References 15

Links, Abstracts, Articles, etc.

These links should work as of 2016; sometimes you have to click on them several times; if they don't work, then Google/search the titles

FQ-Induced Dysglycemia and Diabetes, Diabetes and Tendon Disorders

http://www.ncbi.nlm.nih.gov/pubmed/25960658 **Evaluation of the appropriate use of commonly prescribed fluoroquinolones and the risk of dysglycemia.** *"The final percentage for the appropriate indication, dose, and duration of fluoroquinolone therapy was 93.2%, 74.6%, and 57.6%, respectively. A total of 57.1% of the patients did not receive the appropriate dose adjustment according to their level of renal impairment. In addition, dysglycemia occurred in both diabetic and nondiabetic patients. Dysglycemia was more frequently encountered with ciprofloxacin (50.0%), followed by levofloxacin (42.4%) and moxifloxacin (7.6%). Hyperglycemia was more common than hypoglycemia in all groups. The highest incidence of hyperglycemia occurred with levofloxacin (70.0%), followed by ciprofloxacin (39.0%) and moxifloxacin (33.3%). In contrast, hypoglycemia did not occur in the ciprofloxacin group, but it was more common with moxifloxacin (11.1%) and levofloxacin (6.0%)."*

http://www.ncbi.nlm.nih.gov/pubmed/23948133 **Risk of severe dysglycemia among diabetic patients receiving levofloxacin, ciprofloxacin, or moxifloxacin in Taiwan**. *"Observational studies and fatal case reports raise concern about the safety of severe dysglycemia associated with fluoroquinolone use. The objective of this study was to assess the risk of severe dysglycemia among diabetic patients who received different fluoroquinolones. Diabetics using oral fluoroquinolones faced greater risk of severe dysglycemia. The risk of hypoglycemia varied according to the type of fluoroquinolone administered, and was most commonly associated with moxifloxacin."*

http://www.ncbi.nlm.nih.gov/pubmed/23200776 **Combined contributions of over-secreted glucagon-like peptide 1 and suppressed insulin secretion to hyperglycemia induced by gatifloxacin in rats.** *"Accumulating evidences have showed that gatifloxacin causes dysglycemia in both diabetic and non-diabetic patients. Our preliminary study demonstrated that gatifloxacin stimulated glucagon-like peptide 1 (GLP-1) secretion from intestinal cells. The aim of the study was to investigate the association between gatifloxacin-stimulated GLP-1 release and dysglycemia in both normal and streptozotocin-induced diabetic rats and explore the possible mechanisms. Oral administration of gatifloxacin (100 mg/kg/day and 200 mg/kg/day) for 3 and 12 days led to marked elevation of GLP-1 levels, accompanied by significant decrease in insulin levels and increase in plasma glucose. Similar results were found in normal rats treated with 3-day gatifloxacin. Gatifloxacin-stimulated GLP-1 release was further confirmed in NCI-H716 cells, which was abolished by diazoxide, a K(ATP) channel opener. QT-*

PCR analysis showed that gatifloxacin also upregulated expression of proglucagon and prohormone convertase 3 mRNA. To clarify the contradiction on elevated GLP-1 without insulinotropic effect, effects of GLP-1 and gatifloxacin on insulin release were investigated using INS-1 cells. We found that short exposure (2h) to GLP-1 stimulated insulin secretion and biosynthesis, whereas long exposure (24 h and 48 h) to high level of GLP-1 inhibited insulin secretion and biosynthesis. Moreover, we also confirmed gatifloxacin acutely stimulated insulin secretion while chronically inhibited insulin biosynthesis. All the results gave an inference that gatifloxacin stimulated over-secretion of GLP-1, in turn, high levels of GLP-1 and gatifloxacin synergistically impaired insulin release, worsening hyperglycemia."

