

An old woman with generalized weakness

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IHGM 27 May, 2011

- F/84
- Widow, lives alone
- Unaided, walks with umbrella outdoor
- ADL Independent
- Home helper for IADL
- Non-smoker, non-drinker

- Phoned up regional telephone nursing hotline for
 - generalized weakness ...

DOCTOR

I am unwell

I have ...

generalized weakness

dizziness and headache

muscle ache

LBP



Doctor may probably

- Screen for early URI
- Associated chest pain/ palpitation
- Associated visual impairment/ diplopia
- Tinnitus, vertigo
- History of falls/ head injury
- Any active arthritis

- Reassurance and prescribe symptomatic treatment

She may end up with



- Part of the problems solved
- Main problem is not diagnosed and treated accordingly
- Further deteriorates and ...
 - struggles to live alone with extra support from home helper
 - admit for decreased general condition and decondition
 - admit for found collapse with head injury/ fracture hip

Or the Doctor

- while hearing the complaints of the old lady
- tempted to search the CMS about PMHx, Ix and Rx



Past Medical History

- HT
- Renal impairment due to chronic renal parenchymal disease, Cr \sim 130
- Gout
- Old thalamic infarct
- AF

- Discharge from QEH/ BH 6 weeks ago for dizziness, newly diagnosis AF and gouty arthritis
- Discharged with
 - Antihypertensive drugs and aspirin
 - Colchicine 0.5mg tds a day as needed

the symptoms can be
due to
AF
Electrolytes imbalance
Hypotension

...



She may end up with



- Part of the problems solved
- Main problem is not diagnosed and treated accordingly
- Further deteriorates and ...
 - struggles to live alone with extra support from home helper
 - admit for decreased general condition and decondition
 - admit for found collapse with head injury/ fracture hip

Seen in our geriatrics SOPD

- Take a detail history
- Explore the implication of generalized weakness



Generalized weakness

- progressive weakness of arms and legs
- Generalized muscle ache
- LBP
- Dizziness and headache
- Numbness of both hands and legs, increasing in recent 1 week
- Unable to cope at home alone
- Could not climb up onto minibus

Working diagnosis

- Weakness + muscle ache + sensation involvement
- Diseases of nerve, muscle and neuromuscular junction may present with varying degrees of sensory loss and weakness
- This old lady was admitted for investigation and a course of rehabilitation training

- No history of diabetes
- No history thyroid problem
- No GI disturbances
- No underlying systemic illnesses
- No rheumatic/ genetic diseases
- No family history of muscular weakness/
neuromuscular disorders

Physical examination

- Thin built but well hydrated and nourished
- Afebrile
- BP normal, pulse 80bpm irregularly irregular
- No goitre
- No adenopathy
- No rash/ skin problem

Physical examination

- No muscle atrophy
- Tone normal
- No evidence of active arthritis
- Limb power proximal bilateral grade 4-/5 and distal 4/5 bilateral
- Impaired pin prick sensation over both glove and stocking distribution
- Impaired proprioception over both Lower Limbs
- Reflexes depressed
- Plantar reflex down going

- Compliant with prescribed medications
- Took no over the counter medications or herbal medicine
- No toxic exposures

- Discharge from QEH/ BH 6 weeks ago for dizziness, newly diagnosis AF and gouty arthritis
- Discharged with
 - Antihypertensive drugs and aspirin
 - colchicine 0.5mg tds a day as needed

Drugs

- Aspirin 80mg daily
- Norvasc 2.5mg daily
- Prazosin 1mg tds
- Pepcidine 20mg bd
- Lactulose 10ml tds
- Colchicine 0.5mg tds PRN

- No diuretic / amiodarone/ statin

Working diagnosis

- Myopathy ?cause
- Peripheral neuropathy ?cause
- Endocrine disorders
- Chronic renal impairment/ electrolyte disturbance
- Drug induced
- Rhabdomyolysis

Initial investigations

- CBP normal, NcNc
- ESR 25
- RFT (urea 13, Cr 167)
- Na 143, K 4.8
- ↑ALT 48IU/L, TB 7umol/L, ALP 86IU/L
- Albumin 39, globulin 34
- ↑ CK 1261 (48 on 9/2008),
- ↑ LDH 327
- ↑ Urate 0.53
- Ca 2.24
- Fast glucose 4
- TSH normal
- Vitamin B12 normal
- VDRL NR
- Urine myoglobin negative
- Tn I normal
- ECG AF rate 70, RBBB, no acute ischemic changes

Drugs review

- Taking colchicine 2 to 3 times a day since last discharge because of constant knee pain
- Colchicine induced neuromyopathy was suspected
- Colchicine was stopped after this admission

Electrodiagnostic studies

- Motor studies showed prolonged distal latencies over bilateral tibial nerves. There was slowing of conduction velocities over bilateral tibial nerves and Rt peroneal nerves with markedly reduced CMAP amplitudes
- H reflex on right tibial nerve was prolonged and absent on Lt side
- F-wave studies over left median and ulnar nerves were normal
- Sensory studies on upper limbs were unremarkable
- Sensory studies on bilateral sural and superficial peroneal nerves showed no response in stimulation

- Electromyography studies showed generalized increased insertional activities with needle induced complex discharges over all muscles tested
- Frequent spontaneous activities, mainly positive sharp wave could be detected over the tested muscles

