# Evidence Search Service Results of your search request

## The impact of hydroxychloroquine use and impact on atrial fibrillation (AF)

**ID of request:** 23154  
**Date of request:** 11th May, 2020  
**Date of completion:** 26th May, 2020

If you would like to request any articles or any further help, please contact:  Tom Roper at [tom.roper@nhs.net](mailto:tom.roper@nhs.net)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: The impact of hydroxychloroquine use and impact on atrial fibrillation (AF). Tom Roper. (26th May, 2020). BRIGHTON, UK: Brighton and Sussex Library and Knowledge Service.

**Sources searched**  
Cochrane Central Register of Controlled Trials (1)  
EMBASE (84)  
MEDLINE (49)  
NICE Evidence Search (0)  
TRIP Database (0)  
UpToDate (0)

**Date range used** (5 years, 10 years): 2000 onwards   
**Limits used** (gender, article/study type, etc.): English language   
**Search terms and notes** (full search strategy for database searches below):

Relevant natural language and controlled vocabulary terms were selected and combined. Thesaurus terms were adapted for different databases. Final result sets were de-duplicated and reviewed for relevance by the searcher, irrelevant results being discarded.

In view of the small number of results retrieved by combining atrial fibrillation and hydroxychloroquine (MEDLINE=5, EMBASE=25), the search strategy was expanded to include all forms of cardiac arrhythmia.

For more information about the resources please go to: <https://www.bsuh.nhs.uk/library/>.

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### [B. Search History](#SearchHistory)

## A. Original Research

1. **"Off-label" use of hydroxychloroquine, azithromycin, lopinavir-ritonavir and chloroquine in COVID-19: A survey of cardiac adverse drug reactions by the French Network of Pharmacovigilance Centers.**  
   Gérard Alexandre Therapie 2020;:No page numbers.

INTRODUCTIONCOVID-19 is an unprecedented challenge for physicians and scientists. Several publicized drugs are being used with not much evidence of their efficacy such as hydroxychloroquine, azithromycin or lopinavir-ritonavir. Yet, the cardiac safety of these drugs in COVID-19 deserves scrutiny as they are known to foster cardiac adverse ADRs, notably QTc interval prolongation on the electrocardiogram and its arrhythmogenic consequences.METHODSSince March 27th, 2020, the French Pharmacovigilance Network directed all cardiac adverse drug reactions associated with "off-label" use of hydroxychloroquine, azithromycin and lopinavir-ritonavir in COVID-19 to the Nice Regional Center of Pharmacovigilance. Each Regional Center of Pharmacovigilance first assessed causality of drugs. We performed a specific analysis of these cardiac adverse drug reactions amidst an array of risk factors, reassessed the electrocardiograms and estimated their incidence in coronavirus disease 2019.RESULTSIn one month, 120 reports of cardiac adverse drug reactions have been notified, 103 of which associated with hydroxychloroquine alone (86%), or associated with azithromycin (60%). Their estimated incidence is 0.77% to 1.54% of all patients, notwithstanding strong underreporting. Lopinavir-ritonavir came third with 17 reports (14%) and chloroquine fourth with 3 reports (2.5%). There were 8 sudden, unexplained or aborted deaths (7%), 8 ventricular arrhythmias (7%), 90 reports of prolonged QTc (75%) most of them "serious" (64%), 48 of which proved ≥ 500ms, 20 reports of severe conduction disorders (17%) and 5 reports of other cardiac causes (4%). Six reports derived from automedication.DISCUSSION AND CONCLUSION"Off-label" use of treatments in COVID-19 increases the risk of cardiac ADRs, some of them avoidable. Even if these drugs are perceived as familiar, they are used in patients with added risk factors caused by infection. Precautions should be taken to mitigate the risk, even if they will be proven efficacious.

