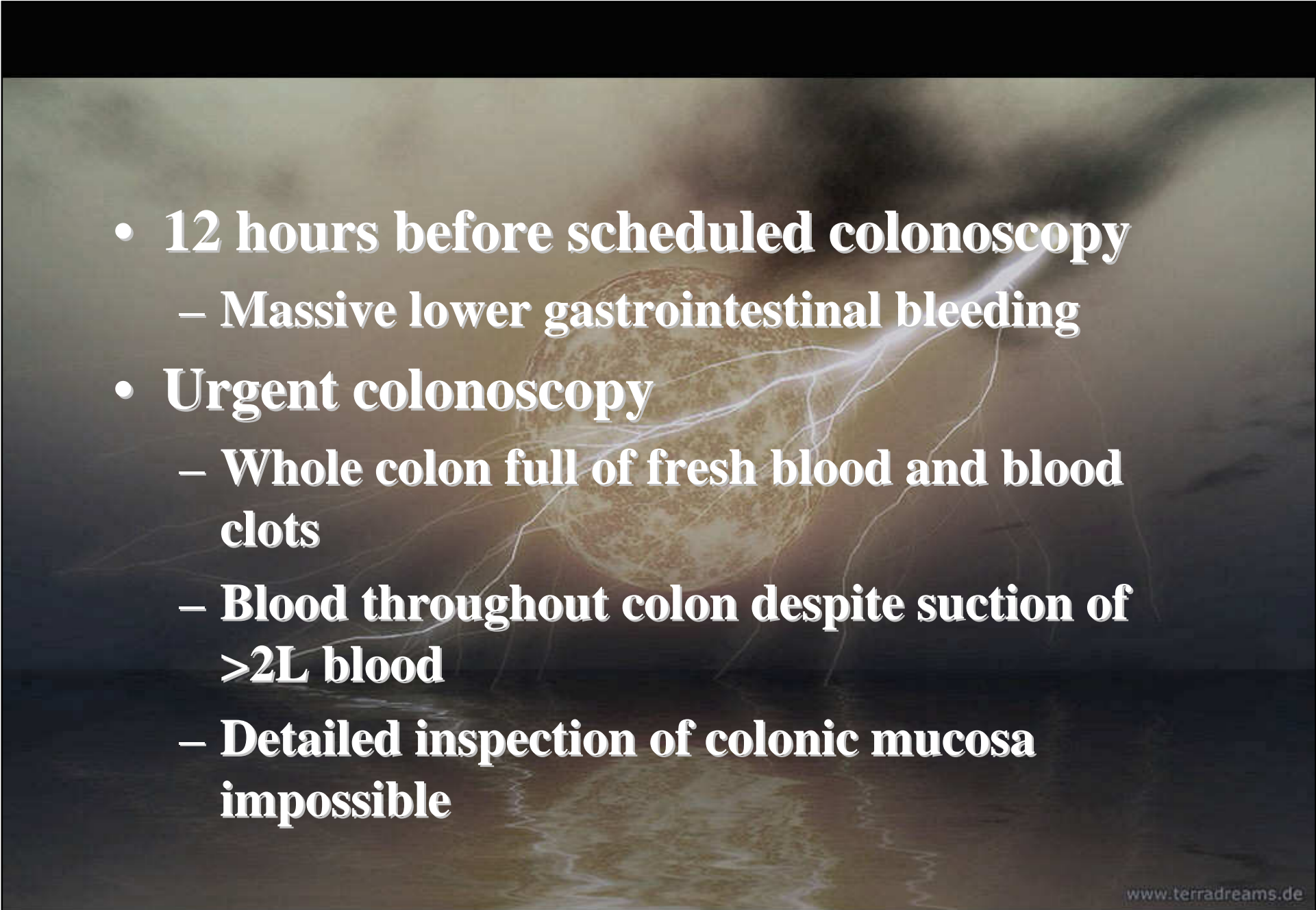
Interhospital Geriatrics Meeting

Final plan

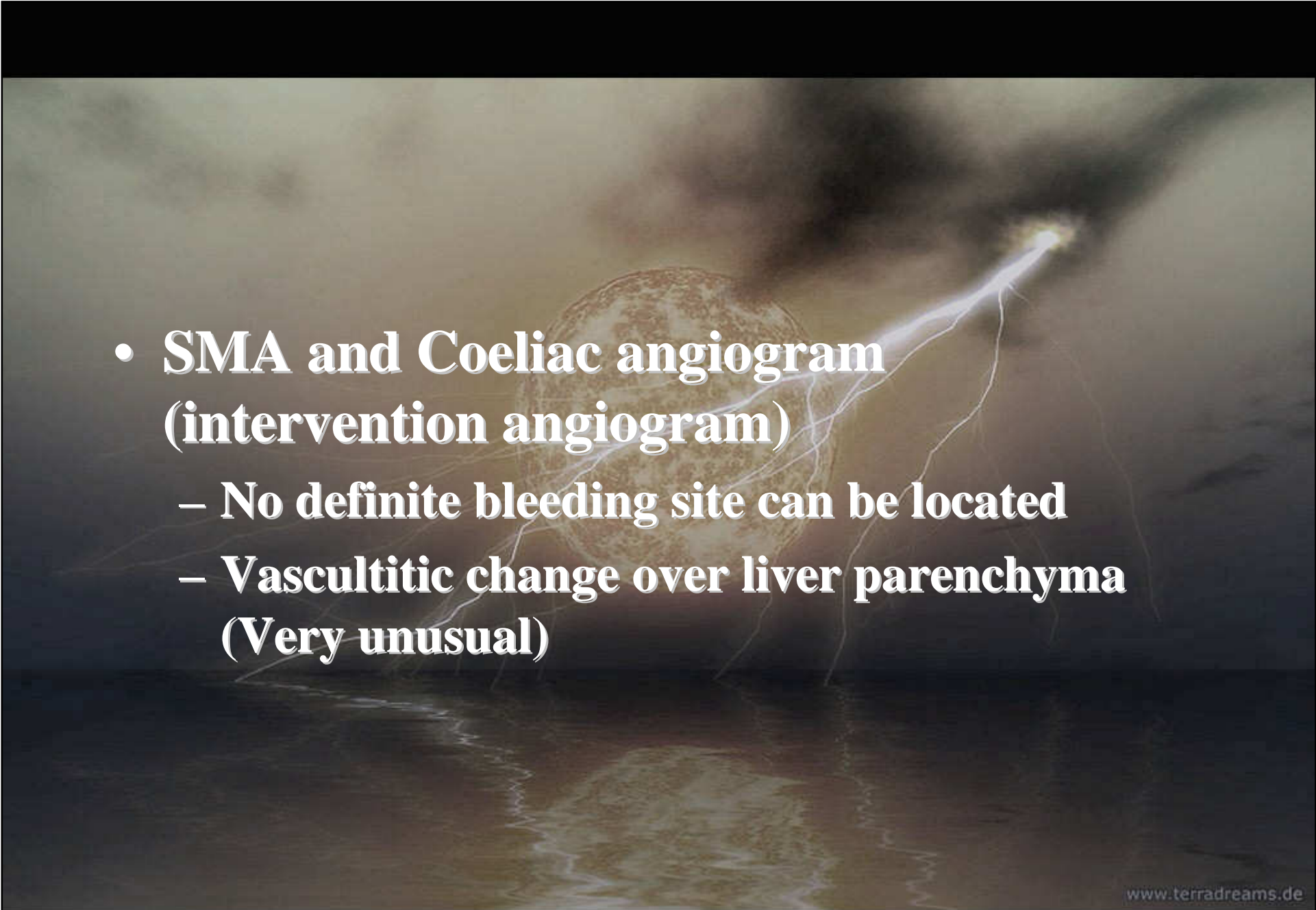
- **Nutrition issue**
 - **Enteral feeding**
- **Disease issue**
 - **Dependent on colonoscopy result**
 - **positive result for TB ileitis or stromal tumor**
 - **Treat according**
 - **negative result and/or vasculitic change and/or non-specific inflammation**
 - **Treat as ANCA +ve vasculitis**