http://www.ncbi.nlm.nih.gov/pubmed/21958023 **Cardiovascular and metabolic safety profiles of the fluoroquinolones.** *"Certain fluoroquinolones share similar indications of use. A comparison among Cardiovascular and metabolic (i.e., dysglycemia) safety profiles of the fluoroquinolones might be particularly useful for the prescribers' decision-making process as well as to hypothesize future researcher purposes."*

http://www.ncbi.nlm.nih.gov/pubmed/21383336 **Life-threatening hypoglycemia with moxifloxacin in a dialysis patient.**

http://onlinelibrary.wiley.com/doi/10.1592/phco.24.17.1807.52348/full **Fatal Hypoglycemia Associated with Levofloxacin**. *"We report a case of fatal hypoglycemia related to levofloxacin administration in an elderly patient with diabetes. As with other fluoroquinolones, levofloxacin can cause profound and prolonged hypoglycemia. Clinicians should be cognizant of this potential adverse effect in patients with diabetes who are receiving levofloxacin therapy."*

http://www.ncbi.nlm.nih.gov/pubmed/20068268 **Clinicopathological aspect of dysglycemia in naive and diabetic rats induced by the fluoroquinolone antibacterial gatifloxacin** *"To ascertain the clinicopathological process underlying dysglycemia induced by the fluoroquinolone antibacterial gatifloxacin (GFLX), we orally administered 100 or 300 mg/kg/day to male clinically healthy (naive) or spontaneous type II (diabetic) Goto-Kakizaki rats for 15 days (days 1 to 15). Treatment of naive rats with GFLX led to decreased blood glucose concentrations at 100 mg/kg/day on day 1. In diabetic animals, markedly increased blood glucose concentrations were noted from 100 mg/kg/day on day 3, and all of the animals given 300 mg/kg/day died or were killed because of moribund conditions by day 9. In a glucose tolerance test, serum insulin concentrations decreased significantly in naive rats receiving 300 mg/kg/day. Microscopically, cytoplasmic vacuolations of the pancreatic islets were observed in naive rats receiving 300 mg/kg/day, and congestion and/or hemorrhage were additionally noted in diabetic rats given 100 mg/kg/day or more. In toxicokinetics with 100 mg/kg/day, AUC(0-8 hr) values for GFLX were higher in diabetic rats than in naive rats, and relatively high serum GFLX concentrations at 8 hr post-dose and extraordinarily high pancreatic GFLX concentrations were also observed in diabetic rats. These results demonstrate that hypoglycemia or hyperglycemia induced by GFLX is associated with higher distribution and retention of GFLX in the pancreas, leading to disturbed insulin secretion"*

http://www.ncbi.nlm.nih.gov/pubmed/19545207 **Severe dysglycemia with the fluoroquinolones: a class effect?** *"Although gatifloxacin is no longer available, other fluoroquinolones may significantly interfere with glucose homeostasis. The objective of the present study was to compare the risk of severe hypo- and hyperglycemia in a cohort of patients treated with gatifloxacin, levofloxacin, ciprofloxacin, or azithromycin . . . The odds of severe hypo- and hyperglycemia were significantly greater with gatifloxacin and levofloxacin, but not ciprofloxacin, than with azithromycin. Thus, the risk of a clinically relevant dysglycemic event appears to vary among the fluoroquinolones."*

http://www.ncbi.nlm.nih.gov/pubmed/19022360 **Disturbance of cellular glucose transport by two prevalently used fluoroquinolone antibiotics ciprofloxacin and levofloxacin involves glucose transporter type 1.**

"Dysglycemia and central nervous system (CNS) complications are the known adverse effects of fluoroquinolone antibiotics. Ciprofloxacin and levofloxacin are among the most prescribed antibiotics. In this study we demonstrate that ciprofloxacin and levofloxacin disturb glucose transport into HepG2 cells and such inhibition is associated with inhibited glucose transporter type 1 (GLUT1) function. When exposed to ciprofloxacin or levofloxacin at maximum plasma concentrations (C(max)) and 5x of C(max) concentrations, GLUT1 mRNA expression, cell surface GLUT1 protein expression and glucose uptake were significantly reduced. These findings imply that disturbed cellular glucose transport and GLUT1 function may underlie the dysglycemic and CNS effects of ciprofloxacin and levofloxacin."

http://www.ncbi.nlm.nih.gov/pubmed/18297409 **An evaluation of the effects of gatifloxacin on glucose homeostasis.** "*Compared to ceftriaxone, gatifloxacin was associated with an increased risk of hypoglycemia . . . The increased risk of hypoglycemia during exposure to gatifloxacin was similar in patients with and without a diagnosis of diabetes mellitus."*

http://www.ncbi.nlm.nih.gov/pubmed/18183859 **Gatifloxacin-associated hypoglycemia**. "While hypoglycemia usually occurs within the first three days of treatment, hyperglycemia often occurs later in the treatment course. The hypoglycemia may be profound and difficult to manage."