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1. **An algorithm for managing QT prolongation in coronavirus disease 2019 (COVID-19) patients treated with either chloroquine or hydroxychloroquine in conjunction with azithromycin: Possible benefits of intravenous lidocaine**  
   Mitra R.L. HeartRhythm Case Reports 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6981eeb72fda8c2df563f3d126197e27)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=10553c2d7be860dc212b021510bde823)

1. **An evaluation of co-use of chloroquine or hydroxychloroquine plus azithromycin on cardiac outcomes: A pharmacoepidemiological study to inform use during the COVID19 pandemic.**  
   Vouri Scott M. Research in social & administrative pharmacy : RSAP 2020;:No page numbers.

BACKGROUNDChloroquine or hydroxychloroquine (chloroquine) plus azithromycin is considered as therapy for COVID-19. With benefit evaluations underway, safety concerns due to potential additive effects on QTc prolongation should be addressed.OBJECTIVEWe compared risk of cardiac adverse events between combinations of chloroquine and azithromycin and chloroquine and amoxicillin.METHODSWe conducted a retrospective cohort study using the IBM MarketScan Commercial Claims and Medicare Supplemental Databases, 2005-2018. We included autoimmune disease patients aged ≥18 years initiating azithromycin or amoxicillin for ≥5 days during chloroquine treatment. Patients had continuous insurance coverage ≥6 months before combination use until 5 days thereafter or inpatient death. Two outcomes were sudden cardiac arrest/ventricular arrhythmias (SCA/VA) and cardiac symptoms. We followed patients for up to 5 days to estimate hazard ratios (HR). Covariates were adjusted using stabilized inverse probability treatment weighting.RESULTSWe identified two SVC/VA events among >145,000 combination users. The adjusted incidence of cardiac symptoms among azithromycin and amoxicillin users was 276 vs 254 per 10,000 person-years with an adjusted HR of 1.10 (95%CI, 0.62-1.95).CONCLUSIONCombination use of chloroquine and azithromycin at routine doses did not show pronounced increases in arrhythmias in this real-world population, though small sample size and outcome rates limit conclusions.

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1. **Antimalarial use and arrhythmias in COVID-19 and rheumatic patients: a matter of dose and inflammation?**  
   Erre G.L. Annals of the rheumatic diseases 2020;:No page numbers.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=12805e7b43e0e33492aedc572c123949)

1. **Arrhythmic profile and 24-hour QT interval variability in COVID-19 patients treated with Hydroxychloroquine and azithromycin.**  
   Cipriani Alberto International journal of cardiology 2020;:No page numbers.

BACKGROUNDHydroxychloroquine and azithromycin combination therapy is often prescribed for coronavirus disease 2019 (COVID-19). Electrocardiographic (ECG) monitoring is warranted because both medications cause corrected QT-interval (QTc) prolongation. Whether QTc duration significantly varies during the day, potentially requiring multiple ECGs, remains to be established.METHODSWe performed 12‑lead ECGs and 12‑lead 24-h Holter ECG monitoring in all patients aged <80 years admitted to our medical unit for COVID-19, in oral therapy with hydroxychloroquine (200 mg, twice daily) and azithromycin (500 mg, once daily) for at least 3 days. A group of healthy individuals matched for age and sex served as control.RESULTSOut of 126 patients, 22 (median age 64, 82% men) met the inclusion criteria. ECG after therapy showed longer QTc-interval than before therapy (450 vs 426 ms, p = .02). Four patients had a QTc ≥ 480 ms: they showed higher values of aspartate aminotransferase (52 vs 30 U/L, p = .03) and alanine aminotransferase (108 vs 33 U/L, p < .01) compared with those with QTc < 480 ms. At 24-h Holter ECG monitoring, 1 COVID-19 patient and no control had ≥1 run of non-sustained ventricular tachycardia (p = .4). No patients showed "R on T" premature ventricular beats. Analysis of 24-h QTc dynamics revealed that COVID-19 patients had higher QTc values than controls, with no significant hourly variability.CONCLUSIONTherapy with hydroxychloroquine and azithromycin prolongs QTc interval in patients with COVID-19, particularly in those with high levels of transaminases. Because QTc duration remains stable during the 24 h, multiple daily ECG are not recommendable.

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1. **Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State.**  
   Rosenberg Eli S. JAMA 2020;:No page numbers.