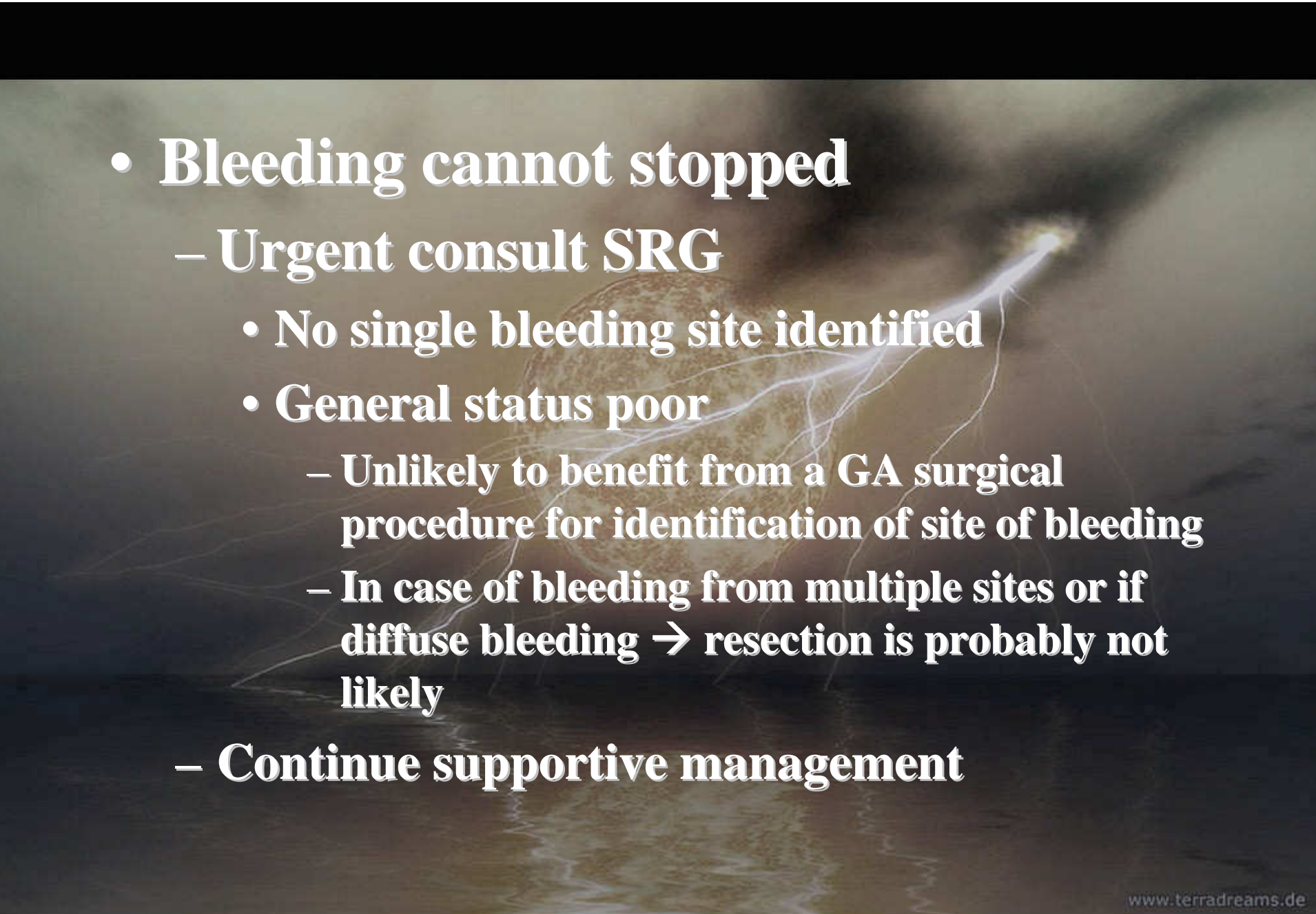


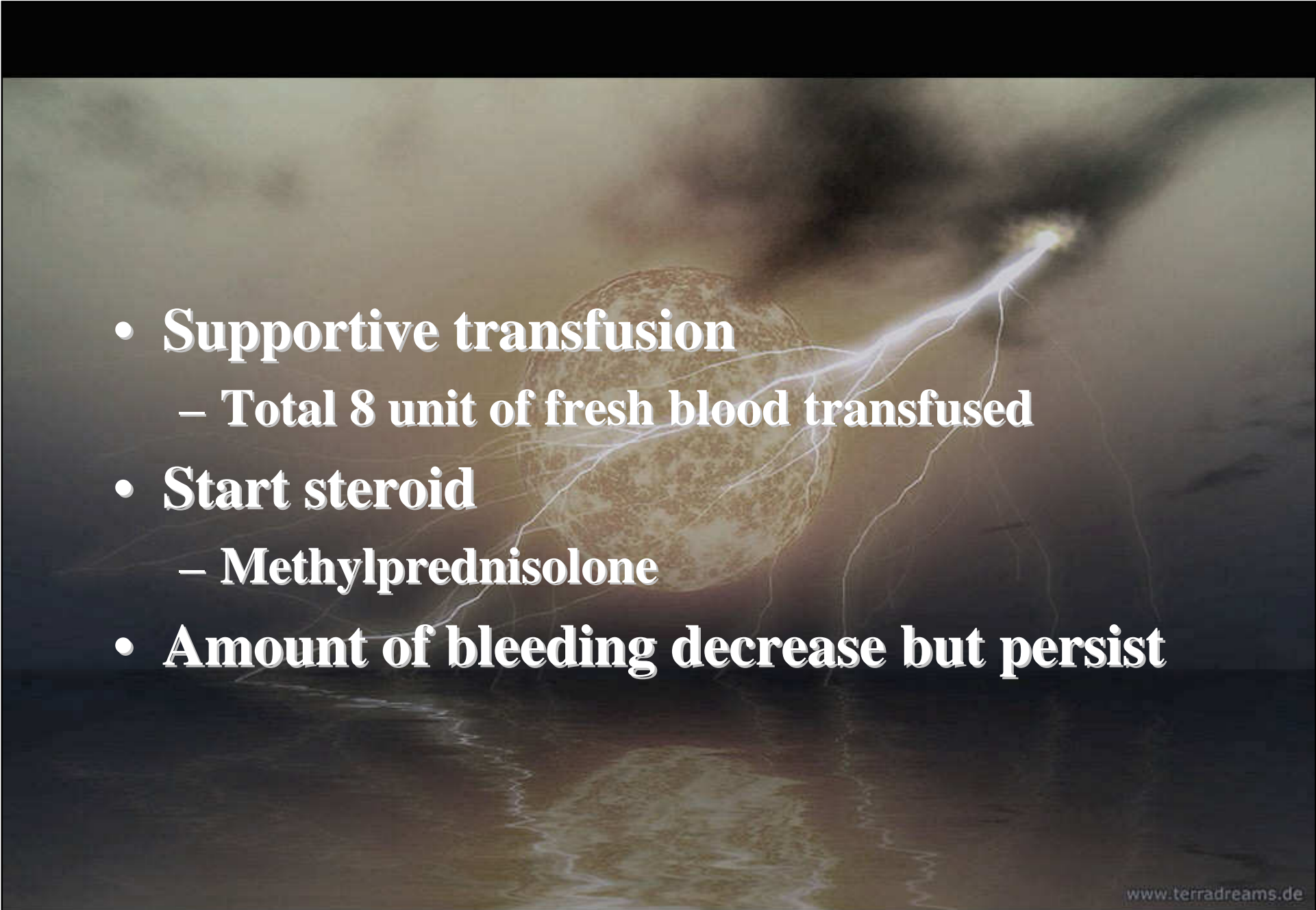
God works in mysterious ways


- 
- **12 hours before scheduled colonoscopy**
 - Massive lower gastrointestinal bleeding
 - **Urgent colonoscopy**
 - Whole colon full of fresh blood and blood clots
 - Blood throughout colon despite suction of >2L blood
 - Detailed inspection of colonic mucosa impossible

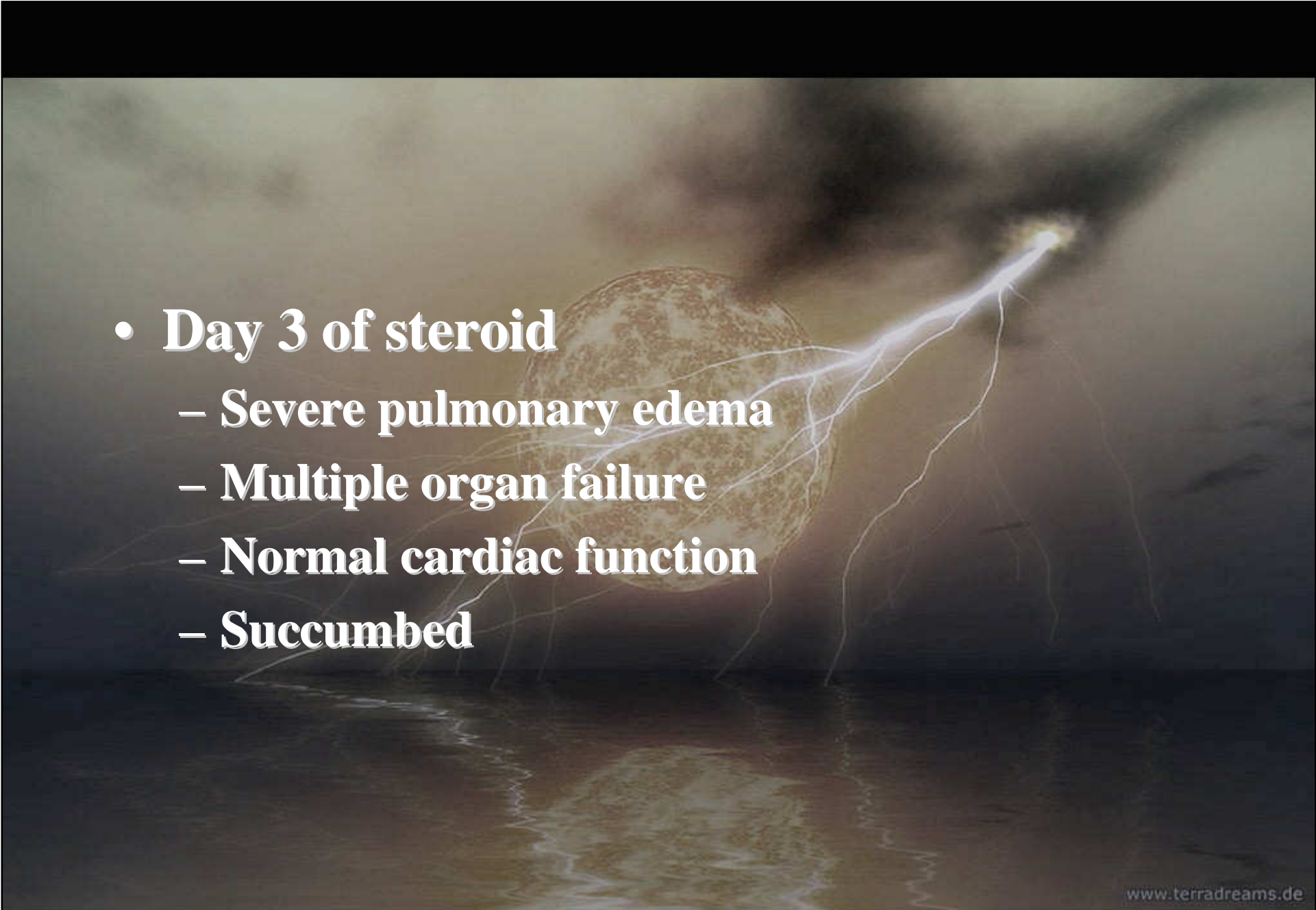
- 
- A dramatic landscape featuring a full moon in the center, a bright lightning bolt striking from the upper right, and a body of water in the foreground reflecting the moon and lightning. The sky is dark and cloudy.
- **CT angiogram**
 - No definite bleeding site can be located
 - **SMA and Coeliac angiogram (intervention angiogram)**

- 
- **SMA and Coeliac angiogram (intervention angiogram)**
 - **No definite bleeding site can be located**
 - **Vasculitic change over liver parenchyma (Very unusual)**

- 
- **Bleeding cannot stopped**
 - **Urgent consult SRG**
 - **No single bleeding site identified**
 - **General status poor**
 - **Unlikely to benefit from a GA surgical procedure for identification of site of bleeding**
 - **In case of bleeding from multiple sites or if diffuse bleeding → resection is probably not likely**
 - **Continue supportive management**

- 
- A dramatic landscape featuring a full moon in a dark, stormy sky. Multiple bright lightning bolts strike down from the clouds. The scene is reflected in a body of water in the foreground. The overall mood is intense and atmospheric.
- **Supportive transfusion**
 - Total 8 unit of fresh blood transfused
 - **Start steroid**
 - Methylprednisolone
 - **Amount of bleeding decrease but persist**

- 
- **Day 2 of steroid**
 - **Sudden deterioration**
 - **Desaturation**
 - **Shock**
 - **CXR**
 - **New right middle zone consolidation + frothy change over other part of chest**
 - **Big gun antibiotics, inotropes, ICU**

- 
- **Day 3 of steroid**
 - **Severe pulmonary edema**
 - **Multiple organ failure**
 - **Normal cardiac function**
 - **Succumbed**

A dramatic night scene of a storm over a body of water. The sky is dark and filled with heavy, grey clouds. Multiple bright, jagged lightning bolts are visible, striking down from the clouds. In the foreground, a wooden pier with several vertical posts extends into the water. In the middle ground, a long bridge with many lights spans across the water. The water is dark and reflects the light from the bridge and the lightning. The overall atmosphere is dark and intense.