http://www.ncbi.nlm.nih.gov/pubmed/18154478 **Prevalence of and risk factors for dysglycemia in patients receiving gatifloxacin and levofloxacin in an outpatient setting**. "*Levofloxacin and gatifloxacin were not significantly associated with increased dysglycemic events compared with azithromycin. Lack of downward fluoroquinolone dosage adjustment for renal function, presence of diabetes, and treatment with insulin or sulfonylureas each independently increased the risk of dysglycemia. Obesity was independently protective against dysglycemia. More data are needed on the contributing effects of diabetes, fluoroquinolone dosage, and concomitant drug therapy so that an appropriate risk-management strategy can be developed."*

http://www.ncbi.nlm.nih.gov/pubmed/18025428 **The effect of publication on Internet-based solicitation of personal-injury litigants.** *(Gatifloxacin used as an example).*

http://www.ncbi.nlm.nih.gov/pubmed/17911203 **Safety concerns with fluoroquinolones.** "*Gatifloxacin has been shown to increase the risk of hospitalization for dysglycemia in patients with and without diabetes. Hyperglycemia may occur with any fluoroquinolone, especially if not properly dose adjusted. Hypoglycemia may occur with any fluoroquinolone and has a higher frequency in patients receiving concomitant oral hypoglycemic drugs or insulin . . . Clinicians should be aware of possible alterations in blood glucose, QTc interval prolongation, seizures, phototoxicity, tendinopathy, or CDAD with the use of any fluoroquinolone."*

http://www.ncbi.nlm.nih.gov/pubmed/17727838 **Gatifloxacin affects GLUT1 gene expression and disturbs glucose homeostasis in vitro.** "*Gatifloxacin may induce life-threatening dysglycemia. The facilitated glucose transporter type 1 (GLUT1) protein is ubiquitously expressed in many tissues. Disturbed GLUT1 protein function weakens the systemic glycemic control and may cause dysglycemia. In this study we demonstrate that gatifloxacin modulates the transcription and reduces the expression and function of GLUT1 gene in HepG2 cells. When treated with gatifloxacin at concentrations of 3.4 mug/ml (8.4 muM) and 17 mug/ml (42 muM), GLUT1 promoter activity was stimulated by 2.8 and 3.8 folds, GLUT1 mRNA expression was decreased by 41% and 31%, and glucose uptake was decreased by 41% and 52%, respectively. Our findings imply that disturbed GLUT1 gene expression and protein function may underlie the dysglycemic effect of gatifloxacin."*

http://www.ncbi.nlm.nih.gov/pubmed/17270116 **Dysglycemia and fluoroquinolones: are you putting patients at risk?**

http://www.ncbi.nlm.nih.gov/pubmed/17070519 **Gatifloxacin acutely stimulates insulin secretion and chronically suppresses insulin biosynthesis.** *"Gatifloxacin can cause both hypoglycemia and hyperglycemia in both diabetic and non-diabetic patients. Gatifloxacin recently has been reported to stimulate insulin secretion by inhibition of ATP-sensitive K(+) (K(ATP)) channels in pancreatic beta-cells . . . We find that gatifloxacin acutely stimulates insulin secretion from mouse pancreatic islets and that glibenclamide has additive effects on gatifloxacin-induced insulin secretion. On the other hand, gatifloxacin-induced hyperglycemia often takes several days to develop. We also demonstrate that chronic gatifloxacin treatment decreases islet insulin content by inhibiting insulin biosynthesis, which process may be associated with gatifloxacin-induced hyperglycemia. Moreover, discontinuation of gatifloxacin results in improved insulin secretory response. These data clarify the differing mechanisms of gatifloxacin-induced hyper- and hypoglycemia, and suggest that blood glucose levels should be carefully monitored during gatifloxacin administration, especially in elderly patients with renal insufficiency, unrecognized diabetes, or other metabolic disorders. Because the risk of potentially life-threatening dysglycemia is increased during gatifloxacin therapy, these findings have important implications for clinical practice."*

http://www.ncbi.nlm.nih.gov/pubmed/17057046 **Gatifloxacin-induced dysglycemia.** *"Although the mechanism of gatifloxacin-induced hyperglycemia is not known, in vitro studies have found that certain quinolone antimicrobials can lower serum glucose levels by blocking adenosine 5'-triphosphate-dependent potassium channels in the pancreatic beta-cell, stimulating insulin release."*

http://www.ncbi.nlm.nih.gov/pubmed/16795151 **Gatifloxacin and dysglycemia in older adults**.