ImportanceHydroxychloroquine, with or without azithromycin, has been considered as a possible therapeutic agent for patients with coronavirus disease 2019 (COVID-19). However, there are limited data on efficacy and associated adverse events.ObjectiveTo describe the association between use of hydroxychloroquine, with or without azithromycin, and clinical outcomes among hospital inpatients diagnosed with COVID-19.Design, Setting, and ParticipantsRetrospective multicenter cohort study of patients from a random sample of all admitted patients with laboratory-confirmed COVID-19 in 25 hospitals, representing 88.2% of patients with COVID-19 in the New York metropolitan region. Eligible patients were admitted for at least 24 hours between March 15 and 28, 2020. Medications, preexisting conditions, clinical measures on admission, outcomes, and adverse events were abstracted from medical records. The date of final follow-up was April 24, 2020.ExposuresReceipt of both hydroxychloroquine and azithromycin, hydroxychloroquine alone, azithromycin alone, or neither.Main Outcomes and MeasuresPrimary outcome was in-hospital mortality. Secondary outcomes were cardiac arrest and abnormal electrocardiogram findings (arrhythmia or QT prolongation).ResultsAmong 1438 hospitalized patients with a diagnosis of COVID-19 (858 [59.7%] male, median age, 63 years), those receiving hydroxychloroquine, azithromycin, or both were more likely than those not receiving either drug to have diabetes, respiratory rate >22/min, abnormal chest imaging findings, O2 saturation lower than 90%, and aspartate aminotransferase greater than 40 U/L. Overall in-hospital mortality was 20.3% (95% CI, 18.2%-22.4%). The probability of death for patients receiving hydroxychloroquine + azithromycin was 189/735 (25.7% [95% CI, 22.3%-28.9%]), hydroxychloroquine alone, 54/271 (19.9% [95% CI, 15.2%-24.7%]), azithromycin alone, 21/211 (10.0% [95% CI, 5.9%-14.0%]), and neither drug, 28/221 (12.7% [95% CI, 8.3%-17.1%]). In adjusted Cox proportional hazards models, compared with patients receiving neither drug, there were no significant differences in mortality for patients receiving hydroxychloroquine + azithromycin (HR, 1.35 [95% CI, 0.76-2.40]), hydroxychloroquine alone (HR, 1.08 [95% CI, 0.63-1.85]), or azithromycin alone (HR, 0.56 [95% CI, 0.26-1.21]). In logistic models, compared with patients receiving neither drug cardiac arrest was significantly more likely in patients receiving hydroxychloroquine + azithromycin (adjusted OR, 2.13 [95% CI, 1.12-4.05]), but not hydroxychloroquine alone (adjusted OR, 1.91 [95% CI, 0.96-3.81]) or azithromycin alone (adjusted OR, 0.64 [95% CI, 0.27-1.56]), . In adjusted logistic regression models, there were no significant differences in the relative likelihood of abnormal electrocardiogram findings.Conclusions and RelevanceAmong patients hospitalized in metropolitan New York with COVID-19, treatment with hydroxychloroquine, azithromycin, or both, compared with neither treatment, was not significantly associated with differences in in-hospital mortality. However, the interpretation of these findings may be limited by the observational design.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e097a22eac7e5003d3539ccf469d1b60)

1. **Cardiac safety of off-label COVID-19 drug therapy: a review and proposed monitoring protocol.**  
   Naksuk Niyada European heart journal. Acute cardiovascular care 2020;:2048872620922784.

More than 2,000,000 individuals worldwide have had coronavirus 2019 disease infection (COVID-19), yet there is no effective medical therapy. Multiple off-label and investigational drugs, such as chloroquine and hydroxychloroquine, have gained broad interest due to positive pre-clinical data and are currently used for treatment of COVID-19. However, some of these medications have potential cardiac adverse effects. This is important because up to one-third of patients with COVID-19 have cardiac injury, which can further increase the risk of cardiomyopathy and arrhythmias. Adverse effects of chloroquine and hydroxychloroquine on cardiac function and conduction are broad and can be fatal. Both drugs have an anti-arrhythmic property and are proarrhythmic. The American Heart Association has listed chloroquine and hydroxychloroquine as agents which can cause direct myocardial toxicity. Similarly, other investigational drugs such as favipiravir and lopinavir/ritonavir can prolong QT interval and cause Torsade de Pointes. Many antibiotics commonly used for the treatment of patients with COVID-19, for instance azithromycin, can also prolong QT interval. This review summarizes evidenced-based data regarding potential cardiac adverse effects due to off-label and investigational drugs including chloroquine and hydroxychloroquine, antiviral therapy, monoclonal antibodies, as well as common antibiotics used for the treatment of COVID-19. The article focuses on practical points and offers a point-of-care protocol for providers who are taking care of patients with COVID-19 in an inpatient and outpatient setting. The proposed protocol is taking into consideration that resources during the pandemic are limited.