**What is the
underlying diagnosis?**

- 
- A dramatic black and white photograph of a lightning storm over a body of water. In the foreground, a wooden pier with several vertical posts extends into the water. The middle ground shows a long pier or bridge structure stretching across the water. The background is dominated by a dark, stormy sky with multiple bright, jagged lightning bolts striking down. The overall mood is intense and ominous.
- **Post mortem**
 - **Answer?**

Interhospital Geriatrics Meeting

- 
- **Polyarteritis Nodosa involving Liver, kidney, GI tract, adrenal...**

Interhospital Geriatrics Meeting

- 
- A dramatic black and white photograph of a lightning storm over a body of water. In the foreground, a wooden pier with several vertical posts extends into the water. In the background, a long pier or bridge structure is visible across the water. The sky is dark and filled with multiple bright, jagged lightning bolts striking down. The overall mood is intense and stormy.
- **PAN is really a kind of vasculitis**
 - **Then...**
 - **Why PAN is not considered?**

Interhospital Geriatrics Meeting

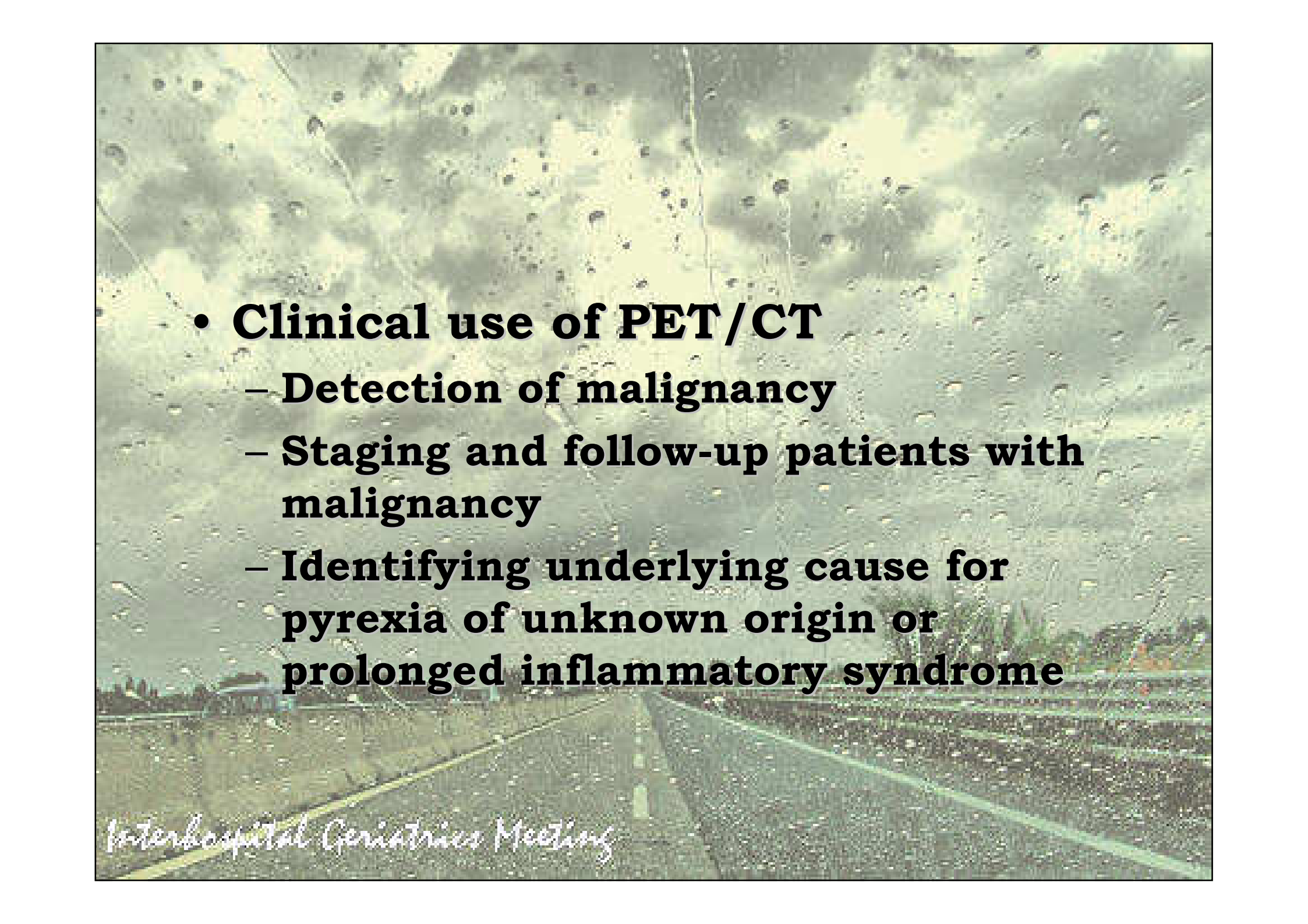
Final outcome

- **We failed to save our patient**
- **But his son highly appreciated our multi disciplinary care, who care his father as a whole**
- **They invited us to join our patient's funeral**

Interhospital Geriatrics Meeting

Review

- **Clinical use of (PET/CT) and its limitation**
- **Clinical significance of ANCA**
- **ANCA associated Vasculitis in Older Patients**
- **Polyarteritis Nodosa**
- **Why PAN is not considered in our patient initially?**
- **Meaning of Decathlon**

- 
- **Clinical use of PET/CT**
 - **Detection of malignancy**
 - **Staging and follow-up patients with malignancy**
 - **Identifying underlying cause for pyrexia of unknown origin or prolonged inflammatory syndrome**

- **Basic knowledge about PET**
 - **A type of radioisotope scan using FDG**
 - **FDG**
 - **Glucose analogue**
 - **Follow a metabolic pathway partially similar to glucose**
 - **When being uptake by cell, only partially metabolized**
 - **Manifested as “hot spots” in FDG imaging**
 - **Some malignancy, infectious process**
 - **Difficulties in interpretation in area with increased normal glucose metabolism**
 - **Brain, bone marrow**

- **Basic knowledge about PET**
 - **Some tumor may have only insignificant FDG uptake**
 - **Highly differentiated tumor**
 - **Tumor with modest glucose activity e.g. prostate cancer, mucinous carcinoma**
 - **Some location may have high distribution and interfere its interpretation**
 - **Urinary system (due to accumulation of FDG activity in urine)**

- **Major malignancy detected by PET**
 - **Head and neck**
 - **Breast**
 - **Lung (small and non-small)**
 - **Colorectal**
 - **Malignant lymphoma (HL and NHL)**
 - **Malignant melanoma**
 - **Gynaecologic tumor**
 - **Iodine-negative thyroid carcinoma**
 - **Malignant bone tumors**
 - **Testicular cancer**
 - **sarcoma**

- **Major malignancy NOT detected by PET**
 - **Malignancy in urinary system**
 - **Malignancy in brain**
 - **Early stage of Ca Lung**
 - **Neuroendocrine tumor (Ga-DOTATOC)**
 - **Prostate tumor (^{11}C - ^{18}F -choline)**

Annals of Nuclear Medicine Vol. 21, No. 1, 65-72, 2007

Interhospital Geriatrics Meeting

Site	Number	PET positive cases	PET negative cases
Colon	15 ^{†,‡}	14	1
Thyroid	11 ^{†,§}	10	1
Lung	10	5	5
Stomach	9 [‡]	7	2
Liver	4	3	1
Bladder	3	0	3
Kidney	3	1	2
Breast	3	2	1
Gallbladder	2	1	1
Prostate	2	0	2
Esophagus	1	1	0
Pancreas	1 [¶]	1	0
UP*	1	1	0
Total	65	46	19

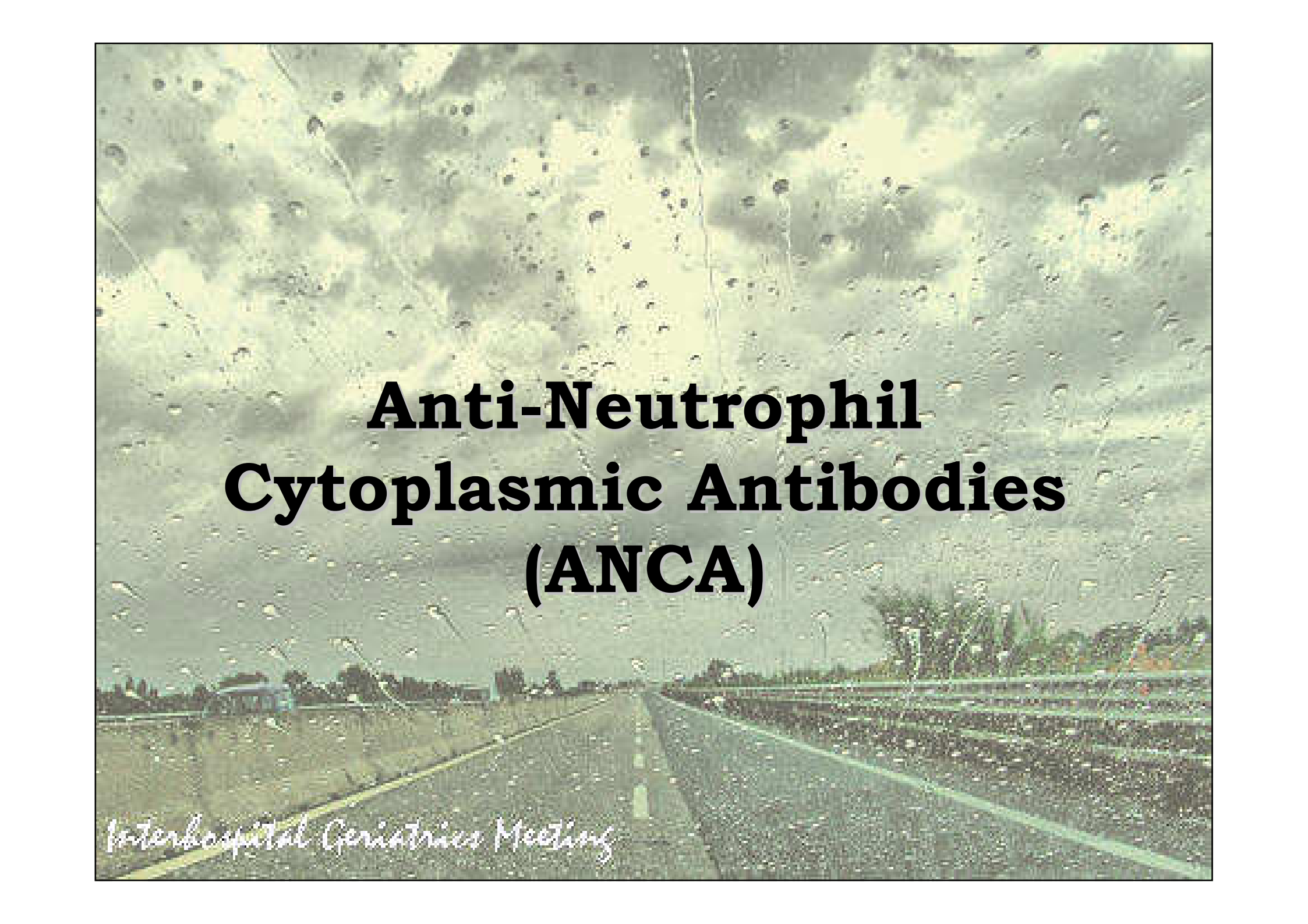
- **Major cause of pyrexia of unknown origin or prolonged inflammatory syndrome that cannot be detected by PET**
 - **Infection in urinary system**
 - **Infection in brain**
 - **Vasculitis of small and medium vessel**
 - **Other rheumatological disease e.g. PMR**

*European Journal of Nuclear Medicine and
Molecular Imaging Vol. 31, No. 1 (2004)*

*European Journal of Nuclear Medicine and
Molecular Imaging Vol 34: 694-703, (2007)*