http://www.nejm.org/doi/full/10.1056/NEJMc066207 **Gatifloxacin and dysglycemia in older adults**.

http://www.ncbi.nlm.nih.gov/pubmed/16510739 **Outpatient gatifloxacin therapy and dysglycemia in older adults**. *"As compared with the use of other broad-spectrum oral antibiotics, including other fluoroquinolones, the use of gatifloxacin among outpatients is associated with an increased risk of in-hospital treatment for both hypoglycemia and hyperglycemia."*

http://www.ncbi.nlm.nih.gov/pubmed/16185173 **A retrospective, comparative evaluation of dysglycemias in hospitalized patients receiving gatifloxacin, levofloxacin, ciprofloxacin, or ceftriaxone**. *"In the 17,108 patients receiving a fluoroquinolone or ceftriaxone, the rate of dysglycemia was greater in those receiving levofloxacin or gatifloxacin than in those receiving ceftriaxone. However, no difference was noted in the rate of glucose abnormalities with levofloxacin versus gatifloxacin. Clinicians should be aware of dysglycemic events that may occur in patients receiving fluoroquinolones, especially in those with diabetes mellitus or those receiving sulfonylureas."*

http://www.ncbi.nlm.nih.gov/pubmed/16185171 **Fluoroquinolone-associated dysglycemias: a tale of two toxicities.**

http://www.ncbi.nlm.nih.gov/pubmed/19073153 **The insulinotropic effect of fluoroquinolones.** *"Antimicrobial fluoroquinolones induce, with strongly varying frequency, life-threatening hypoglycemias, which is explained by their ability to block K(ATP) channels in pancreatic B-cells and thus to initiate insulin secretion . . . In the presence of 10mM glucose all fluoroquinolones which enhanced secretion markedly elevated cytosolic calcium concentration ([Ca(2+)](i)). In the presence of 5mM glucose gatifloxacin and moxifloxacin at 500microM but not at 100microM elevated [Ca(2+)](i). It is concluded that fluoroquinolones in the clinically relevant concentration range are not initiators, but rather enhancers of glucose-induced insulin secretion. The block of K(ATP) channels appears necessary but not sufficient to explain the hypoglycemic effect of fluoroquinolones."*

http://www.ncbi.nlm.nih.gov/pubmed/24947193 **Fluoroquinolone antibiotics and type 2 diabetes mellitus**.

http://www.ncbi.nlm.nih.gov/pubmed/17027138 **Effects of fluoroquinolones on HERG channels and on pancreatic beta-cell ATP-sensitive K+ channels.** *"An inhibition of the cardiac rapid delayed rectifier K(+) current (I(Kr)) and of the ATP-sensitive K(+) (K(ATP)) current seems to be involved in the mechanisms of the cardiotoxic effects and the alterations in glucose homeostasis, respectively, induced by some fluoroquinolones . . . In conclusion, the structural requirements for fluoroquinolones to inhibit I(Kr) currents and K(ATP) currents appear to differ. The amino group at position C(5) seems to be primarily responsible for the strong HERG current blocking property of sparfloxacin. In contrast, for the block of pancreatic beta-cell K(ATP) currents by fluoroquinolones the substituents at positions N(1), C(7) and C(8) all might play a role."*

http://www.ncbi.nlm.nih.gov/pubmed/12759137 **Effects of lomefloxacin and norfloxacin on pancreatic beta-cell ATP-sensitive K(+) channels**.

