

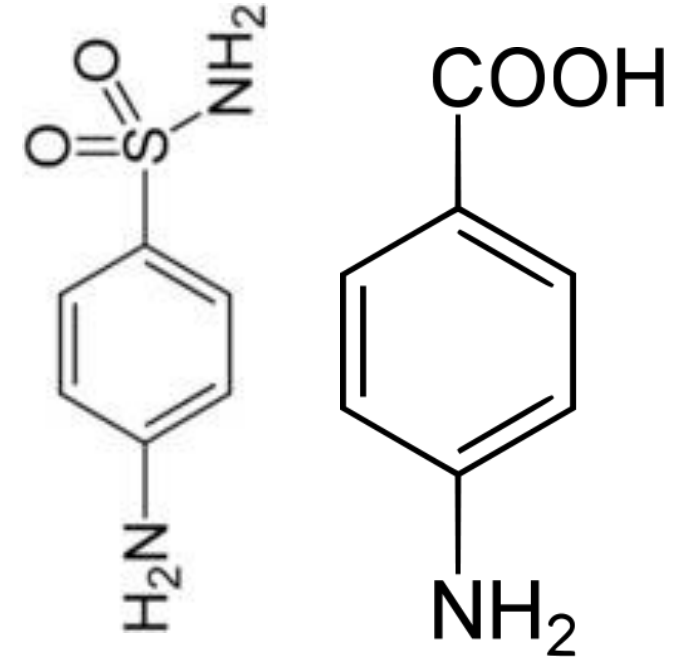
Inhibitors of NA synthesis

- Sulphonamides and trimethoprim
- Metronidazole
- Quinolones
- Rifampicin

Sulphonamides & Trimethoprim

- مع بعض يعطوني synergistic effect

- Bacteria can not utilize external folic acid (FA) for DNA synthesis(human cell can)
- البشر قادرين يحصلوا على الفوليك أسيد من الغذاء، لكن البكتيريا ما عندها هاي القدرة بالتالي من هون جاي ال specific of action of sulphonamides. ☒
- Bacteria must synthesize FA from PABA.
- Sulphonamides are similar to PABA and inhibits the enzyme dihydro folate synthetase in synthetic pathway of FA.
- ال active form'folic acid isn't، الأكتيف فورم هو ال Dihydro folate (اللي بستخدمه لبناء ال DNA)
- They are bacteriostatic.
- كمان ال trimethoprim عنده Bacteriostatic، لكن مع بعض يعطوا synergistic effect.