- NCS - Polyneuropathy over bilateral lower limbs with both motor and sensory nerves involvement
- EMG - Diffuse neuropathic changes over both proximal and distal muscles in lower limbs
- Muscle biopsy not done

Progress

- Given rehabilitation training
- Knee pain controlled with panadol and physical methods
- Limbs power improved
- Her muscle strength, mobility and activities of daily living were close to pre-morbid levels
- CK down to 177

Rehabilitation training

On Admission

- MMSE 26/30
- Monofilament test showed diminished or loss of protective sensation
- Dressing lower garment, lying to sitting, bed to chair transfer, sit to standing needs mild assistance

- Quad strength

- Admission R 4.6 L 1.5 kg

- Discharge 4.8 2.6 kg

- Grip/ pinch strength

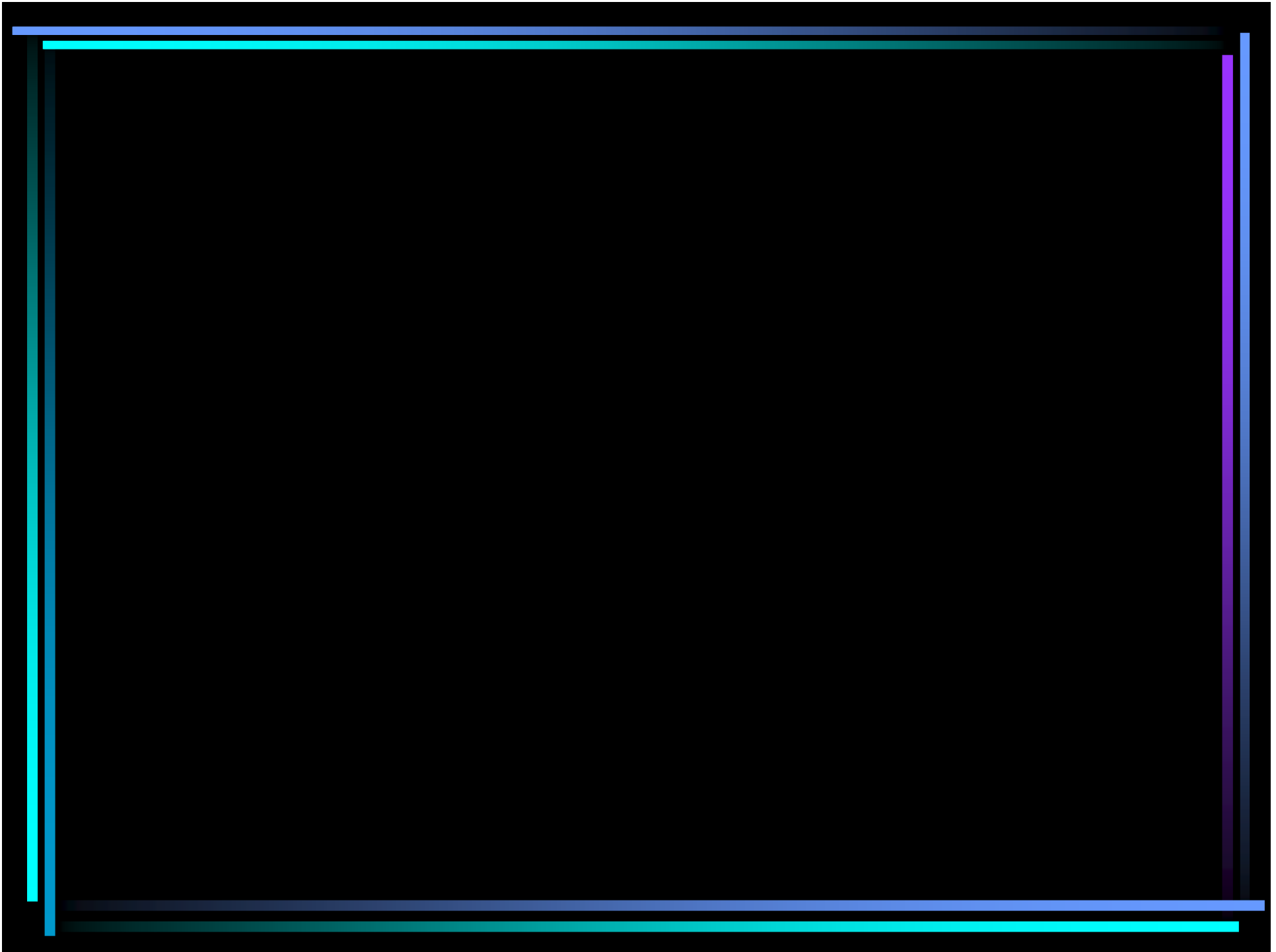
- Admission R 8 / 2 L 7 / 2 kg

- Discharge 14 / 3 11 / 3 kg

- Timed up and go 36 sec to 25 sec
- Climb one flight of stairs with rail support, stick and supervision
- Dressing, transfer, lying to sitting – independent
- Toilet transfer – supervised, bathing with set up
- Numbness over both hands and feet have subsided

Diagnosis

- Drug induced neuromuscular toxicity due to regular use of colchicine by an old woman with renal impairment