http://www.ncbi.nlm.nih.gov/pubmed/17026994 **Effect of levofloxacin on serum glucose concentration in rats**. "*Levofloxacin can induce hypoglycemia and hyperglycemia in rats. Levofloxacin can promote histamine release, leading to an increased serum epinephrine concentration and hyperglycemia."*

http://www.ncbi.nlm.nih.gov/pubmed/20674567 **Gatifloxacin-induced histamine release and hyperglycemia in rats.** "In conclusion, gatifloxacin-induced release of histamine can contribute to an increase in the serum epinephrine concentration and hyperglycemia in normal rats. In diabetic rats, lower doses of gatifloxacin can induce hyperglycemia owing to the low level of insulin secretion that they exhibit compared with normal animals."

http://www.ncbi.nlm.nih.gov/pubmed/23358329 **Effects of moxifloxacin on serum glucose concentrations in rats**.

http://www.ncbi.nlm.nih.gov/pubmed/16503322 **Hyperglycemia and gatifloxacin: a case report and summary of current literature.**

http://www.ncbi.nlm.nih.gov/pubmed/18236349 **Fluoroquinolone-induced Achilles tendon rupture**. *"A 72-year-old female dialysis patient with insulin-dependent diabetes mellitus who was under long-term medication with oral prednisolone due to chronic obstructive pulmonary disease was given levofloxacin for one week to treat an acute bronchitis (one 500 mg dose on the first day, 125 mg/day orally from second day onwards) . . . A typical feature of fluoroquinolone-induced tendinopathy (FIT) is a considerable latency period in some cases between the commencement of treatment with a fluoroquinolone and the onset of FIT symptoms. In addition to fluoroquinolone intake, there are three other predisposing risk factors for tendinopathy: age over 60 years, long-term treatment with systemic glucocorticoids, and chronic kidney disease. The patient showed a combination of all the aforementioned risk factors. In patients with these risk factors, especially among people with a combination of said risk factors - which is frequently the case with nephrologic and dialysis patients, especially -, fluoroquinolones should be administered only after critical evaluation and with a dosage that is adapted to renal function."*

http://www.ncbi.nlm.nih.gov/pubmed/10850524 **Effect of multiple-dose gatifloxacin or ciprofloxacin on glucose homeostasis and insulin production in patients with noninsulin-dependent diabetes mellitus maintained with diet and exercise**.

https://www.ncbi.nlm.nih.gov/pubmed/24028371 **Severe hypoglycemia associated with levofloxacin in a healthy older woman.**

http://jamanetwork.com/journals/jama/article-abstract/1737039 **FDA Warning and Study Highlight Fluoroquinolone Risks**. *"Taking fluoroquinolones, a class of antibiotics commonly used to treat pneumonia and urinary tract infections, may cause serious blood glucose fluctuations or permanent nerve damage, according to a new study and warning from the US Food and Drug Administration (FDA). Previous studies have linked the use of fluoroquinolones with an increased risk of tendon rupture or cardiac disturbances in the general population. One drug in this class of medications, gatifloxacin, was pulled from the market in 2006 because it can cause severe fluctuations in blood glucose in patients with and without diabetes. Recently, new data have emerged suggesting blood glucose disturbances may be a class effect, a particular concern for people with diabetes."*

https://www.ncbi.nlm.nih.gov/pubmed/23896743 **Life-threatening metabolic coma caused by levofloxacin**.