PABA & SA Structures

Sulfonamides adverse effect

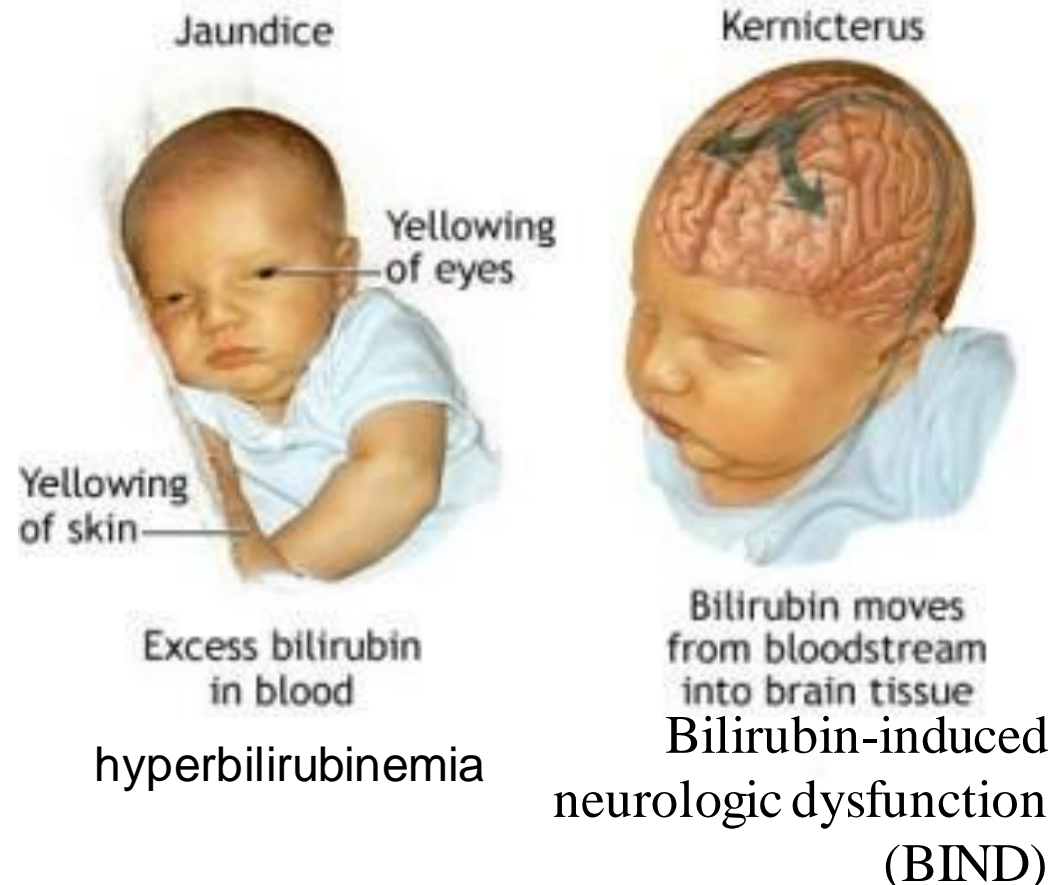
Kernicterus

- سواء استخدمنا الـ sulphonamides لحاله أو Combinations بعملية Kernicterus

Should be avoided after 32 weeks of gestation.

Sulfonamides should never be used in infants under the age of two months

This disorder may occur in newborns, because sulfa drugs displace bilirubin from binding sites on serum albumin. The bilirubin is then free to pass into the CNS, because the baby's blood-brain barrier is not fully developed and this lead to brain damage



Other combination

ORAL PYRIMETHAMINE WITH SULFONAMIDE

Pyrimethamine and sulfadiazine are used in the treatment of **toxoplasmosis** and **falciparum malaria**.

- Pyrimethamine نفس الـ Trimethprime دائماً folate reductase inhibitors.
- فيني أستخدامه كـ Anti combination with sulphonamides which has malaria effect and for the treatment toxoplasmosis (هي بتكون بسبب دودة الأرض)

Adverse Drug Reactions

- فيها توخده المرأة الحامل، لكن في الـ end term بوقفه تماماً

- **TM:** * Folic acid deficiency :megaloplastic

anemia, agranulocytosis leucopenia “preg. & poor and diet”.

TT: folinic acid

Cotrimoxazole: Dermatologic, gastrointestinal & hematological

- مشكلتي هون دائماً إنه الـ side effects بييجي من شغلتي، الأولى من الـ sulphonamides، والثانية من الـ Trimethprime.

- الـ sulphonamides السايڊ إيفكت تبعها جاية من الـ phototoxicity, hypersensitivity, contraindicated .P Defeciency patients, and crystil urea6with G-

- السايڊ إيفيكت بالنسبة للـ Trimethprime : folic acid Defeciency because impaired folic acid
☑ acteviation and lead to megaplastic anemia

- هاي حكت ندور على أجوبتهم (اعملوا سكيب خلص ضمانتي
(🤔🤔)

Drug Interactions

- On the basis of protien binding displacement →
Potention of effect of(?)

- عشان هيك تحديداً بصير عند الأطفال Kernicterus، عشان ال
sulphonamides بزيد من ال albumin والبيلوروبين. ☒

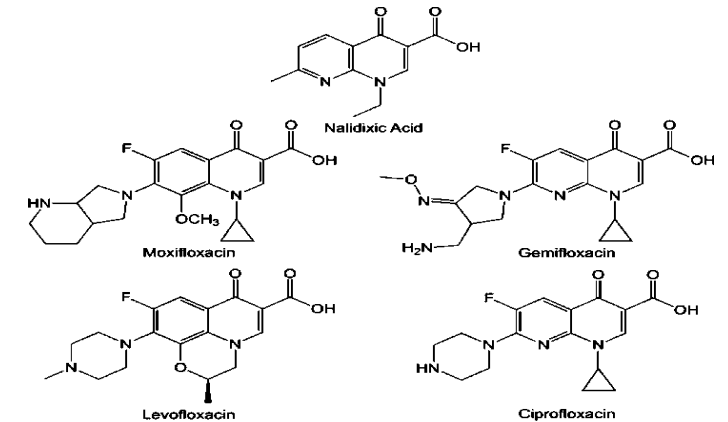
- And on the basis of Inhibition of metabolism →
Potentiation of effect of (?)