Drug induced Neuromuscular toxicity

Colchicine

Prevalence/ incidence

- Precise incidence of drug-induced myopathies / neuropathies is unknown
- Drug-induced myopathy is among the most common causes of muscle disease
- Ranges from mild myalgia with or without mild weakness to chronic myopathy with severe weakness, to massive rhabdomyolysis with acute renal failure

Mechanism – drug-induced myopathy

- Direct myotoxicity
 - eg. alcohol, cocaine, glucocorticoids, lipid lowering agents, antimalarials, colchicine (vacuolar myopathy) and zidovudine (mitochondrial myopathy)
- Immunologically induced inflammatory myopathy
 - eg. D-penicillamine
- Indirect muscle damage
 - Drug-induced coma and subsequent ischemic muscle compression, drug-induced hypokalemia (e.g. diuretics), drug-induced hyperkinetic states (eg. Delirium tremens or seizures secondary to alcohol), dystonic states associated with phenothiazines and hyperthermia related to cocaine use or the neuroleptic malignant syndrome

Mechanism – drug-induced peripheral neuropathy

- Axonal degeneration
 - Occurs over weeks to months after exposure
 - electrophysiological testing will detect changes prior to the development of clinical symptoms
 - damage is only to the axon, the neuropathy will resolve completely with cessation of the medications in many cases
 - eg. Colchicine, dapsons, dilsulfiram, HMG-CoA reductase inhibitors, hydralazine, isoniazid, ...

Amanda C Peltier, James W Russell. Advances in understanding drug-induced neuropathies. Drug safety 2006; 29(1): 23-30

Mechanism – drug-induced peripheral neuropathy

- Cell death, usually dorsal root ganglion cells
 - These cells are vulnerable as they are not protected by the blood-brain barrier
 - This causes a sensory predominant, irreversible neuropathy that is more physically debilitating
 - eg. Cisplatin, carboplatin, ocaliplatin, suramin sodium and thalidomide
- Demyelinating neuropathy
 - Less common
 - e.g. amiodarone, interferon α , suramin sodium, perhexiline, chloroquine and tacrolimus

Colchicine

- Colchicine is an alkaloid derived from the plant of the Lily family *Colchicum autumnale*
- used to treat gout for more than 2000 years, and pseudogout and familial Mediterranean fever (FMF) for several decades
- On July, 2009 U.S. Food and Drug Administration (FDA) approved colchicine as a monotherapy for the treatment of familial Mediterranean fever and acute gout flares
- Pain relief involves blockage of the inflammatory response to uric acid crystals, through inhibition of crystal phagocytosis and neutrophil migration
- Exploring for therapeutic uses in other rheumatic and nonrheumatic disorders, such as pulmonary fibrosis, liver cirrhosis, pericarditis, psoriatic arthritis, vasculitis, scleroderma, familial Mediterranean fever, amyloidosis and Behcet's disease

Kerry Wilbur, Mark Makowsky. Colchicine Myotoxicity: Case Reports and Literature Review. *Pharmacotherapy* 2004;24(12):1784–1792

Adverse effects

- The most prevalent adverse effect is dose-related gastrointestinal intolerance (nausea, vomiting, abdominal pain)
- Occurrence of bone marrow suppression, dermatitis, and alopecia is low
- Colchicine-induced myopathy/ neuropathy is rare
- It can occur in the setting of acute overdose, or even chronic administration in therapeutic doses

Kerry Wilbur, Mark Makowsky. Colchicine Myotoxicity: Case Reports and Literature Review. *Pharmacotherapy* 2004;24(12):1784–1792

- There are many drugs (including chloroquine, amiodarone, and vincristine) as well as conditions such as alcohol abuse, paraneoplastic syndrome, hypothyroidism, connective tissue disorder, and uraemia that cause combined myopathy and peripheral neuropathy
- colchicine use is one of the less recognized causes
- Kuncel et al were the first to report on patients with colchicine-induced myopathy and neuropathy in 1987
- In many case reports, patients take customary levels of colchicine but toxicity develops due to varying degrees of renal impairment

SSL Choi, KF Chan, HK Ng, WP Mak. Colchicine-induced myopathy and neuropathy. HKMJ 1999;5:204-7

- Colchicine myotoxicity has been reported in a wide range of age groups after variable durations of therapy
- A study searched databases such as MEDLINE, EMBASE, Health Star, International Pharmaceutical Abstracts, and Web of Science from 1966–2003, combining the key words colchicine, toxicity, myotoxicity, and myopathy as medical subject headings. Documents retrieved were limited to those published in English and involving adult patients
- 75 cases had been identified with colchicine-induced myopathy

Kerry Wilbur, Mark Makowsky. Colchicine Myotoxicity: Case Reports and Literature Review. *Pharmacotherapy* 2004;24(12):1784–1792

- The mean \pm SD age in patients identified was 58 ± 16 years
- Duration of colchicine therapy ranged from 4 days–11 years (mean \pm SD 40 ± 64 mo)
- at reported mean \pm SD cumulative daily doses of colchicine 1.4 ± 0.96 mg
- Although many patients had been receiving standard-dose therapy for long periods, colchicine toxicity often became apparent after recent changes in underlying disease states (e.g., solid organ transplantation, decline in renal function, start of dialysis) or short-term use of increased dosages