https://www.ncbi.nlm.nih.gov/pubmed/26649323 **HERG Protein Plays a Role in Moxifloxacin-Induced Hypoglycemia.** *"The purpose of this study was to investigate the effect of moxifloxacin on HERG channel protein and glucose metabolism . . . The moxifloxacin-induced decrease in blood glucose and increase in insulin secretion occurred via the HERG protein; thus, HERG protein plays a role in insulin secretion. Human ether-a-go-go-related gene (HERG) encodes the HERG ion channel, which is a member of the voltage-dependent potassium channel (Kv) family. HERG mutations reduce the outward flow of potassium during repolarization and elongate the QT interval leading to polymorphic ventricular tachycardia, cardiac syncope, and sudden death. This is known as the long-QT syndrome (LQTS). HERG ion channels are expressed in the human pancreas where it has been shown to negatively regulate insulin secretion and positively regulate glucagon secretion . . . With the widespread clinical use of FQs, dysglycemia has been reported as an adverse effect. . . . gatifloxacin, ofloxacin, and lomefloxacin have been reported to lead to hypoglycemia, whereas ofloxacin and gatifloxacin have been reported to result in hyperglycemia. Although these side effects are rare, they require hospitalization and can endanger the life of a patient; thus, patients taking fluoroquinolones should be monitored for dysglycemia. Some fluoroquinolones cause hypoglycemia by blocking ATP-sensitive potassium channels (K-ATP) in pancreatic β-cells leading to stimulation of insulin secretion. By stimulating histamine secretion, gatifloxacin can indirectly induce adrenaline release and elevate blood sugar levels. Gatifloxacin can also cause vacuolization of islet β-cells leading to a decrease in insulin production and hyperglycemia. K-ATP channels and other ion channels have been found to synergistically regulate insulin secretion; thus, HERG potassium channels and K-ATP channels together may regulate insulin secretion by pancreatic β-cells. Because the ability of moxifloxacin to inhibit HERG channels is unknown, this study explored the effect of moxifloxacin on HERG channel currents and glucose metabolism in mice . . . Fluoroquinolones can block HERG channels and pancreatic β-cell K-ATP channels; however, the structures of the fluoroquinolones that inhibit HERG channels and KATP channels differ. The amino group at position C5 of fluoroquinolones plays a major role in blocking HERG channels, whereas the substituents at positions N1, C7, and C8 of fluoroquinolones are responsible for the inhibition of K-ATP channels . Inhibition of K-ATP channels is required for fluoroquinolone-induced hypoglycemia, but channel inhibition alone does not sufficiently explain this side effect . . . The fluoroquinolone moxifloxacin has been associated with the highest risk of hypoglycemia followed by levofloxacin and ciprofloxacin."*

https://www.ncbi.nlm.nih.gov/pubmed/23358329 **Effects of moxifloxacin on serum glucose concentrations in rats**. *"Abnormalities in serum glucose concentrations are well-documented adverse effects of fluoroquinolones. Previously, enoxacin, lomefloxacin, norfloxacin, ofloxacin, levofloxacin, ciprofloxacin and gatifloxacin have been reported to cause hypoglycemia, and ofloxacin and gatifloxacin have been reported to cause hyperglycemia. It has been thought that gatifloxacin-induced glucose abnormalities are more frequent than those by other fluoroquinolones. Since some fluoroquinolones are known to stimulate the secretion of insulin by blocking the ATP-*

sensitive potassium channels of pancreatic β-cells, it is thought that fluoroquinolone-induced hypoglycemia is caused by an increase in insulin secretion. As for hyperglycemia, it has been reported that, in animal studies, oral administration of gatifloxacin at 270 or 810 mg/kg/d for 1 month caused the vacuolation of pancreatic β-cells. In addition, it has been reported that gatifloxacin can decrease islet insulin content by using isolated pancreatic islets, suggesting that repeated doses of gatifloxacin can reduce serum insulin concentrations by a disorder in pancreatic β-cells. Previously, we reported that a single intravenous injection of gatifloxacin and levofloxacin induced an increase or decrease in serum glucose concentrations that was dose dependent, and that increased release of histamine led to an increase in epinephrine secretion and hyperglycemia. In the present study, we investigated the effect of moxifloxacin on serum glucose concentrations in rats in order to clarify the mechanisms of moxifloxacin-induced abnormalities in serum glucose concentrations . . . Several studies to investigate the mechanism of fluoroquinolone-induced histamine release have been reported previously. Furuhata et al. showed that ciprofloxacin can induce the release of histamine from rat peripheral mast cells in a dose-dependent manner. Mori et al. reported that intravenous injection of levofloxacin and ciprofloxacin produced dose-related elevations in plasma histamine level in anaesthetized dogs and rats, and that, in vitro study, levofloxacin and ciprofloxacin induced non-cytotoxic secretion of histamine from canine or rat skin mast cells in a concentration-dependent manner. In addition, Mori et al. demonstrated that the mechanism of levofloxacin-induced histamine release may be closely linked to activation of pertussis toxin-sensitive G proteins. These findings suggest that moxifloxacin can also cause histamine release from mast cells . . . Following intravenous injection, moxifloxacin is rapidly metabolized to acyl glucuronide and N-sulfate in the liver, unlike gatifloxacin and levofloxacin, which are mainly excreted by the kidneys. It has been reported that the rate of renal excretion of moxifloxacin in unchanged compound is 8.4% of the dose after intravenous injection in rats. These findings suggest that the conjugation of moxifloxacin in the liver may be saturated at a high dose of moxifloxacin, resulting in a decrease in total body clearance. Renal failure has been recognized as one of the risk factors for gatifloxacin-induced dysglycemia because serum concentrations of gatifloxacin were relatively high due to the delayed renal excretion of gatifloxacin. In moxifloxacin, severe hepatic impairment may be a risk factor for moxifloxacin-induced dysglycemia. Diabetes mellitus is also recognized as a risk factor for gatifloxacin-induced hyper- and hypoglycemia because these adverse effects mainly occurred in patients with diabetes mellitus. Previously, we reported that gatifloxacin-induced histamine release and epinephrine secretion were not different between normal and diabetic rats, and that the shortage of insulin secretion can induce hyperglycemia at a lower drug concentration in diabetic rats. On the other hand, intravenous administration of moxifloxacin at 100 mg/kg induced histamine release and epinephrine secretion without affecting serum immunoreactive insulin concentrations. This result suggests that the effect of diabetes mellitus on drug-induced hyperglycemia may be different between gatifloxacin and moxifloxacin. Further investigation will be needed to clarify the effect of diabetes mellitus on moxifloxacin-induced dysglycemia. In conclusion, moxifloxacin can induce histamine release, leading to an increase in serum epinephrine concentrations and hyperglycemia."