- وكمان بعملوا inhibition of hepatic Enzyme ☒.

Fluroquinolones

The least group in Antibacterial agents

- The fluroquinolones are a family of bactericidal broad spectrum drugs
- The fluoroquinolones interfere with bacterial DNA synthesis by inhibiting topoisomerase II (DNA gyrase), especially in Gram-negative organisms, and topoisomerase IV, especially in Gram-positive organisms



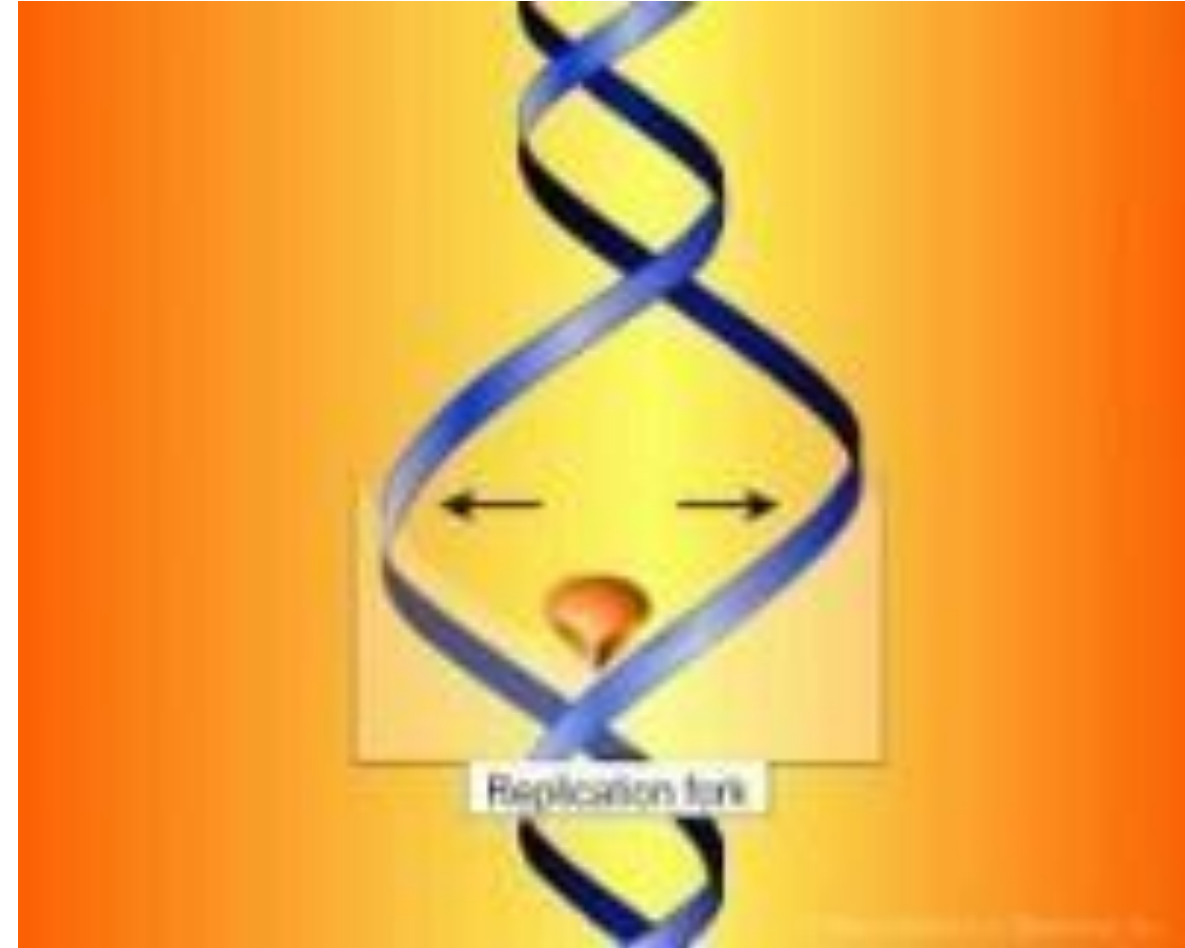
المشكلة mechanism of action -
تعتبر مختلفة عن الباقين وفريدة، إنه يعمل
inhibition of DNA gyrase