Kerry Wilbur, Mark Makowsky. Colchicine Myotoxicity: Case Reports and Literature Review. *Pharmacotherapy* 2004;24(12):1784–1792

Table 1. Summary of Colchicine-Induced Myopathy Case Reports

Age (yrs)	Sex	Length of Therapy	Dosage	Symptoms	CK (U/L)
48 ¹⁶	M	2 yrs	1.0 mg t.i.d.	Weakness	NR
43 ¹⁷	F	5 yrs	1.2 mg q4h 2-3 x/wk	Weakness, numbness	1160
60 ¹⁸	F	1.5 yrs	0.6 mg b.i.d.	Weakness, myalgia, fatigue	518
59 ¹⁹	M	2 yrs	0.6 mg b.i.d.	Weakness	1550
86 ¹⁹	M	3 yrs	0.6 mg b.i.d.	Weakness	11 x ^a
60 ¹⁹	M	5 yrs	0.6 mg b.i.d.	Weakness, atrophy	746
85 ¹⁹	M	Yrs	0.6 mg b.i.d.	Weakness	NR
64 ²⁰	F	2 wks	1.5 mg q.d.	Weakness, myalgia	416
44 ²¹	M	Yrs	0.6 mg b.i.d.	Weakness	600
57 ²²	F	4 days	2.0 mg q.d.	Myalgia	2344

ALT, AST (U/L)	Vacuolar Myopathy on Muscle Biopsy	Procedures, Comorbidities, Drug Therapy	EMG	Time to Resolution
NR	-	NR	+	6 wks
NR	+	NR	+	Ataxia remained at 1 yr
135, 47	NP	RF, Pred	NP	In-hospital death
NR	+	RF	+	3 wks
NR	+	Noncontributory	NP	2 wks
NR	+	HD, Pred	+	1 mo
NR	NP	RF	NP	2 mo
43, NR	NP	Liver disease	+	2 wks
288, 929	+	HD, CsA, Pred	+	1 mo
NR	NP	RTx, CsA, Pred	-	1 wk

Kerry Wilbur, Mark Makowsky. Colchicine Myotoxicity: Case Reports and Literature Review. *Pharmacotherapy* 2004;24(12):1784-1792

Pathogenesis

- Classically, neurotoxins or neurotoxic drugs induce axonal-type neuronal damage
- Mechanism of acute colchicine neuromyopathy is unknown
- Thought to be related to the inhibitory effect of colchicine on microtubule formation
- Microtubules are involved in cell motility and also form an intracellular transport network along which materials move by saltatory movements within cells
- Colchicine binds to tubulin reversibly at a high-affinity site and prevents the polymerisation of tubulin into microtubules, thereby impairing axoplasmic transport in peripheral nerves

- Colchicine also alters the microtubular network that localises, moves, or allows the normal extrusion of lysosomes and autophagosomes in skeletal muscle cells
- the overdevelopment of autophagic vacuoles, which subsequently injure the lysosomal membrane, thereby increasing its permeability
- Proteolytic enzymes may be released from these secondary lysosomes into the cytoplasm and may cause myofibril degenerative changes similar to chloroquine-induced vacuole myopathy

Pharmacokinetics and Pharmacodynamics

- The risk of combined myopathy and peripheral neuropathy is predominantly related to the presence of chronic renal insufficiency (Cr >140 mmol/L)
- Colchicine is readily absorbed and a peak serum level is reached 30 to 120 minutes after oral ingestion; the serum half-life is approximately 20 minutes
- Colchicine becomes distributed into tissue space of a volume larger than that of body water within half an hour of administration
- When given orally or intravenously, colchicine undergoes enterohepatic circulation and accumulates in the liver, bone marrow, leukocytes, kidneys, intestines, spleen, and testes

- Colchicine is partially demethylated in the liver by the cytochrome P450 system, mainly by the isoenzyme CYP3A4 and excreted as a metabolite or unchanged in the bile. 10-20% is excreted in urine by the P-glycoprotein
- In normal human beings, 15% to 40% of the colchicine is excreted unchanged and 4% to 15% is excreted as metabolites within 48 hours
- In the presence of hepatic or renal failure, accumulation occurs and toxicity is promoted at normal therapeutic doses
- Terminal elimination of colchicine with normal hepatic and renal function is approximately 9 hours
- prolonged 2–3-fold in patients with severe kidney failure and up to 10-fold in the presence of additional liver cirrhosis
- Colchicine is not removed by dialysis

SSL Choi, KF Chan, HK Ng, WP Mak. Colchicine-induced myopathy and neuropathy. HKMJ 1999;5:204-7

•Kerry Wilbur and Mark Makowsky. Colchicine Myotoxicity: Case Reports and Literature Review. Pharmacotherapy Vol 24, No 12, 2004; 1784-1792

Interaction

- Toxicity can be increased by daily consumption of a liter of grapefruit, hepatic/renal impairment, statins, fibrates and digoxin
- Drugs interacting with colchicine metabolism (Inhibitors of CYP3A4 and P-glycoprotein) increase the colchicine serum level and accelerate accumulation and toxicity
 - eg. cyclosporin, clarithromycin, erythromycin, verapamil, diltiazem, statins, ketoconazole, HIV protease inhibitors