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1. **Cardiovascular risks of hydroxychloroquine in treatment and prophylaxis of COVID-19 patients: A scientific statement from the Indian Heart Rhythm Society**  
   Kapoor A. Indian Pacing and Electrophysiology Journal 2020;:No page numbers.

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1. **Conduction abnormalities in hydroxychloroquine add on therapy to lopinavir/ritonavir in COVID-19**  
   Chong V.H. Journal of medical virology 2020;:No page numbers.

COVID-19 is a contagious disease caused by Severe Adult Respiratory Syndrome Corona Virus-2 (SARS-CoV-2). Currently the role of HCQ in COVID-19 remains controversial but HCQ continued to be used in the absence of any effective therapy. We showed that cardiac conduction abnormalities were common in patients with HCQ added on to lopinavir/ritonavir. After starting HCQ, there were 5 (45.5%) new events of which four (36.3%) were attributed to HCQ: QTc prolongations in 3 patients with additional development of conduction blocks (fascicular block and right bundle brunch block in one patient respectively) and one patient with bradycardia. All conduction abnormalities settled after discontinuation of HCQ. Therefore monitoring is recommended when considering HCQ in treating patients with COVID-19. This article is protected by copyright. All rights reserved.

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1. **COVID-19 and (hydroxy)chloroquine-Azithromycin combination: Should we take the risk for our patients?**  
   Javelot H. British journal of clinical pharmacology 2020;:No page numbers.

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1. **COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options.**  
   Guzik Tomasz J. Cardiovascular research 2020;:No page numbers.

The novel coronavirus disease (COVID-19) outbreak, caused by SARS-CoV-2, represents the greatest medical challenge in decades. We provide a comprehensive review of the clinical course of COVID-19, its comorbidities, and mechanistic considerations for future therapies. While COVID-19 primarily affects the lungs, causing interstitial pneumonitis and severe acute respiratory distress syndrome (ARDS), it also affects multiple organs, particularly the cardiovascular system. Risk of severe infection and mortality increase with advancing age and male sex. Mortality is increased by comorbidities: cardiovascular disease, hypertension, diabetes, chronic pulmonary disease, and cancer. The most common complications include arrhythmia (atrial fibrillation, ventricular tachyarrhythmia, and ventricular fibrillation), cardiac injury [elevated highly sensitive troponin I (hs-cTnI) and creatine kinase (CK) levels], fulminant myocarditis, heart failure, pulmonary embolism, and disseminated intravascular coagulation (DIC). Mechanistically, SARS-CoV-2, following proteolytic cleavage of its S protein by a serine protease, binds to the transmembrane angiotensin-converting enzyme 2 (ACE2) -a homologue of ACE-to enter type 2 pneumocytes, macrophages, perivascular pericytes, and cardiomyocytes. This may lead to myocardial dysfunction and damage, endothelial dysfunction, microvascular dysfunction, plaque instability, and myocardial infarction (MI). While ACE2 is essential for viral invasion, there is no evidence that ACE inhibitors or angiotensin receptor blockers (ARBs) worsen prognosis. Hence, patients should not discontinue their use. Moreover, renin-angiotensin-aldosterone system (RAAS) inhibitors might be beneficial in COVID-19. Initial immune and inflammatory responses induce a severe cytokine storm [interleukin (IL)-6, IL-7, IL-22, IL-17, etc.] during the rapid progression phase of COVID-19. Early evaluation and continued monitoring of cardiac damage (cTnI and NT-proBNP) and coagulation (D-dimer) after hospitalization may identify patients with cardiac injury and predict COVID-19 complications. Preventive measures (social distancing and social isolation) also increase cardiovascular risk. Cardiovascular considerations of therapies currently used, including remdesivir, chloroquine, hydroxychloroquine, tocilizumab, ribavirin, interferons, and lopinavir/ritonavir, as well as experimental therapies, such as human recombinant ACE2 (rhACE2), are discussed.