Fluoroquinolones mechanism of action

مراجعة سريعة كده شوية للميديسنال :

هسة أنا الطبيعي عندي يكون في double DNA strains ، لازم ينفصلوا وأثناء الانفصال رح يصير عندي supercoiling للـ Two strains ؛ فالـ DNA gyrase بمنع هاد الـ super coiling إنه يصير فبعمل enhances DNA replication . ☒

لكن لما آخذ Fluroquinolones ؛ فأنا بعمل تشبيط للـ DNA gyrase وبالتالي بحقّر الـ super coiling إنها تصير وهاد impaired DNA replication = ☒



Classification


- Fluoroquinolones are classified by “generation” based on their antimicrobial spectrum of activity
- First-generation fluoroquinolone (nalidixic acid)
- Use limited because it's Toxicity
- Second-generation fluoroquinolones (Norfloxacin, Ciprofloxacin and ofloxacin)
 - عشان ضفت الهالوجينات، صارت اسمها fluoroquinolones. ✓
 - كما إنه ال second generation هي الأشهر خاصة ال Ciprofloxacin.
- Third-generation fluoroquinolones (levofloxacin, Gemifloxacin).
 - ال levofloxacin is use mainly in respiratory infection. ✓
- Fourth-generation fluoroquinolones (moxifloxacin)
 - Unlike other fluoroquinolones, the moxifloxacin is NOT use to -
 - ✓ treat Urinary tract infection (يستخدم زي ال levofloxacin لل (respiratory infection

Generation	Drugs
First	Nalidixic acid Cinoxacin
Second	Norfloxacin Ciprofloxacin Ofloxacin Lomefloxacin Enoxacin
Third	Levofloxacin Sparfloxacin Gatifloxacin Gemifloxacin
Fourth	Trovafoxacin Moxifloxacin Clinafloxacin Sitafoxacin