Interhospital Geriatrics Meeting

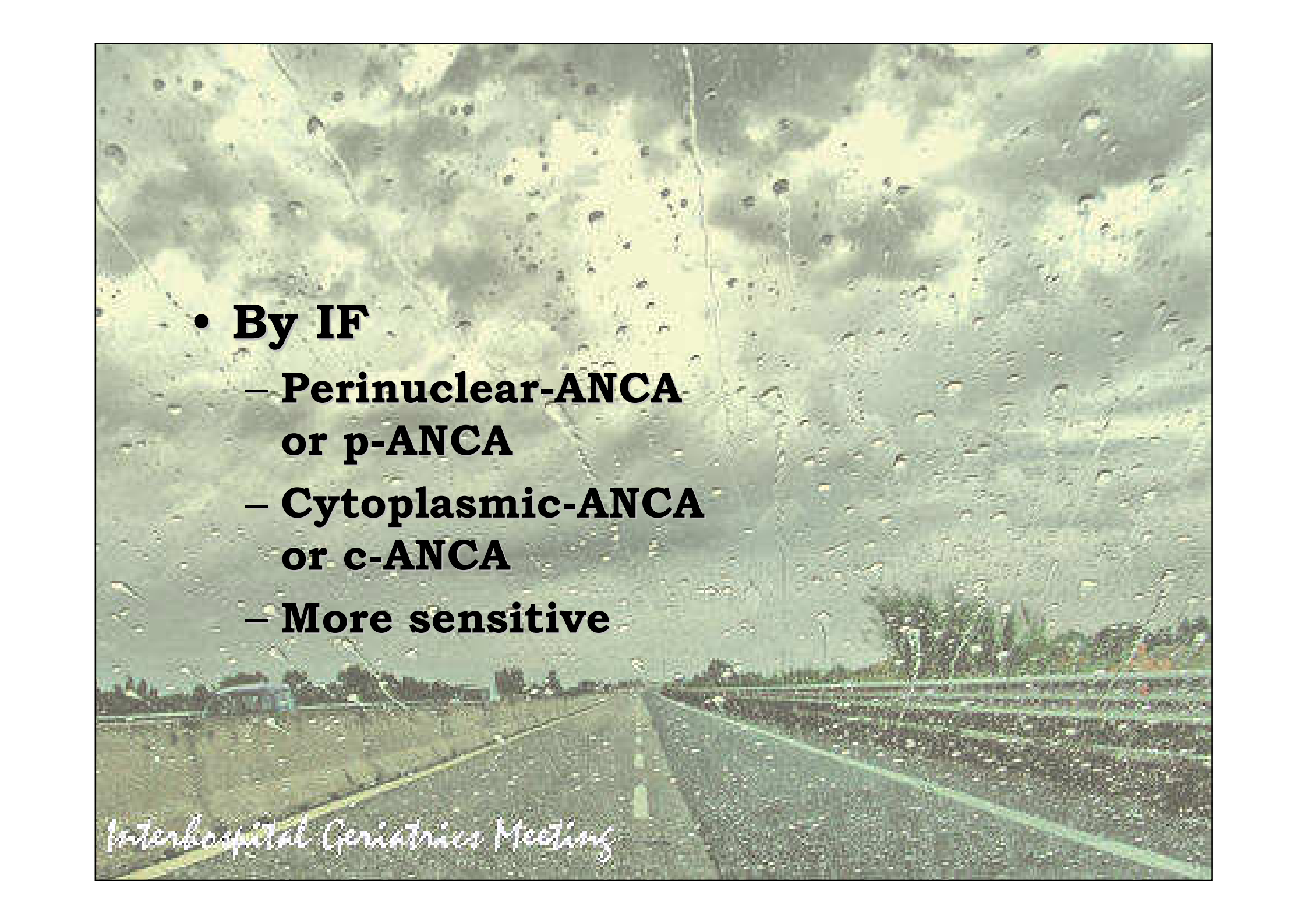
Category	No. of cases	True positive	True negative	False positive	False negative
Infection	12 (17%)	11	–	–	1
Bronchiectasia/pneumonia	2	2	–	–	–
Diverticulitis	1	1	–	–	–
Pyelonephritis	1	–	–	–	1
Abdominal abscesses	1	1	–	–	–
Osteomyelitis	2	2	–	–	–
Tonsillitis	1	1	–	–	–
Chronic persistent yersiniosis	4	4	–	–	–
Neoplasm	5 (7%)	5	–	–	–
Non-Hodgkin's lymphoma	3	3	–	–	–
Metastatic breast cancer	1	1	–	–	–
Adenocarcinoma with unknown primary	1	1	–	–	–
Non-infectious inflammatory disease	16 (23%)	6	7	1	2
Large-vessel vasculitis	2	2	–	–	–
Polymyalgia rheumatica	3	–	3	–	–
Henoch-Schönlein purpura	1	–	1	–	–
Microscopic polyangiitis	1	–	1	–	–
Psoriatic arthritis	1	1	–	–	–
Adult-onset Still's disease	3	1	2	–	–
Systemic lupus erythematosus	4	2	–	–	2
Cryoglobulinaemia	1	–	–	1	–
Miscellaneous	2 (3%)	1	1	–	–
Drug fever	1	1	–	–	–
Hypertriglyceridaemia	1	–	1	–	–
No diagnosis	35 (50%)	–	26	9	–

The background of the slide is a photograph of a road stretching into the distance, viewed through a windshield covered in rain. The rain streaks are prominent, creating a textured, somewhat blurred effect over the scene. The road has white lane markings and a yellow center line. In the distance, there are some trees and buildings under a grey, overcast sky.

Anti-Neutrophil Cytoplasmic Antibodies (ANCA)

Interhospital Geriatrics Meeting


- **1st introduced in 1982**
 - **A kind of antibody directed against neutrophil cytoplasmic antigens in patient with pauci-immune glomerulonephritis**
- **2 ways of identifying**
 - **Indirect immunofluorescence assay (IF)**
 - **Enzyme-linked immunosorbent assay (ELISA)**

- 
- **By IF**
 - **Perinuclear-ANCA
or p-ANCA**
 - **Cytoplasmic-ANCA
or c-ANCA**
 - **More sensitive**



- **By ELISA**

- **Antibodies towards proteinase 3 antigen or PR3-ANCA**
- **Antibodies towards myeloperoxidase antigen or MPO-ANCA**
- **More specific**

- 
- **Clinical practice**
 - **+ve IF → screening with ELISA**
 - **c-ANCA → PR3-ANCA**
 - **p-ANCA → MPO-ANCA**

A photograph of a road with a rain-streaked windshield overlay. The road is paved and has white lane markings. The sky is overcast and grey. The text "5 major principles for ANCA" is centered on the image in a bold, black, sans-serif font.

5 major principles for ANCA

Interhospital Geriatrics Meeting

- **Significance of positive finding**
 - Principle 1
 - +ve IF alone is inadequate
 - **Common false +ve finding**
 - Especially p-ANCA
 - **False +ve in nearly all immune mediated conditions** e.g. connective tissue disorders, inflammatory disease, autoimmune hepatitis etc
 - Atypical patterns are commonly seen
 - **Subjective component to the interpretation of IF assays**
 - Visual interpretation
 - **Must followed with ELISA assay**

- **Significance of positive finding**
 - **Principle 2**
 - **According to Chapel Hill Definition 1994**
 - **The Landmark conference which incorporate ANCA into its diagnostic purpose for different vasculitis**
 - **Major vasculitis with ANCA +ve**
 - **Wegener's granulomatosis**
 - **Microscopic polyangiitis**
 - **Churg-Strauss Syndrome**
 - **Pauci-immune GN**
 - **Drug related vasculitis**

Nomenclature of systemic vasculitides. Proposal of an internal consensus conference. Arthritis Rheum. 1994; 37: 187-192

Interhospital Geriatrics Meeting

A positive ANCA, particularly if confirmed to be due to antibody with a specificity for PR3 or MPO argues against PAN and in favor of one of the ANCA-associated vasculitides

Nomenclature of systemic vasculitides. Proposal of an internal consensus conference. Arthritis Rheum. 1994; 37: 187-192

Anti-neutrophil cytoplasmic antibodies: Current diagnostic and pathophysiological potential. Kidney Int 1994; 46:1

Interhospital Geriatrics Meeting



*Diagnostic value of standardized assay for
ANCA in idiopathic systemic vasculitis.*

Kidney Int 1998; 53:743

Interhospital Geriatrics Meeting

Diagnosis	New patients		Historical patients	
	No therapy	All	No therapy	All
All diagnoses	126	169	59	106
Wegener's granulomatosis (all)	73	97	37	75
a WG, granulomas in biopsy	21	31	13	26
b WG, glomerulonephritis in biopsy	37	44	14	28
c WG, vasculitis in biopsy, no GN	7	9	4	8
d WG, no histology support	8	13	6	13
Microscopic polyangiitis	34	44	13	19
Idiopathic RPGN	10	12	3	6
Classical polyarteritis nodosa	5	10	3	3
Churg-Strauss syndrome	4	6	3	3

Abbreviations are: WG, Wegener's granulomatosis; RPGN, rapidly progressive glomerulonephritis.

Diagnostic value of standardized assay for ANCA in idiopathic systemic vasculitis. Kidney Int 1998; 53:743

Interhospital Geriatrics Meeting

Table 2. Disease control patients

Diagnosis	N
Temporal arteritis	13
Takayasu arteritis	3
Rheumatoid arthritis with vasculitis	7
Systemic lupus erythematosus	45
Mixed essential cryoglobulinemia	9
Henoch-Schönlein purpura	14
Other glomerulonephritis (GN)	
Membranous nephropathy	5
IgA nephropathy	13
MPGN	10
Minimal lesions	4
FSGS	2
Crescentic GN (not pauci-immune)	2
Chronic sclerosing GN	6
Immune-complex GN	1
Post-streptococcal GN	2
Anti-GBM disease	6
Tuberculosis	4
Sarcoidosis	14
Ulcerative colitis	7
Crohn's disease	6
Other vasculitides	
Serum sickness	1
Infective endocarditis	3
Visceral sepsis	1
Behçet's disease	3
Scleroderma/MCTD with vasculitis	3
Total	184

Diagnostic value of standardized assay for ANCA in idiopathic systemic vasculitis. Kidney Int 1998; 53:743

Interhospital Geriatrics Meeting

Table 5. Sensitivity and specificity of the combination of IIF-test and ELISA results in patients with systemic vasculitis

	N	Sensitivity %				
		cANCA + anti-PR3			pANCA + anti-MPO	cANCA/PR3 ^a or pANCA/MPO
		Copenhagen	Raisdorf	Leiden		
New patients						
Wegener's granulomatosis	97	55 (57)	56 (58)	54 (56)	16 (16)	71 (73)
Microscopic polyangiitis	44	7 (16)	5 (12)	7 (16)	22 (49)	30 (67)
Idiopathic RPGN	12	4 (36)	4 (36)	4 (36)	6 (46)	10 (82)
Classical polyarteritis nodosa	10	1 (10)	1 (10)	1 (10)	1 (10)	2 (20)
Churg-Strauss syndrome	6	2 (33)	2 (33)	0 (0)	2 (33)	3 (56)
Historical patients						
Wegener's granulomatosis	75	32 (43)	31 (41)	36 (48)	15 (19)	46 (62)
Microscopic polyangiitis	19	1 (5)	1 (6)	1 (6)	7 (36)	8 (42)
Idiopathic RPGN	6	0 (0)	0 (0)	0 (0)	4 (60)	4 (60)
Classical polyarteritis nodosa	3	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Churg-Strauss syndrome	3	1 (33)	0 (0)	1 (33)	0 (0)	1 (33)
Specificity %						
Control patients						
Disease controls	184	1 (99)	1 (99)	1 (99)	2 (99)	3 (98)
Healthy controls	740	1 (100)	1 (100)	1 (100)	0 (100)	1 (100)

RPGN is rapidly progressive glomerulonephritis. New patients were newly diagnosed after the start of the study, old patients were analyzed retrospectively.