- One retrospective study reported an incidence of severe toxicity in as much as 10% of patients receiving concomitant therapy with colchicine and clarithromycin. It did not specifically regard the occurrence of neuromyopathy
- The co-administration of cimetidine has been reported to decrease colchicine clearance by 32% and to increase the half-life of colchicine by 33%

Van der Velden, et al. Colchicine-induced neuromyopathy in a patient with chronic renal failure: the role of clarithromycin. *The Netherlands journal of medicine*. May 2008, Vol 66(5) pp 204-206

- Statins are also metabolised by the cytochrome P450 system, in which CYP3A4 is the major isoenzyme
- Co-administration of colchicine with statins may lead to accumulation of both substrates and resulted in increase myotoxic effect, causing myopathy and varying degree of rhabdomyolysis

Manifestations

- Subacute proximal muscle weakness, often more prominent in the lower than upper extremities
- CK levels are elevated, usually 10 to 20-fold above normal
- Asymptomatic or causes mild sensory symptoms
- diminished deep tendon reflexes

Electrodiagnostic testing

- Nerve conduction studies show prolongation of distal motor and sensory latencies in both UL and LL
 - Reduced in CMAP and SNAP amplitudes
 - F waves prolonged
 - H reflexes may be absent or prolonged
- Electromyography show prominent fibrillations, positive sharp waves and excessive polyphasic MUP in proximal muscle (acute destructive myopathic process)
- Myopathic changes and an accompanying axonal polyneuropathy that is usually asymptomatic or causes mild sensory symptoms and diminished deep tendon reflexes

Rutkove SB; De Girolami U; Preston DC; Freeman R; Nardin RA; Gouras GK; Johns DR; Raynor EM. Mytonia in colchicine myoneuropathy. *Muscle Nerve* 1996 July 19(7): 870-5
Daniel Dumitru. *Electrodiagnostic Medicine*, second edition. Hanley & Belfus. Page 1408

Muscle biopsy

- Accumulation of autophagic vacuoles in muscle and nerve cells
- The vacuoles have been shown to be of lysosomal origin by special stains (acid phosphatase +ve) and electron microscopy

Kissin et al. Colchicine Myopathy in a Patient With Familial Mediterranean Fever and Normal Renal Function. *Arthritis & Rheumatism*. Vol 49, No 4, August 15, 2003 pp 614-616

H & E stain

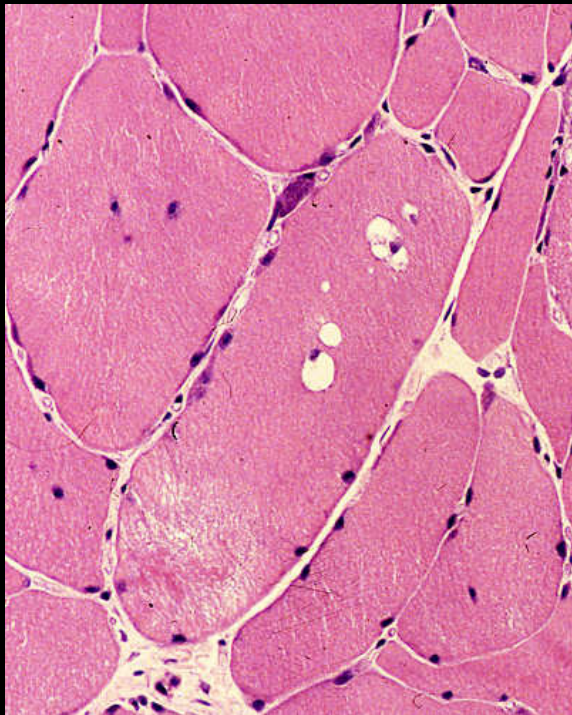
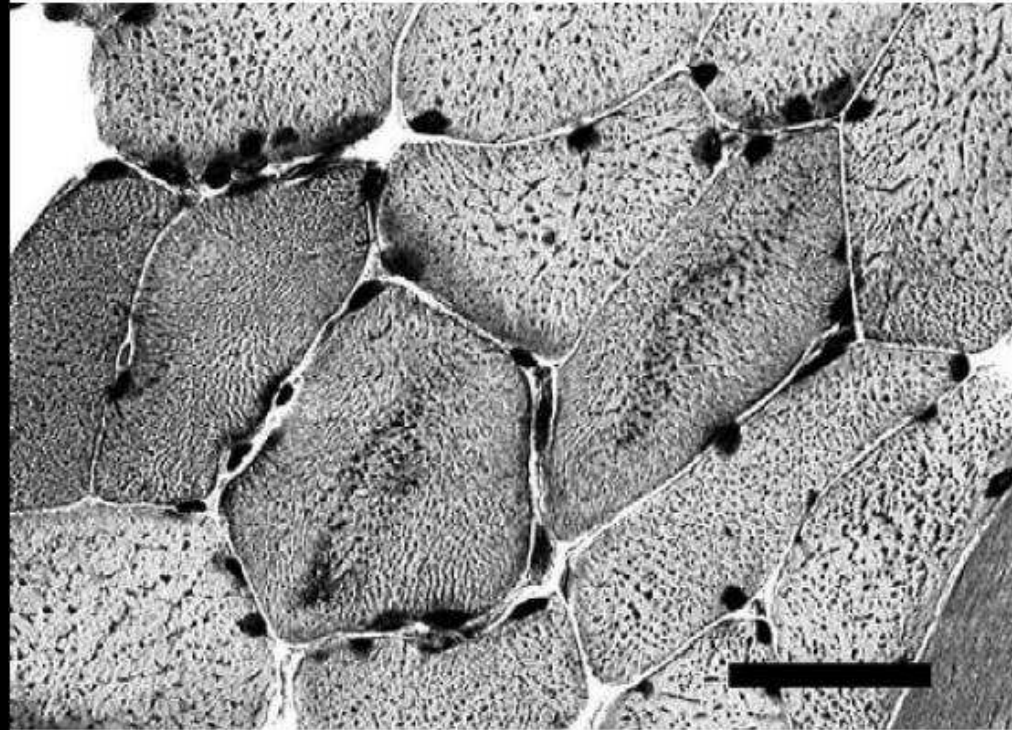