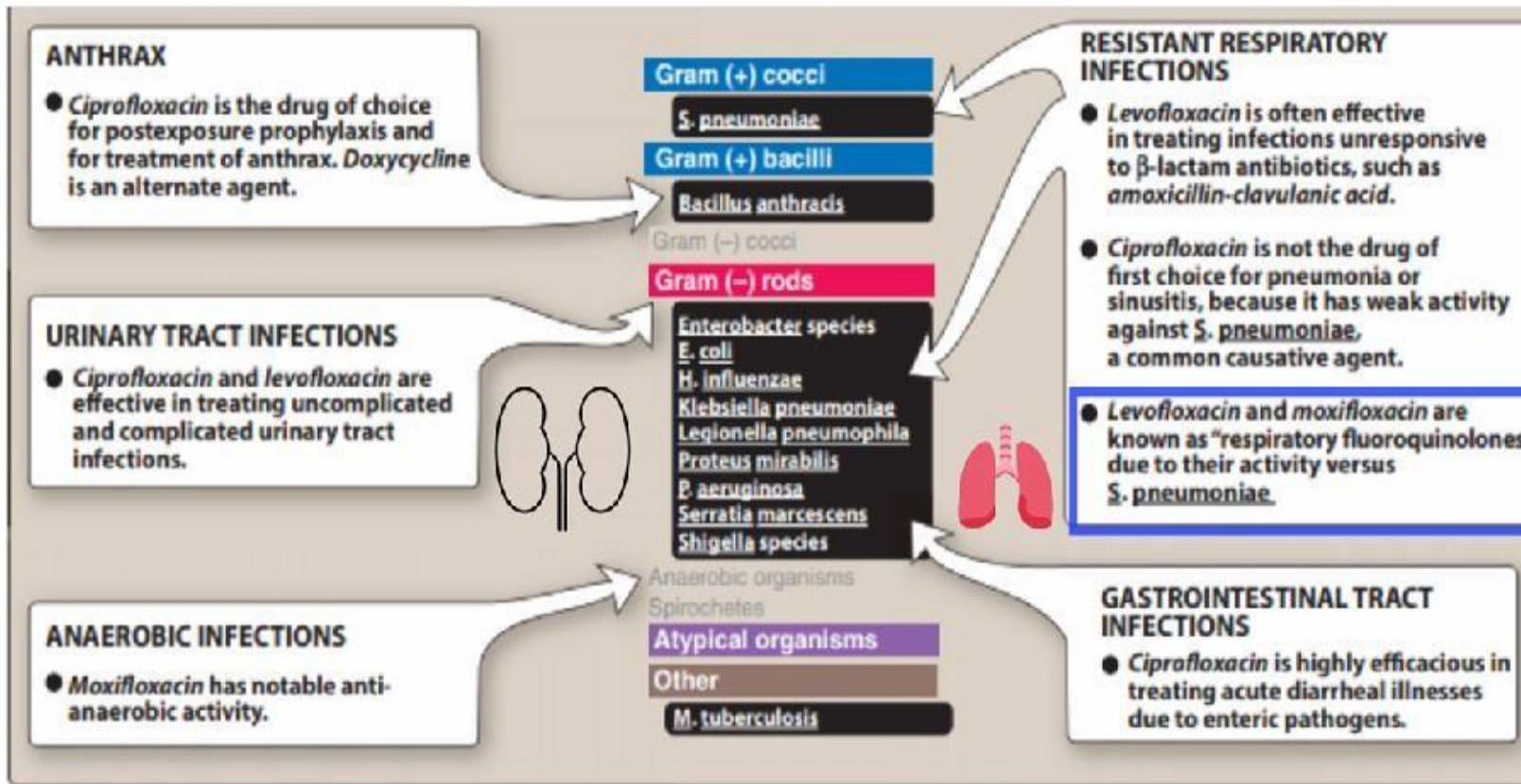
- كل ما رُحنا من ال first generation to other modern generation the Activity Against
 ✓ Gram + bacteria will INCREASE

Antimicrobial spectrum of fluoroquinolones

FQ are classified into 4 generations based on their antimicrobial targets:

- 1st generation: Nonfluorinated quinolone(ex. Nalidixic acid): usually confined to the **urinary tract infections by G-ve.**
- 2nd generation (ex. Ciprofloxacin and norfloxacin): for G-ve and exhibit significant intracellular penetration (used for chlamydia, mycoplasma, and legionella) and some activity against **G+ve.**
 - هاد الـ generation بشتغل ضد الـ **Atypical Bacteria** .
- 3rd generation (ex. Levofloxacin): G-ve and increased activity against **G+ve**
- 4th generation (ex. Moxifloxacin): G-ve, active against **anaerobic & G+ve**

Typical therapeutic applications of fluoroquinolones.



- زي ما حكينا إنه الـ *levofloxacin* and *moxifloxacin* يستخدموا للـ respiratory infection التي بسببها Gram + bacteria .☒

- الـ *Ciprofloxacin* can use to treat GI infection and treating the diarrhea .thet cause by E. COLI

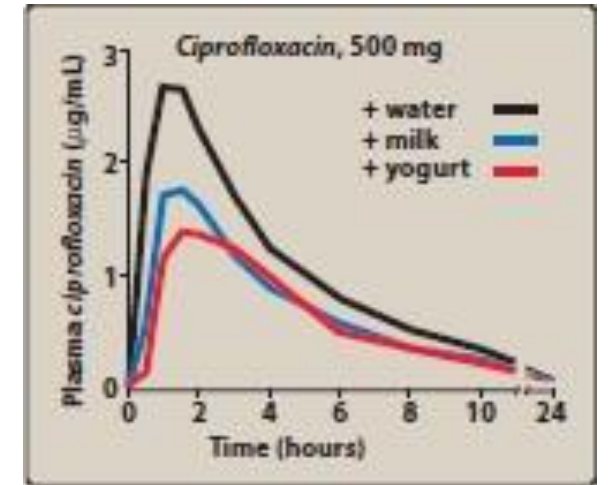
- الـ Anaerobic infection can be .treated with fourth generation

***Moxifloxacin* has poor activity against *P. aeruginosa*.
It does not concentrate in urine and is not indicated for the treatment of UTIs**

Kinetics

- ❑ Well absorbed orally.
- ❑ Oral absorption is impaired by divalent and trivalent cations, including those in antacids. Therefore, oral fluoroquinolones should be taken 2 hours before or 4 hours after any products containing these cations.