^a Anti-PR3 result is average of the sensitivity of the 3 anti-PR3 ELISAs

Sensitivity 70%, specificity 99% for small vessel vasculitis

Diagnostic value of standardized assay for ANCA in idiopathic systemic vasculitis. Kidney Int 1998; 53:743

Interhospital Geriatrics Meeting

- **Significance of positive finding**
 - **Principle 3**
 - **Should not rely on +ve ANCA for definitive diagnosis of small vessel vasculitis**
 - **I. Histological proof is essential**
 - **II. Exclude other differentiate diagnosis**



- **4 major organs commonly involved**

- **Renal**

- **Rapidly deteriorating renal function**
- **Significant proteinuria**
- **Haematuria with cast**

- **Skin**

- **Palpable purpura**

- **Nerve**

- **Mononeuritis multiplex**

- **Lung**


- **haemoptysis**



- **Significance of positive finding**

- **Principle 4**

- **Can it be false positive?**
- **Positive predictive value of ANCA**
 - **Very much dependent on the clinical presentation**
- **Proper ordering of ANCA**
 - **Decrease false positive**



**Using Antineutrophil Cytoplasmic
Antibody Testing to Diagnose Vasculitis:
Can Test-Ordering Guidelines improve
Diagnostic Accuracy?**

Arch Intern Med. 2002; 162: 1509-1514

Interhospital Geriatrics Meeting

- **Retrospective study for all ordered ANCA from 1997 to 1998**
- **To analyze**
 - **sensitivity, specificity, positive predictive value and negative predictive value**
 - **towards ANCA associated vasculitis**
 - **before and after imposing guideline criterion for ordering an ANCA test**

Table 1. Clinical Indications for ANCA Testing*

Guidelines†	Clinical Definition
1. Glomerulonephritis, especially rapidly progressive	(A) Creatinine level >2.0 mg/dL (>176.8 µmol/L) (normal range, 0.7-1.3 mg/dL [61.9-114.9 µmol/L]) immediately prior to ANCA testing or (B) urinary red blood cell casts or hematuria with >5 red blood cells per high-powered microscopic field
2. Pulmonary hemorrhage, especially pulmonary renal syndrome	Hemoptysis or pulmonary hemorrhage
3. Cutaneous vasculitis with systemic features myalgias, arthralgias, or arthritis	Purpura, rash or livedo with concurrent fever, weight loss, myalgias, arthralgias, or arthritis
4. Multiple lung nodules	At least 1 nodule seen on any imaging study‡
5. Chronic destructive disease of the upper airways	Epistaxis or erosive changes seen on clinical examination or imaging studies not due to previous surgery
6. Long-standing sinusitis or otitis	(A) Hearing loss, blocked ears, or ear pain or (B) sinusitis or otitis specified as the reason for ANCA test ordering by the physician
7. Subglottic, tracheal stenosis	(A) Visualized on imaging studies or (B) tracheal stenosis specified as the reason for ANCA test ordering by the physician
8. Mononeuritis multiplex or other peripheral neuropathy	Sensory or motor changes, including cranial nerve palsies
9. Retro-orbital mass	Radiographic visualization of a mass lesion

*ANCA indicates antineutrophil cytoplasmic antibody.

†Based on the article by Hagen et al.¹²

‡Not all patients had specialized imaging studies to detect multiple lesions, so a single nodule was accepted.

Before imposing guideline

ANCA Test Result	AVV Present	AVV Absent
Positive	13	11
Negative	3	470

Sensitivity: 81% Specificity 98%


PPV: 54% NPV: 99%

After imposing guideline

ANCA Test Result	AVV Present	AVV Absent
Positive	13	8
Negative	3	357

Sensitivity: 81% Specificity: 98%

PPV: 62% NPV: 99%

- 
- **Significance of positive finding**
 - **Principle 5**
 - **Arteriography**
 - **Useful in large and medium sized vasculitis**
 - **Not useful in small sized vasculitis**
 - » **Affected vessels are below the resolution of usual angiograms**

Clinically suspected case

+ve ANCA IF

Further confirmed with ELISA

**Small vessel
vasculitis**

+ve

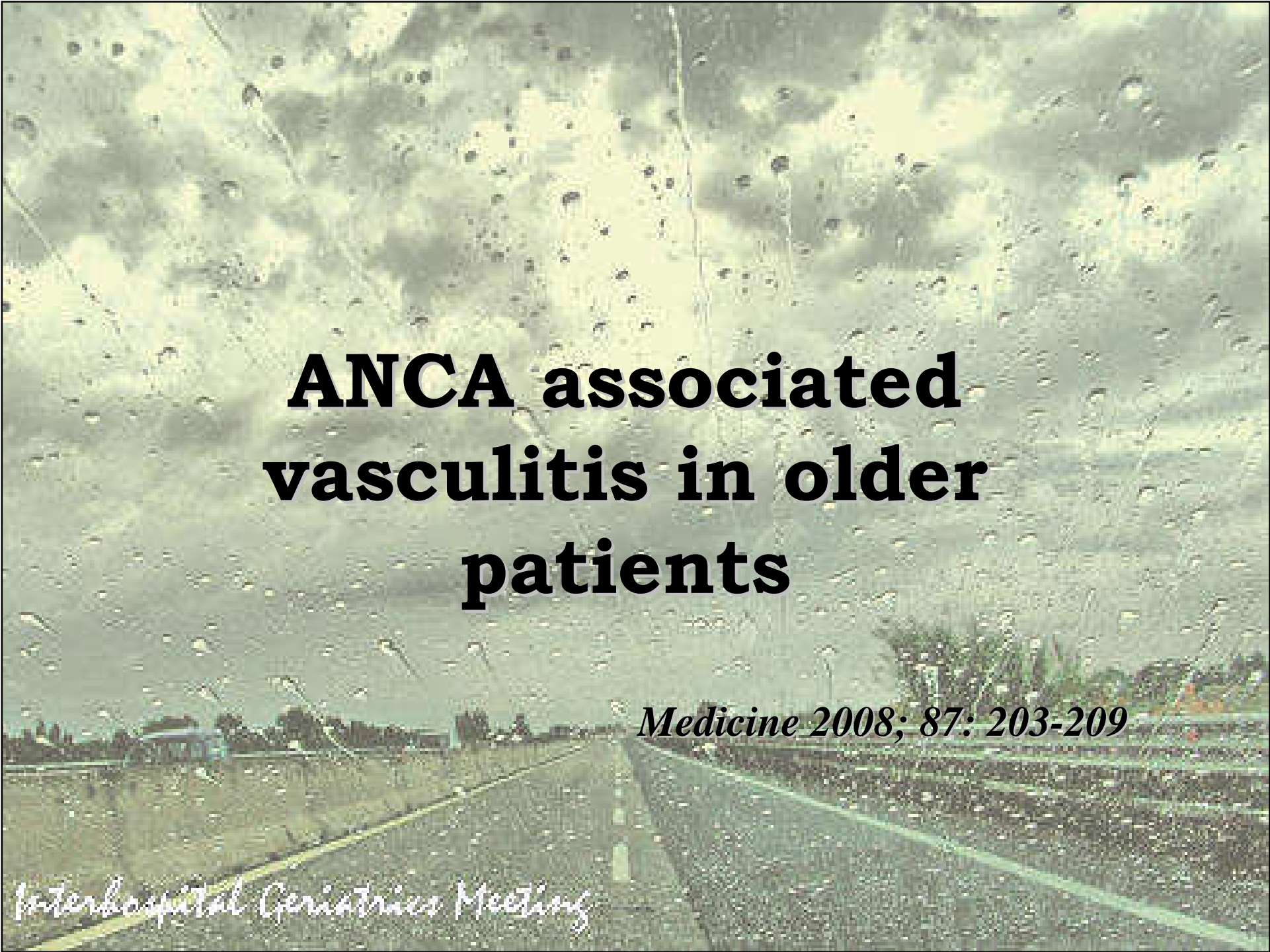
-ve

**Medium and large
vessel vasculitis**

-Exclude other DDx
-Biopsy of affected organ

-Exclude other DDx
-Biopsy of affected organ
**-Digital Subtraction
Arteriogram**

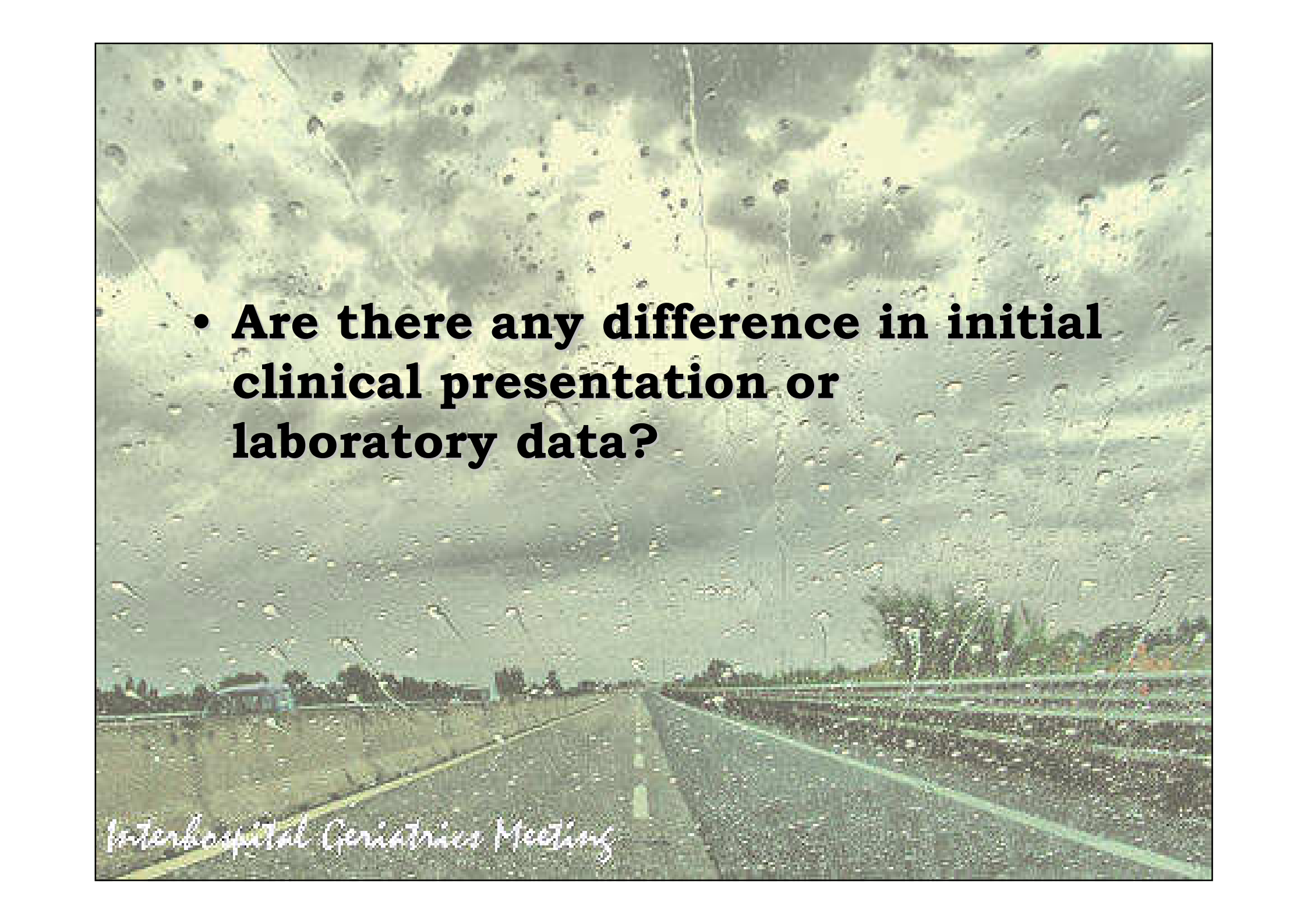
Interhospital Geriatrics Meeting



**ANCA associated
vasculitis in older
patients**

Medicine 2008; 87: 203-209

Interhospital Geriatrics Meeting

- 
- A photograph of a road with a rain-streaked windshield overlay. The road is paved and has a dashed white line down the center. The background shows a cloudy sky and some distant buildings. The text is overlaid on the left side of the image.
- **Are there any difference in initial clinical presentation or laboratory data?**