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1. **ENHANCED ECG MONITORING OF COVID-19 PATIENTS**  
   Jain S. Heart rhythm 2020;:No page numbers.

BACKGROUND: Many of the drugs being used in the treatment of the ongoing pandemic coronavirus disease 2019 (COVID-19) are associated with QT prolongation. Expert guidance supports ECG monitoring to optimize patient safety. <br/>OBJECTIVE(S): To establish an enhanced process for ECG monitoring of patients being treated for COVID-19. <br/>METHOD(S): We created an SBAR (Situation Background Assessment Recommendation Tool) identifying the indication for ECGs in COVID-19 patients, and tagged these ECGs to ensure prompt over reading and identification of those with QT prolongation (QTc &gt;470 ms for QRS &lt; 120 ms, QTc &gt; 500 ms for QRS &gt; 120 ms). This triggered a phone call from the electrophysiology service to the primary team to provide management guidance and a formal consultation if requested. <br/>RESULT(S): During a 2-week period we reviewed 2006 ECGs, corresponding to 524 unique patients, of whom 103 (19.7%) met SBAR defined criteria for QT prolongation. When compared to those without QT prolongation, these patients were more often in the intensive care unit (58.3% vs 35.4%) and more likely to be intubated (31.1 vs 18.1%). Fifty patients with QT prolongation (48.5%) had electrolyte abnormalities, 98 (95.1%) were on COVID-19 related QT prolonging medications, and 62 (60.2%) were on 1-4 additional non COVID-19 related QT prolonging drugs. Electrophysiology recommendations were given to limit modifiable risk factors. No patient developed torsade de pointes. <br/>CONCLUSION(S): This process functioned efficiently, identified a high percentage of patients with QT prolongation, and led to relevant interventions. Arrhythmias were rare. No patient developed torsade de pointes.<br/>Copyright &#xa9; 2020. Published by Elsevier Inc.

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1. **Guidance on Minimizing Risk of Drug-Induced Ventricular Arrhythmia During Treatment of COVID-19: A Statement from the Canadian Heart Rhythm Society.**  
   Sapp John L. The Canadian journal of cardiology 2020;:No page numbers.

The COVID-19 pandemic has led to efforts at rapid investigation and application of drugs which may improve prognosis but for which safety and efficacy are not yet established. This document attempts to provide reasonable guidance for the use of antimicrobials which have uncertain benefit but may increase risk of QT interval prolongation and ventricular proarrhythmia, notably, chloroquine, hydroxychloroquine, azithromycin, and lopinavir/ritonavir. During the pandemic, efforts to reduce spread and minimize effects on health care resources mandate minimization of unnecessary medical procedures and testing. We recommend that the risk of drug proarrhythmia be minimized by 1) discontinuing unnecessary medications that may also increase the QT interval, 2) identifying outpatients who are likely to be at low risk and do not need further testing (no history of prolonged QT interval, unexplained syncope, or family history of premature sudden cardiac death, no medications that may prolong the QT interval, and/or a previous known normal corrected QT interval [QTc]), and 3) performing baseline testing in hospitalized patients or those who may be at higher risk. If baseline electrocardiographic testing reveals a moderately prolonged QTc, optimization of medications and electrolytes may permit therapy. If the QTc is markedly prolonged, drugs that further prolong it should be avoided, or expert consultation may permit administration with mitigating precautions. These recommendations are made while there are no known effective treatments for COVID-19 and should be revisited when further data on efficacy and safety become available.

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1. **Hydroxychloroquine, Coronavirus Disease 2019, and QT Prolongation**  
   Bonow R.O. JAMA Cardiology 2020;:No page numbers.