- نفس قصة التيتراسايكلين، ال fluoroquinolones effective
☑ by cations



Kinetics

- Widely distributed in the body----- Levels are high in bone, urine (except *moxifloxacin*), kidney, and prostatic tissue (but not prostatic fluid), and concentrations in the lungs exceed those in serum.
 - حكت الدكتور إنه ال Clindamycin يعتبر drug of Choice to treat osteotits (التهاب العظام).
 - وحتى كونه ال fluoroquinolones تركيزها عالي جداً في ال prostatic tissue؛ فأنا مُمكن أستفيد منها بعلاج ال prostatic infection.
- Most fluoroquinolones are excreted renally. Therefore, dosage adjustments are needed in renal dysfunction. *Moxifloxacin* is excreted primarily by the liver, and no dose adjustment is required for renal impairment.
 - ال safty of fluoroquinolones better than aminoglycosides (مُهم جداً أعملهم TDM زي ال ☒). (Aminoglycosides

Adverse reactions

Have a wide Adverse effects

- In general, these agents are well tolerated. Like most antibiotics, the most common adverse effects of fluoroquinolones are **nausea**, **vomiting**, and **diarrhea**.
- الدكتور حكت إنه أهم شي تعرفوا إنه ال Diarrhea بتكون كثير واضحة مع ال broad and extend Antibacterial agents.
- **Headache** and **lightheadedness** may occur. Patients with central nervous system (CNS) disorders, such as epilepsy, should be treated cautiously with these drugs.
- مشكلة كبيرة إنه بحفز نوبات الصرع للأشخاص اللي عندهم **history of epilepsy**.
- **Phototoxicity** (if it occurs, the drugs should be discontinued)
- **Articular cartilage erosion (arthropathy)** has been observed in immature animals exposed to fluoroquinolones.
- An increased risk of **tendinitis** or **tendon rupture**
- **Prolongation of the QTc interval**
- **CAUTIONS:** These agents should be avoided in pregnancy and lactation and in children under 18 years of age
- وهاد بسبب ال ☒ **Articular cartilage erosion**.

Drug-drug interaction

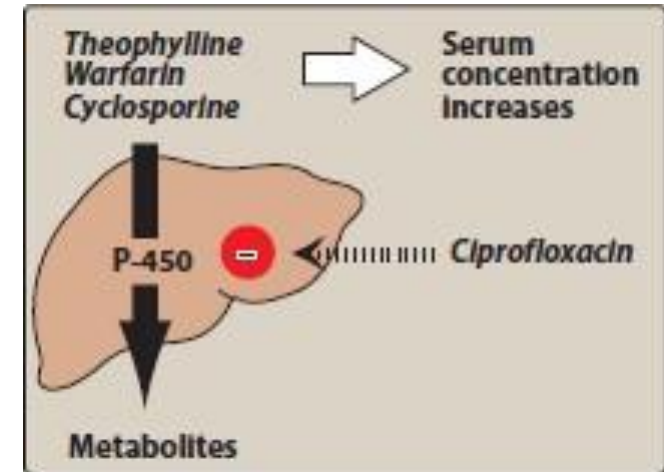
- *Ciprofloxacin* can increase serum levels of *theophylline* by inhibiting its metabolism.

- يعتبر **hepatic Enzyme inhibitors**.

- Quinolones may also raise the serum levels of *warfarin*, *caffeine*, and *cyclosporine*.

- إله Interaction مع ال *caffeine*؛ فاللي بوخدوا ال
fluoroquinolones وبشربوا قهوة بصير عندهم
accumulation or rise in level of caffeine (فبتزيد ال
insomnia and CNS activation).

- Antacids and minerals decrease fluoroquinolones absorption.



Gatifloxacin was banned in the United States and Canada for use as an oral dosage form as it is posed high threat of severe hyperglycemia or high blood sugar among elderly citizens