Interhospital Geriatrics Meeting

TABLE 2. Clinical and Laboratory Data at Presentation, by Age

	Older Patients (≥65 yr) (n = 99) No. (%)	Younger Patients (<65 yr) (n = 135) No. (%)	p Value
Male/female	49/50	58/77	>0.05
Age (yr)	72.1 ± 5.6	49.3 ± 13.1	-
MPO-ANCA/PR3-ANCA	94/5	108/26	<0.01
Fever	63/99 (63.6)	84/135 (62.2)	>0.05
Fatigue	57/99 (57.6)	79/135 (58.5)	>0.05
Weight loss	45/99 (45.5)	64/135 (47.4)	>0.05
Muscle pain	28/99 (28.3)	43/135 (31.9)	>0.05
Arthralgia	35/99 (35.4)	61/135 (45.2)	>0.05
Skin rash	17/99 (17.2)	28/135 (20.7)	>0.05
Pulmonary involvement	75/99 (75.8)	66/135 (48.9)	<0.001
Hemoptysis	33/99 (33.3)	41/135 (30.4)	>0.05
Nodules or cavities	8/99 (8.1)	17/135 (12.6)	>0.05
Alveolar or interstitial infiltration	47/99 (47.5)	43/135 (31.9)	<0.05
Pulmonary interstitial fibrosis	37/99 (37.4)	25/135 (18.5)	<0.01
Mechanical ventilation	9/99 (9.1)	2/135 (1.5)	<0.05
Urinary protein (g/24 h)	1.67 ± 1.79	2.45 ± 2.29	<0.05
Initial Scr (μmol/L)	399.7 ± 255.7	446.7 ± 371.5	>0.05
eGFR (mL/min per 1.73 m ²) (median and range)*	12.5 (2.70–153.7)	13.3 (1.87–156.8)	>0.05
Ophthalmic	18/99 (18.2)	38/135 (28.1)	>0.05
Otic	35/99 (35.4)	46/135 (34.1)	>0.05
Upper respiratory tract	15/99 (15.2)	37/135 (27.4)	<0.05
Gastrointestinal	5/99 (5.1)	11/135 (8.1)	>0.05
Nervous system	21/99 (21.2)	24/135 (17.8)	>0.05
Anemia	87/99 (87.9)	105/135 (77.8)	>0.05
Leukocytosis	56/99 (56.6)	57/135 (42.2)	<0.05
Thrombocytosis	31/99 (31.3)	47/135 (34.8)	>0.05
Elevated ESR	91/99 (91.9)	109/135 (80.7)	<0.05
Elevated CRP	61/99 (61.6)	60/135 (44.4)	<0.01
BVAS	21.3 ± 6.7	20.4 ± 5.3	>0.05

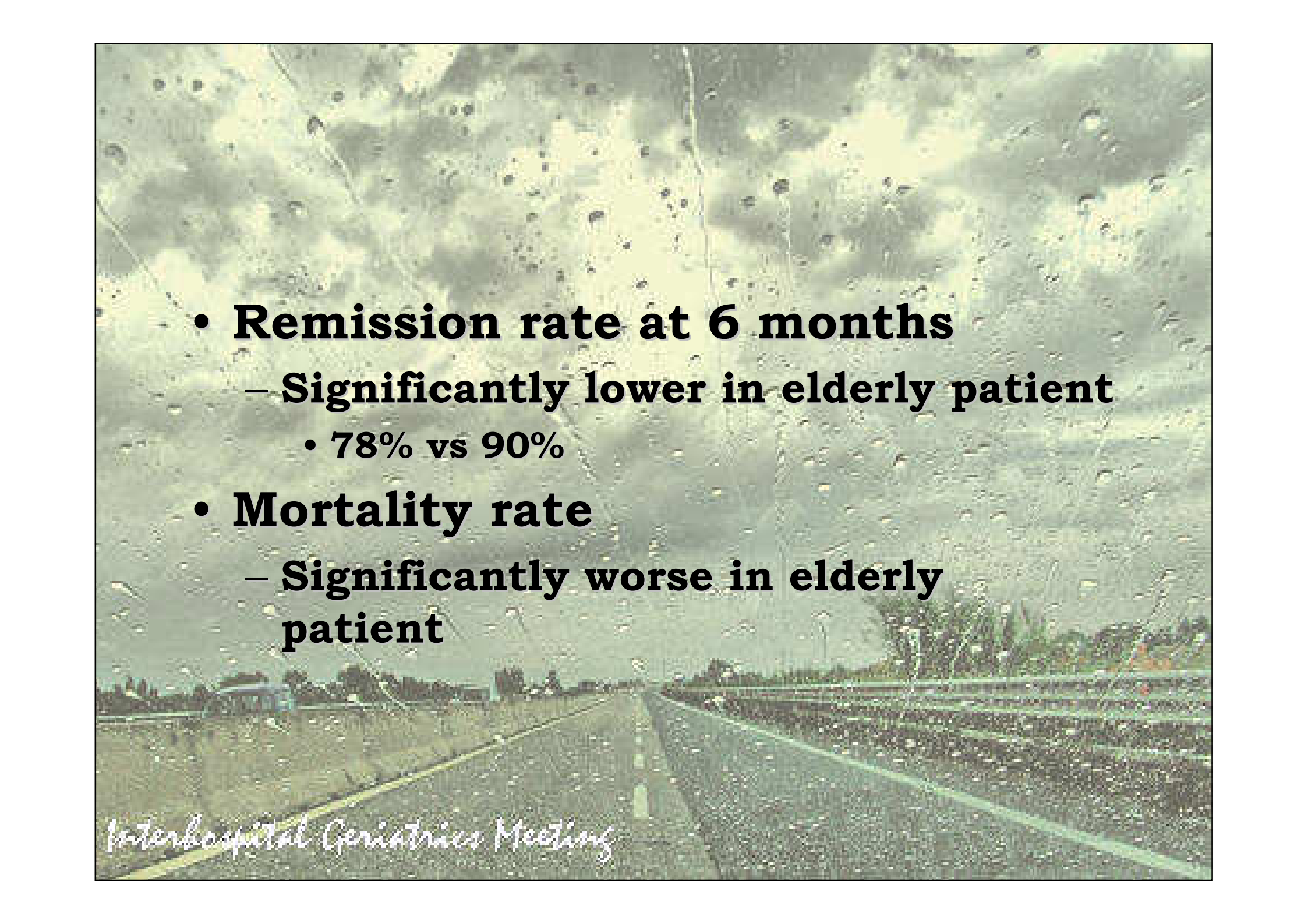
Abbreviations: Scr = serum creatinine, eGFR = estimated glomerular filtration rate, BVAS = Birmingham vasculitis activity score.

*eGFR (mL/min per 1.73 m²) = 175 × (plasma creatinine)^{-1.234} × age^{-0.179} × 0.79 (if female) (from reference 11).

- **Elderly patient (>65)**
 - **More significant**
 - **Pulmonary involvement**
 - **Increase ESR**
 - **Increase CRP**
 - **Leucocytosis**
 - **Less significant**
 - **Upper respiratory tract involvement**
 - **24 hour urinary protein**

- 
- **Are there any difference in treatment outcome?**

Interhospital Geriatrics Meeting

- 
- **Remission rate at 6 months**
 - **Significantly lower in elderly patient**
 - **78% vs 90%**
 - **Mortality rate**
 - **Significantly worse in elderly patient**

Survival

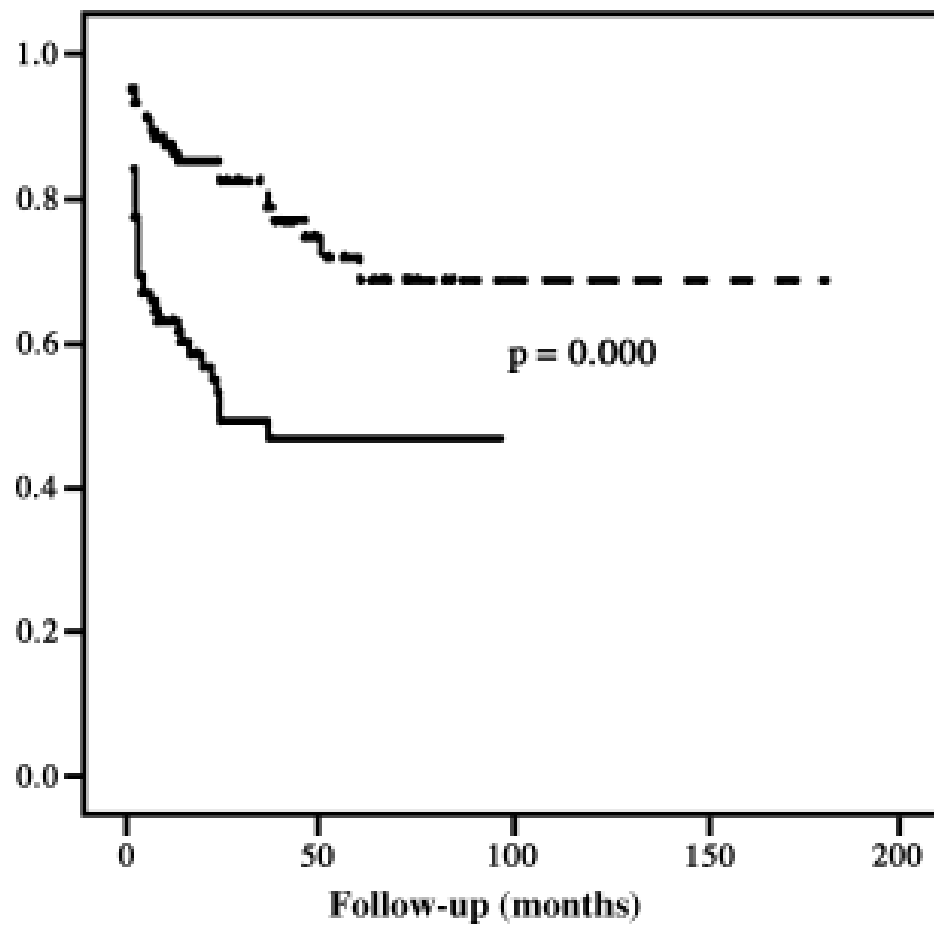


FIGURE 2. Kaplan-Meier analysis of survival of older and younger patients (log-rank test). Solid line: age ≥ 65 yr; dashed line: age < 65 yr.