Diabetes and Tendon Issues

Incidence and predictors of hospitalization for tendon rupture in type 2 diabetes: the Fremantle diabetes study.
http://www.ncbi.nlm.nih.gov/pubmed/24151882

Thickness of the Supraspinatus and Biceps Tendons in Diabetic Patients
http://care.diabetesjournals.org/content/25/2/408.1.full

Carpal Tunnel May Predict Diabetes http://www.webmd.com/pain-management/carpal-tunnel/news/20060822/carpal-tunnel-predict-diabetes

Musculoskeletal Complications of Diabetes http://eradiology.bidmc.harvard.edu/LearningLab/musculo/chen.pdf (Tendonopathies (tendonitis, tendon rupture and tenosynovitis)

SOME LONG-TERM SEQUELAE OF POORLY CONTROLLED DIABETES THAT ARE FREQUENTLY UNDIAGNOSED, MISDIAGNOSED OR MISTREATED http://ec2-184-73-33-13.compute-1.amazonaws.com/html/diabetes-book.com/wp-content/uploads/2015/01/bernstein.pdf

Painless rupture of the Achilles tendon in a diabetic patient with sensory neuropathy http://onlinelibrary.wiley.com/doi/10.1002/pdi.1043/abstract

Musculoskeletal disorders in diabetes mellitus: an update. http://www.ncbi.nlm.nih.gov/pubmed/15123045

Musculoskeletal manifestations of diabetes mellitus. http://www.ncbi.nlm.nih.gov/pubmed/20469786

Achilles tendons in people with type 2 diabetes show mildly compromised structure: an ultrasound tissue characterisation study. http://www.ncbi.nlm.nih.gov/pubmed/25586910

Evaluation of Achilles tendon thickening in type 2 diabetes mellitus. http://www.ncbi.nlm.nih.gov/pubmed/17318767

Biomechanical Properties of Achilles Tendon in Diabetic vs. Non-diabetic Patients. http://www.ncbi.nlm.nih.gov/pubmed/25918879

Achilles tendons in people with type 2 diabetes show mildly compromised structure: an ultrasound tissue characterisation study. http://www.ncbi.nlm.nih.gov/pubmed/25586910

Diabetes alters mechanical properties and collagen fiber re-alignment in multiple mouse tendons. http://www.ncbi.nlm.nih.gov/pubmed/24833253

Diabetes and rheumatic diseases. http://www.ncbi.nlm.nih.gov/pubmed/19077719

Type 2 diabetes impairs tendon repair after injury in a rat model. http://www.ncbi.nlm.nih.gov/pubmed/23042903

The effect of exercise, thyroid status and insulin-induced hypoglycaemia on the Achilles tendon reflex time in man. http://www.ncbi.nlm.nih.gov/pubmed/7014217