Figure 1. Muscle biopsy: characteristic multiple small basophilic vacuoles accumulated in the central part of several muscle fibers



The black bar represents 50 μm . (Hematoxylin-Phloxine stained frozen section).

Van der Velden, et al. Colchicine-induced neuromyopathy in a patient with chronic renal failure: the role of clarithromycin. *The Netherlands journal of medicine*. May 2008, Vol 66(5) pp 204-206

Blood tests

- Investigations are necessary to exclude
 - myopathy caused by thyroid disease, viral infection and other drugs
 - common causes of peripheral neuropathy
 - Liver/ renal function, electrolytes, fasting glucose, B12, TSH, VDRL, inflammatory markers, muscle enzyme

Consequences

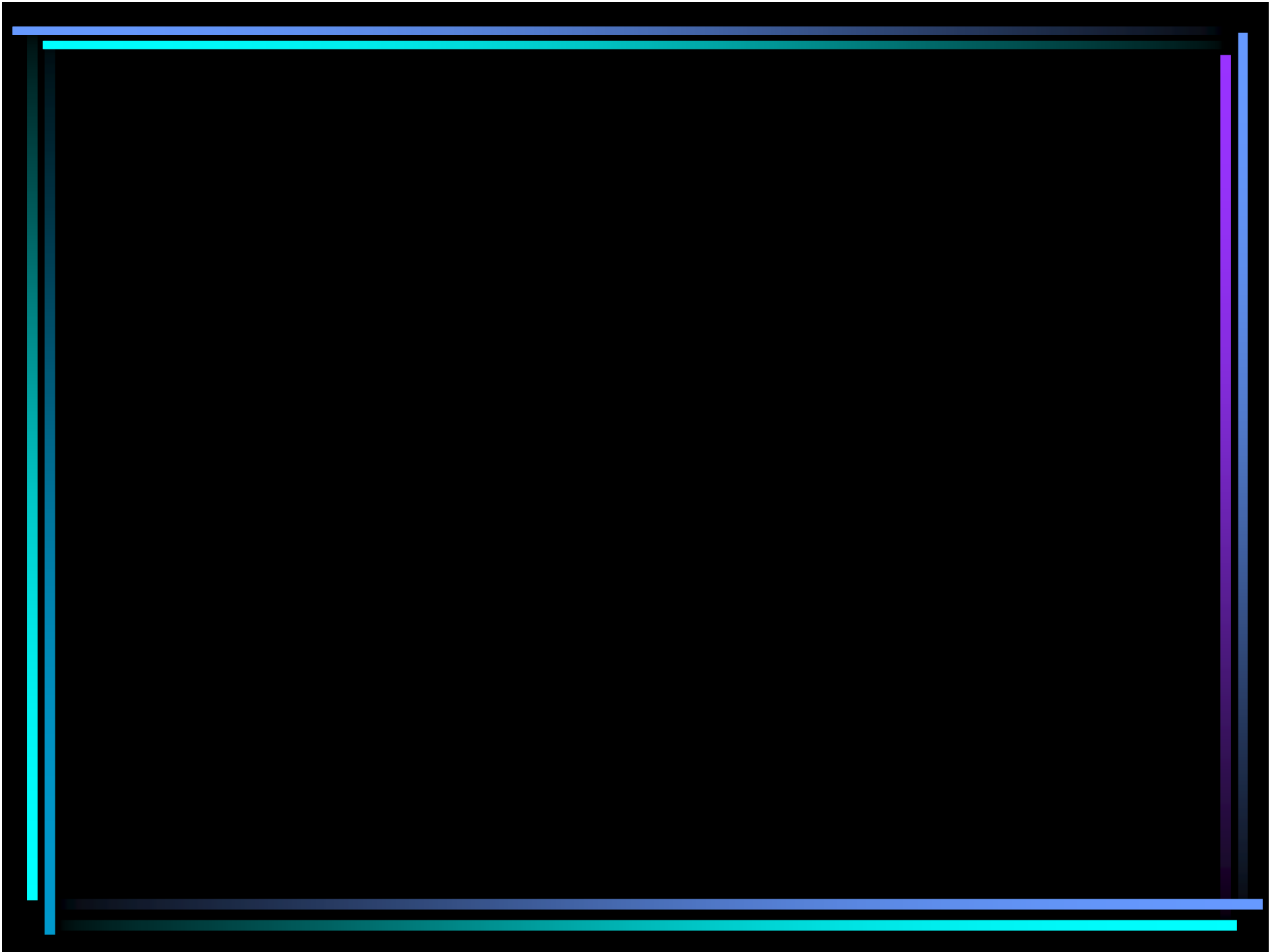
- If myopathy is suspected, colchicine and possible interacting drugs should be discontinued
- Serum CK levels should be monitored
- Therapy is supportive as there are no specific antidotes or methods to decrease toxic plasma levels