- 
- **Are there any difference in treatment related complication rate?**

Interhospital Geriatrics Meeting

- 
- A photograph of a road with a rain-streaked windshield overlay. The road is a two-lane asphalt road with a dashed white center line and solid white edge lines. The background shows a cloudy sky and some distant trees and buildings. The text is overlaid on the left side of the image.
- **More significant secondary pulmonary infection rate in elderly**

– **29% vs 7%**

Interhospital Geriatrics Meeting

- 
- A photograph of a road with a rain-streaked windshield overlay. The road is a two-lane asphalt road with a dashed white center line and solid white edge lines. The sky is overcast and grey. The windshield has numerous vertical streaks of water, suggesting it is raining. The overall tone is somber and atmospheric.
- **Are there any difference in relapse rate for those respond patient?**

Interhospital Geriatrics Meeting

- 
- **Relapse rate**
 - **No significant difference between young and old for those who respond**

Interhospital Geriatrics Meeting

Major message

- **Although elderly patient may associated with increased complication from conventional treatment, if successfully treated, the relapse rate is NOT higher**

A photograph of a road with a rain-streaked windshield overlay. The road is paved and has white lane markings. The sky is overcast and grey. The windshield has many vertical streaks of water, creating a distorted view of the road and sky. The text "Polyarteritis Nodosa" is overlaid in the center in a bold, black, sans-serif font.

Polyarteritis Nodosa

Interhospital Geriatrics Meeting

Polyarteritis Nodosa

- **Systemic necrotizing vasculitis typically affects medium sized muscular arteries**

- **Epidemiology**

- **Prevalence: 2-33 per million**

- **Etiology**

- **Idiopathic**

- **Hepatitis B virus (Oriental)**

- **Up to 33%**

- **Hairy cell leukaemia**

*Hepatitis B virus-associated polyarteritis nodosa:
clinical characteristics, outcome, and impact of
treatment in 115 patients. Medicine 2005; 84: 313*

Interhospital Geriatrics Meeting



- **Pathogenesis**

- **Immune complexes mediated disease**

- **Medium sized arterial inflammation**

- **Inflammation of vessel wall**

- **weakening of vessel wall**

- **aneurysm formation**

- **rupture and life threatening bleeding**

- **Clinical feature**

- **Constitutional**

- Fatigue, weakness, fever, arthralgia

- **Skin**

- Livedo reticularis, skin ulcer, tender erythematous
- Palpable purpuric lesion

- **Renal disease**

- Renal impairment, hypertension
- Urinalysis: **sub-nephrotic proteinuria, modest haematuria, absent red blood cell casts**

- **Neurologic disease**

- Mononeuritis multiplex
- Stroke (rare)

- **Lung**

- Rarely involved

- **Gastrointestinal disease**

TABLE 1. Demographics, Gastrointestinal Manifestations and Radiologic Findings in 62 Patients With Small and Medium-Sized Vessel Vasculitides*

	All (n = 62)	PAN (n = 38)	CSS (n = 11)	WG (n = 6)	MPA (n = 4)	RAAV (n = 3)
Age, yr, mean \pm SD	48 \pm 18	47 \pm 18	37 \pm 15	49 \pm 7	48 \pm 27	70 \pm 9
M:F ratio, n	46/16	27/11	10/1	6/0	1/3	2/1
Abdominal pain	60 (97)	37	10	6	4	3
Nausea or vomiting	21 (34)	12	2	2	3	2
Diarrhea	17 (27)	6	5	3	2	1
Hematochezia or melena	10 (16)	2	4	2	1	1
Hematemesis	4 (6)	3	0	0	0	1
Esophageal ulcerations	7 (11)	5	0	1	0	1
Gastroduodenal ulcers	17 (27)	12	2	2	0	1
Colorectal ulcerations	6 (10)	2	2	2	0	0
Gastritis	4 (6)	2	0	1	1	0
Surgical abdomen [†]	21 (34)	12	4	0	2	3
Peritonitis	11 (18)	5	2	0	2	2
Bowel perforations	9 (15)	6	1	0	1	1
Intestinal occlusion	4 (6)	2	0	0	1	1
GI ischemia/infarction	10 (16)	5	2	0	1	2
Appendicitis	6 (10)	4	1	0	1	0
Cholecystitis	5 (8)	3	1	0	0	1
Acute pancreatitis	3 (5)	2	0	0	1	0
Abnormal angiography (n = 39)	26/39 (67)	23/31	3/5	0/2	0	0/1
Abnormal abdominal CT (n = 24)	18/24 (75)	11/16	1/1	3/3	2/3	1/1

*Values are numbers (with percentages in parentheses when meaningful) of patients per group, unless indicated otherwise.


[†]A single patient may have 2 or more surgical complications, for example, pancreatitis and perforations and peritonitis.

Interhospital Geriatrics Meeting
Presentation and outcome of gastrointestinal involvement in systemic necrotizing vasculitides. Medicine 2005; 84:115

- **Investigation (Chapel Hill definition)**
 - **ANCA –ve**
 - **Digital subtraction Arteriogram**
 - **Show characteristic multiple aneurysm**
 - **Tissue biopsy**
 - **Definitive but with higher risk of bleeding due to presence of aneurysm**
 - **Hepatitis B serology**

Nomenclature of systemic vasculitides. Proposal of an internal consensus conference. Arthritis Rheum. 1994; 37: 187-192

Interhospital Geriatrics Meeting



**Why PAN is not
considered in our
patient initially?**

Interhospital Geriatrics Meeting

Clinically suspected case

+ve ANCA IF

Further confirmed with ELISA

**Small vessel
vasculitis**

+ve

-ve

**Medium and large
vessel vasculitis**

-Exclude other DDx
-Biopsy of affected organ

-Exclude other DDx
-Biopsy of affected organ
**-Digital Subtraction
Arteriogram**

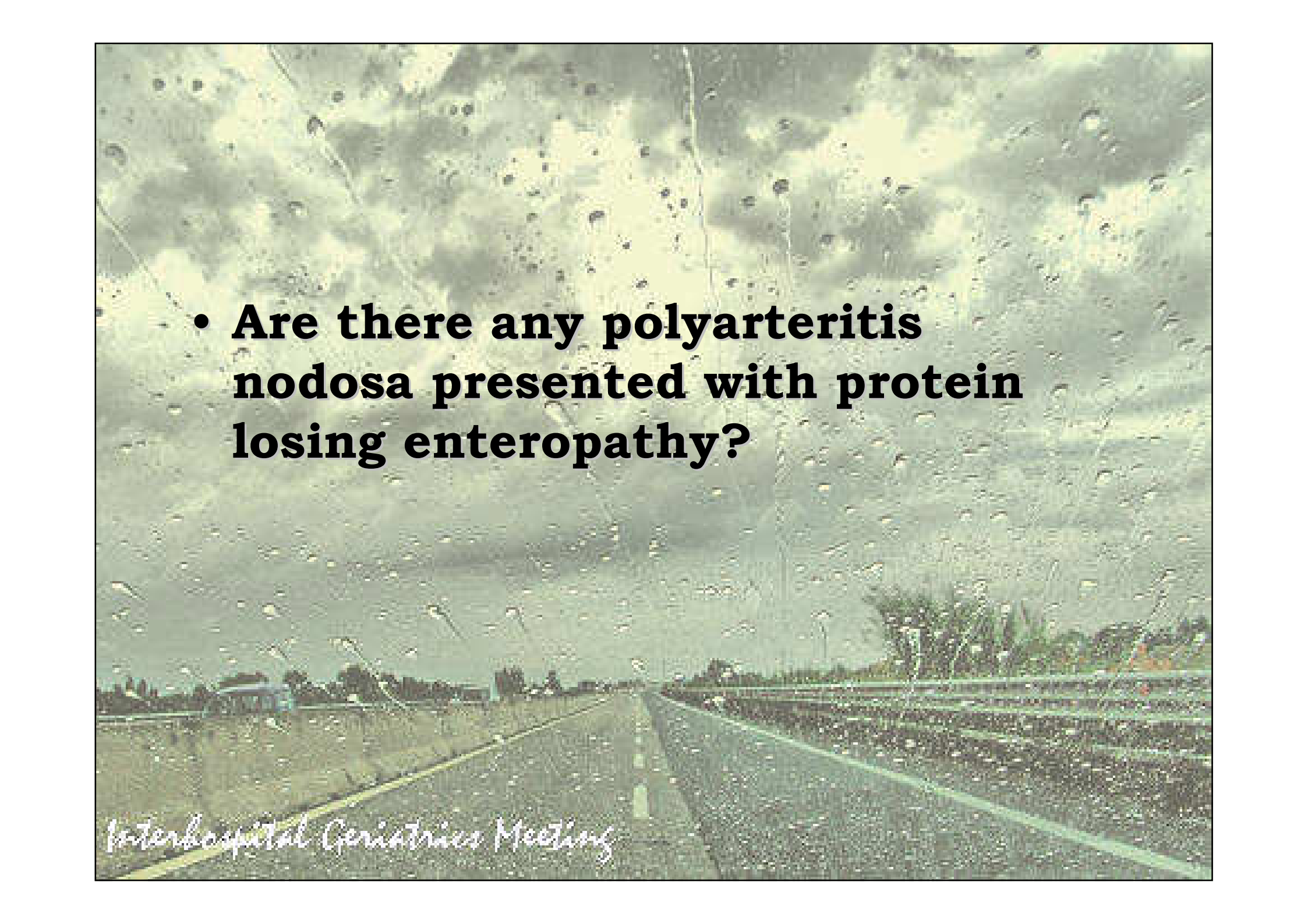
Interhospital Geriatrics Meeting

- 
- **Are there any report of polyarteritis nodosa with +ve MPO-ANCA+p-ANCA OR c-ANCA+PR3-ANCA ?**

- **PUBMED search**
 - **2 case reports only**
 - **Both initially diagnosed as microscopic polyangiitis but subsequent confirm PAN by autopsy or arteriogram**
 - **Initially with classical multi-organ involvement**

A case of MPO-ANCA positive PAN complicated by interstitial pneumonia and rapidly progressive renal failure. Clin Rheumatol 2007; 26:429-432