- Muscles weakness resolves and CK levels return to normal within a few days to several weeks after discontinuation of colchicine
- Neuropathy resolves more slowly

Kissin et al. Colchicine Myopathy in a Patient With Familial Mediterranean Fever and Normal Renal Function. *Arthritis & Rheumatism*. Vol 49, No 4, August 15, 2003 pp 614-616

Risk factors of Neuromuscular toxicity

- Age > 75
- Chronic kidney disease (increased plasma colchicine levels)
- Liver disease (80% excreted by liver metabolism)
- Not removed by dialysis
- Organ transplant recipients who are treated with cyclosporine (impairs the metabolism of colchicine)
- Concomittent drugs – tolbutamide, erythromycin, cyclosporine, statins



Use of Colchicine in the treatment of Gout

- In July 2010, the New Zealand Rheumatology Association (NZRA) updated a consensus statement on the safe use of colchicine in the treatment of gout
- In most patients, non steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are the treatment of choice for acute gout
- When NSAIDs are contraindicated and corticosteroids are not providing an adequate response, colchicine is an option, particularly if taken within the first 24 hours of the onset of pain
- The use of two hourly dosing of colchicine to treat acute gout is no longer appropriate, especially in older patients, because of the serious adverse effects arising from large doses

- The recommended dose for colchicine in the treatment of acute gout is 1.0 mg stat, followed by 0.5 mg stat six hourly, up to a maximum dose of 2.0 mg per 24 hours on the first day
- An alternative regimen to consider in acute gout of less than 12 hours duration is 1.0 mg stat followed by 0.5 mg one hour later. On the subsequent days, the total dose should not exceed 1.5 mg daily. The total dose should not exceed 6 mg over four days
- A prophylactic dose of Colchicine may be started after three days. Corticosteroids can be used in combination with NSAIDs or colchicine to provide further relief during acute gout

Adjustment in renal impairment

- Flares
 - CrCl > 30: dosage adjustment not required, monitor closely for adverse effects
 - CrCl < 30: dosage reduction not required but may be considered, treatment course should not be repeated more frequently than every 14 days
 - Dialysis: 0.6mg as a single dose, treatment course should be repeated more frequently than every 14 days. Not removed by dialysis

Adjustment in renal impairment

- Because of impaired colchicine pharmacokinetics in the elderly
 - reduce prophylactic daily dose by 50% in patients older than age 70 years
- Concurrent use of colchicine and CYP3A4 or P-GP inhibitors is contraindicated in renal impairment
- Treatment of gout flares is not recommended in patients with renal impairment receiving prophylactic colchicine

- Gout prophylaxis
 - CrCl >50 ml/min: 0.6mg twice daily
 - CrCl 35-49 ml/min: 0.6mg once daily
 - CrCl 10-34 ml/min: 0.6mg every 2-3 days
 - CrCl < 10 ml/min: avoid chronic use of colchicine
 - Hemodialysis: avoid chronic use of colchicine

Hanlon JT, et al. Consensus guidelines for oral dosing of primarily renally cleared medications in older adults. *JAGS* 2009; 57:335-340