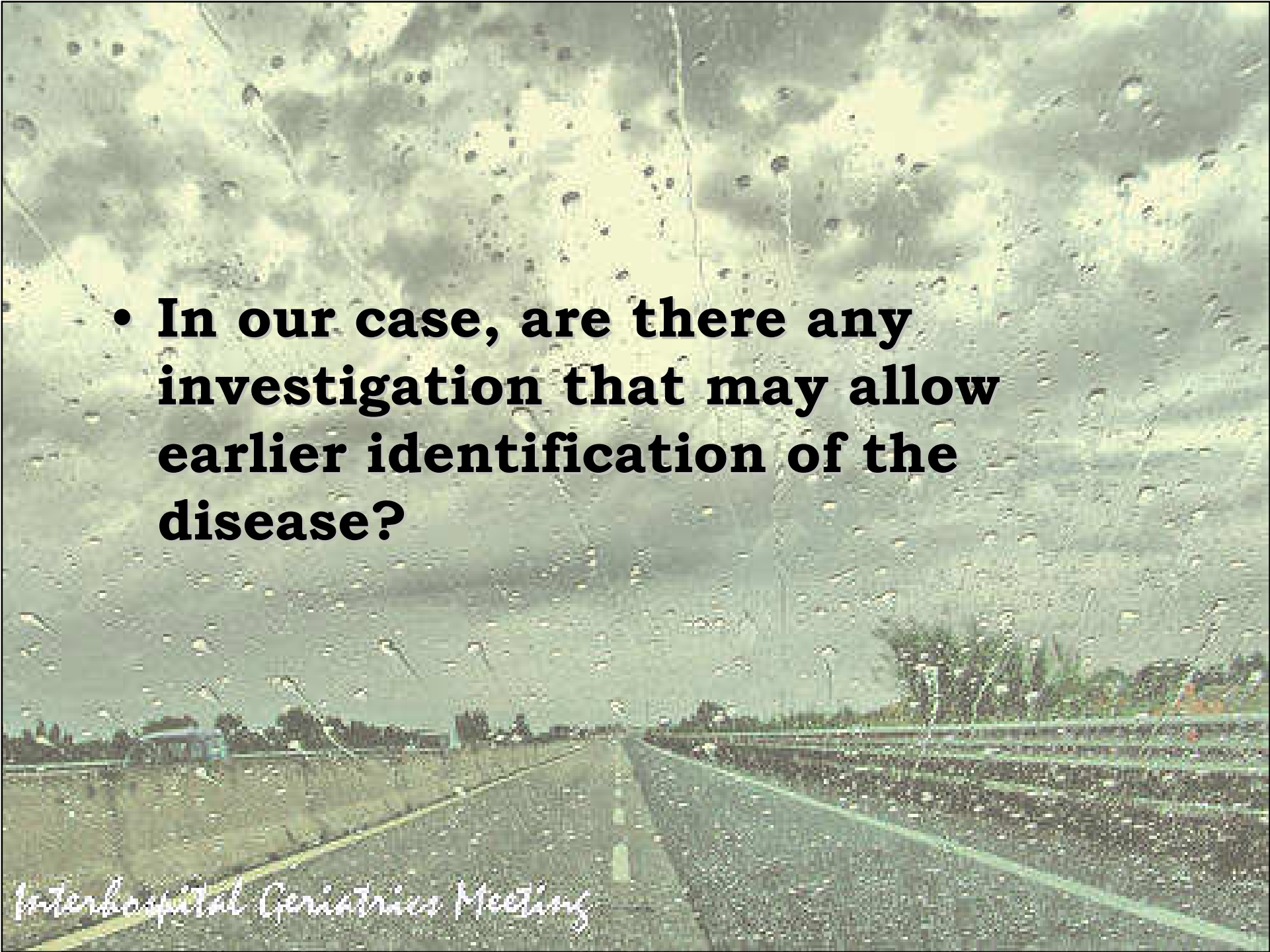
Two cases of classical PAN associated with MPO-ANCA. Nippon Jinzo Gakkai Shi. 2006; 48(4): 371-376

- 
- A photograph of a road with a rain-streaked windshield overlay. The road is a two-lane asphalt road with a dashed white center line and solid white edge lines. The background shows a cloudy sky and some distant buildings and trees. The text is overlaid on the left side of the image.
- **Are there any polyarteritis nodosa presented with protein losing enteropathy?**

Interhospital Geriatrics Meeting

- **PUBMED search**
– **NO**

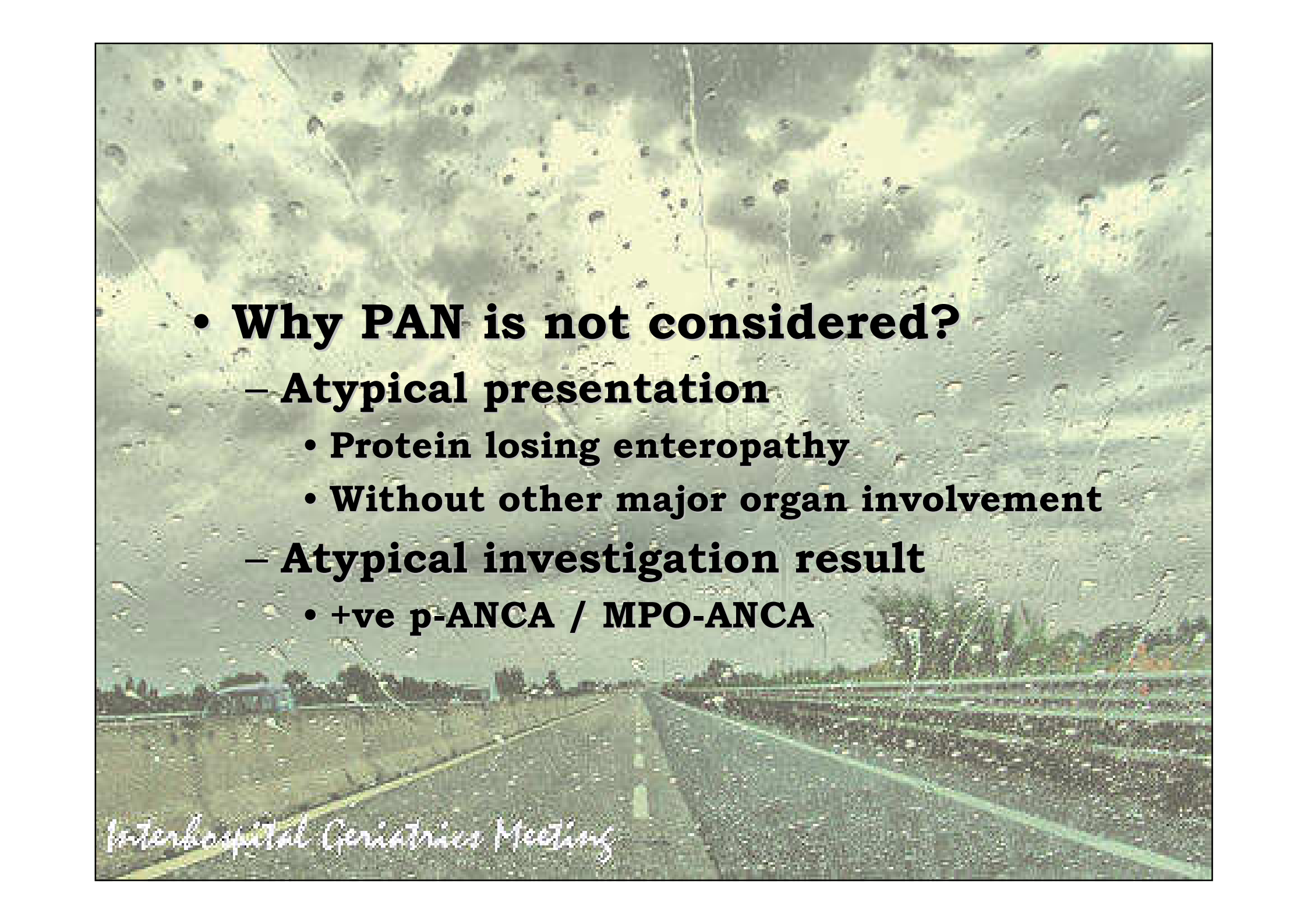
Interhospital Geriatrics Meeting

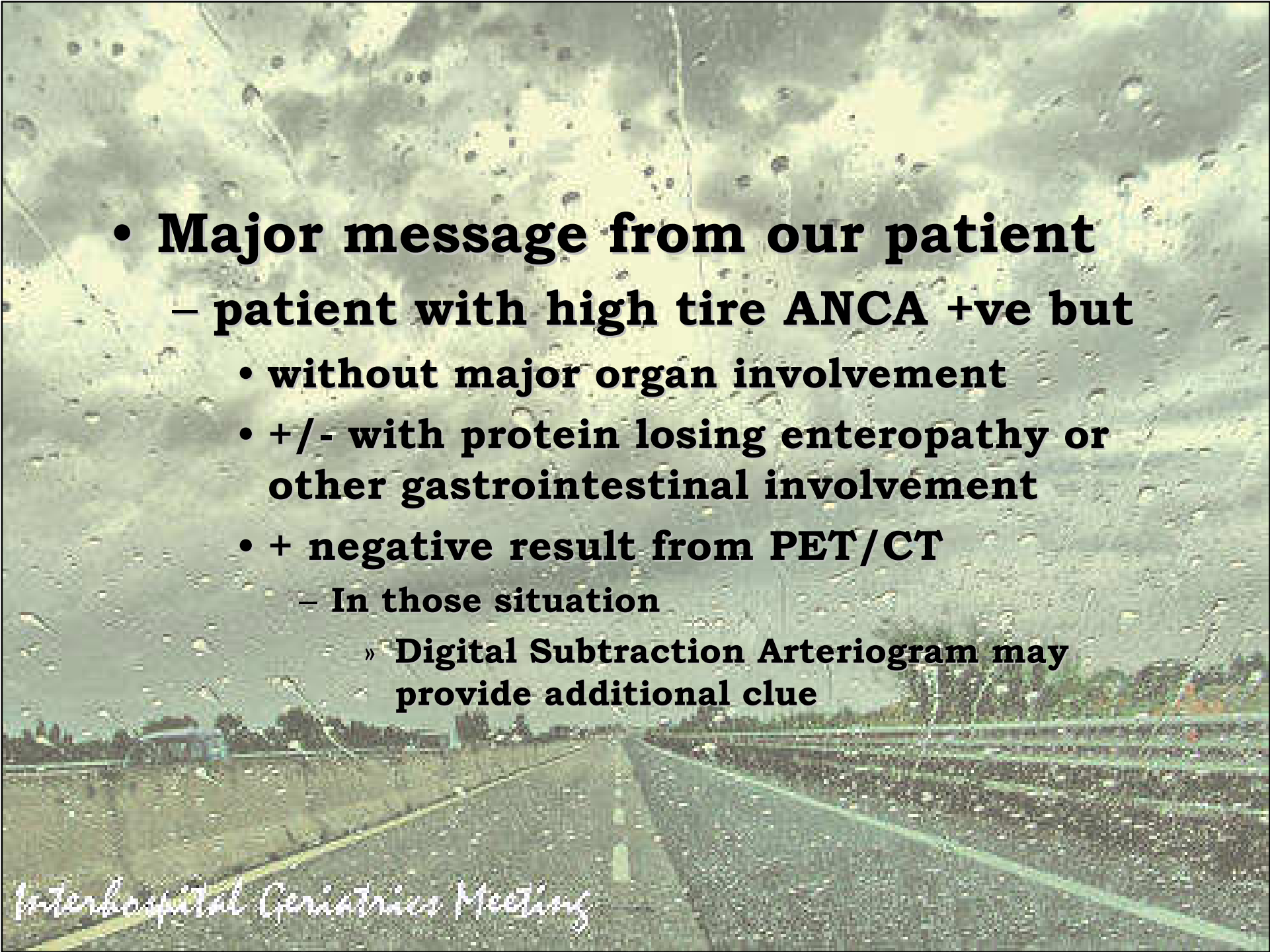
- 
- **In our case, are there any investigation that may allow earlier identification of the disease?**

Interhospital Geriatrics Meeting

- **Digital subtraction arteriogram**

Interhospital Geriatrics Meeting

- 
- **Why PAN is not considered?**
 - **Atypical presentation**
 - **Protein losing enteropathy**
 - **Without other major organ involvement**
 - **Atypical investigation result**
 - **+ve p-ANCA / MPO-ANCA**

- 
- **Major message from our patient**
 - **patient with high titer ANCA +ve but**
 - **without major organ involvement**
 - **+/- with protein losing enteropathy or other gastrointestinal involvement**
 - **+ negative result from PET/CT**
 - **In those situation**
 - » **Digital Subtraction Arteriogram may provide additional clue**

A dramatic night sky with a bright lightning bolt striking down over a city at night. The lightning bolt is the central focus, illuminating the surrounding clouds and the city below. The city lights are visible in the foreground, and the sky is a deep blue with some lighter clouds. The text "Thank you very much" is overlaid on the left side of the image.

Thank you
very much