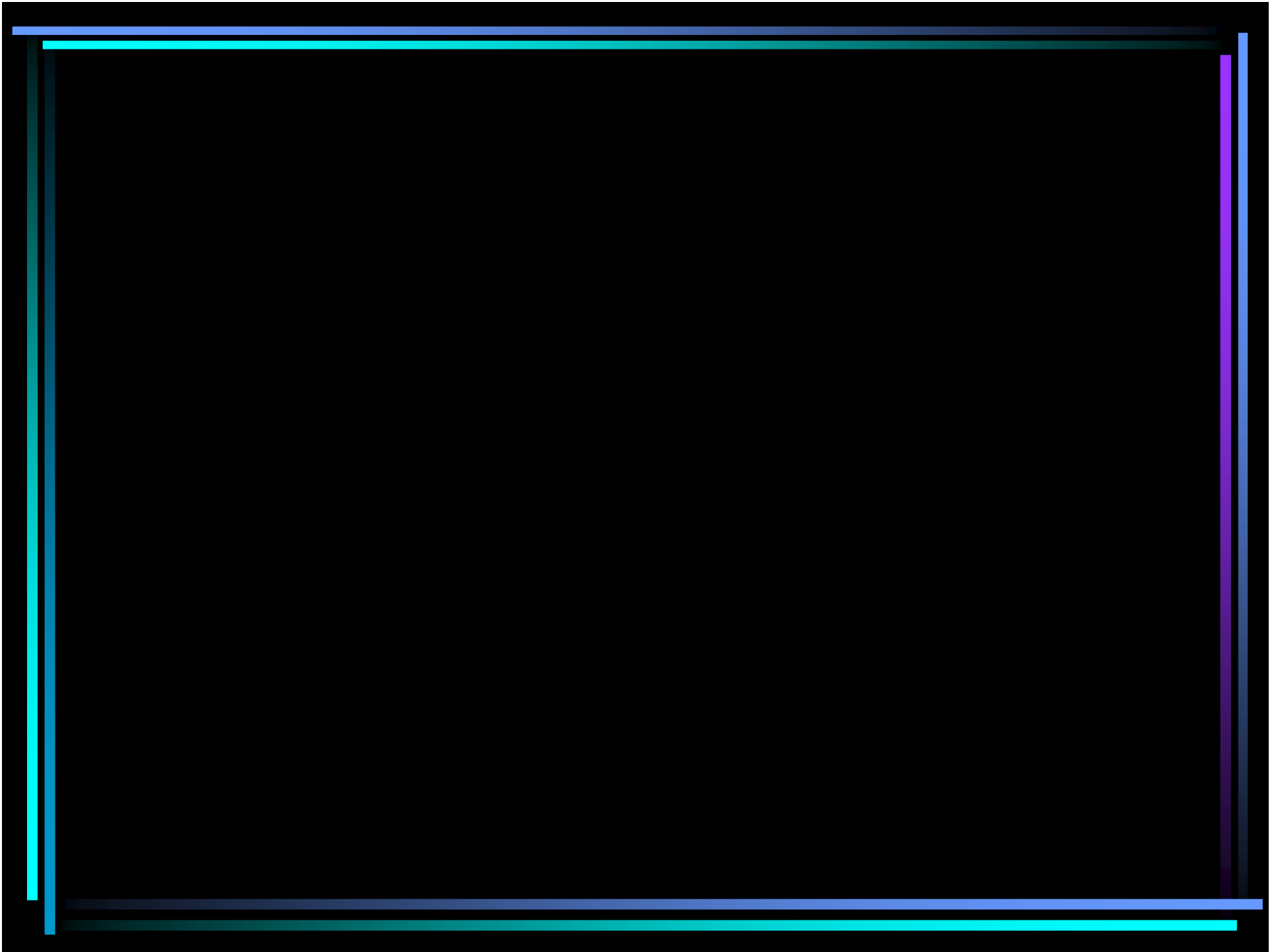
Zhang W, et al. EULAR evidence based recommendations for gout. Part II: Management. Reporting of a task force of the EULAR standing committee for International Clinical Studies including Therapeutics (ESCISIT). *Ann Rheum Dis* 2006; 65; 1312-24

Ly J, Gow P, Dalbeth N. Colchicine prescribing and safety monitoring in patients with gout. *New Zealand Medical Journal*. 2007; 120(1265)

Terkeltaub RA. Colchicine Update: 2008. *Semin Arthritis Rheum*, 2009, 38(6): 411-9

- Colchicine is of proven benefit in patients with chronic gout, as prophylaxis therapy to prevent acute attacks, particularly when establishing urate-lowering therapy
- If a gout patient
 - receives long term prophylactic oral colchicine (a minimum daily dose of 0.5mg for a duration of 6 months or longer) and
 - has significant renal insufficiency (creatinine clearance \leq 50ml/min)
 - a complete blood cell count and creatine kinase (CK) should be evaluated a minimum of one time for every 6 months of continued use
- BECAUSE the risk of colchicine related myopathy and myelosuppression appears to be substantially increased in the context of reduced renal function

• Jason Ly, Peter Gow, Nicola Dalbeth. Colchicine prescribing and safety monitoring in patients with gout. Journal of New Zealand Medical Association, 09/11/2007, 120(1265)



Take home message

- This case demonstrated the immobility and iatrogenesis in old people



Take home message - Start LOW, Go SLOW



- Drug review is important
- Drug-drug interaction is common
- Advice and education of drug dosage and use should be given to patient and carer carefully
- (eg. PRN use of colchicine)
- Caution about patients with liver/ renal impairment

General recommendations for geriatric prescribing



TABLE 14-8 GENERAL RECOMMENDATIONS FOR GERIATRIC PRESCRIBING

1. Evaluate geriatric patients thoroughly in order to identify all conditions that could (a) benefit from drug treatment; (b) be adversely affected by drug treatment; (c) influence the efficacy of drug treatment.
2. Manage medical conditions without drugs as often as possible.
3. Know the pharmacology of the drug(s) being prescribed.
4. Consider how the clinical status of each patient could influence the pharmacology of the drug(s).
5. Avoid potential adverse drug interactions.
6. For drugs or their active metabolites eliminated predominantly by the kidney, use a formula or nomogram to approximate age-related changes in renal function and adjust dosages accordingly.
7. If there is a question about drug dosage, start with smaller doses and increase gradually.
8. Drug blood concentrations can be helpful in monitoring several potentially toxic drugs used frequently in the geriatric population.
9. Help to ensure compliance by paying attention to impaired intellectual function, diminished hearing, and poor vision when instructing patients and labeling prescriptions (and by using other techniques listed in Table 14-1).
10. Monitor older patients frequently for compliance, drug effects, and toxicity.

Robert Kane. Essentials of clinical geriatrics. McGraw-Hill; 5 ed, 2003 P. 380



End