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1. **Inpatient use of mobile continuous telemetry for COVID-19 patients treated with hydroxychloroquine and azithromycin**  
   Gabriels J. HeartRhythm Case Reports 2020;:No page numbers.

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1. **Massive nonfatal pediatric ingestion of hydroxychloroquine**  
   Srihari P. Journal of Medical Toxicology 2020;16(2):122-123.

Background: Hydroxychloroquine is a 4-aminoquinoline used to treat malaria and inflammatory diseases. In toxicity, it can cause arrhythmia and cardiovascular collapse. Here we present a massive hydroxychloroquine ingestion in a pediatric patient who survived with early intubation, electrolyte repletion, and high-dose epinephrine and diazepam infusions. <br/>Method(s): This is a single patient chart review. A 15-year-old female presented after an intentional ingestion of approximately 10-11 g of hydroxychloroquine. On arrival to the emergency department (ED), she was awake with vital signs showing heart rate 154 beats perminute and blood pressure (BP) 106/68 mmHg. Shortly after, she became hypotensive to BP 69/39 mmHg. Poison control was contacted. An urgent call back placed by the consulting toxicologist advocated for early and aggressive care. The patient was then intubated and started on high-dose epinephrine and diazepam infusions. Prompt electrolyte repletion was initiated, and she was transferred to the regional children's hospital. <br/>Result(s): Initial ED laboratory studies were significant for potassium 3.0mmol/L (normal 3.4-5.0 mmol/L).After transfer to the pediatric intensive care unit (PICU), repeat labs showed serum hydroxychloroquine level of 13,000 ng/mL (reporting limit &gt; 100 mg) and potassium of 2.8 mmol/L (normal 3.5-5.5 mmol/L). Her electrocardiogram was significant for a QRS of 102ms andQTc of 575ms.Asecond hydroxychloroquine level at 24 hours post-ingestion was 5600 ng/mL. An arterial line was placed for BP monitoring and a central line was placed to continue electrolyte repletion. Twentyfour hours after PICU presentation, her BP began to improve, and her infusions were titrated down and discontinued. On hospital day 3, she was successfully extubated, and at time of discharge, her cardiovascular status was normal, and she made a full recovery. <br/>Conclusion(s): Massive hydroxychloroquine ingestions can be successfully treated with early aggressive supportive care.

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1. **QT Interval Prolongation and Torsade De Pointes in Patients with COVID-19 treated with Hydroxychloroquine/Azithromycin.**  
   Chorin Ehud Heart rhythm 2020;:No page numbers.

BACKGROUNDThere is no known effective therapy for patients with COVID-19. Initial reports suggesting the potential benefit of Hydroxychloroquine/Azithromycin (HY/AZ) have resulted in massive adoption of this combination worldwide. However, while the true efficacy of this regimen is unknown, initial reports have raised concerns regarding the potential risk of QT prolongation and induction of torsade de pointes (TdP).OBJECTIVEto assess the change in QTc interval and arrhythmic events in patients with COVID-19 treated with HY/AZ METHODS: This is a retrospective study of 251 patients from two centers, diagnosed with COVID-19 and treated with HY/AZ. We reviewed ECG tracings from baseline and until 3 days after completion of therapy to determine the progression of QTc and incidence of arrhythmia and mortality.RESULTSQTc prolonged in parallel with increasing drug exposure and incompletely shortened after its completion. Extreme new QTc prolongation to > 500 ms, a known marker of high risk for TdP had developed in 23% of patients. One patient developed polymorphic ventricular tachycardia (VT) suspected as TdP, requiring emergent cardioversion. Seven patients required premature termination of therapy. The baseline QTc of patients exhibiting extreme QTc prolongation was normal.CONCLUSIONThe combination of HY/AZ significantly prolongs the QTc in patients with COVID-19. This prolongation may be responsible for life threating arrhythmia in the form of TdP. This risk mandates careful consideration of HY/AZ therapy in lights of its unproven efficacy. Strict QTc monitoring should be performed if the regimen is given.

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1. **QT prolongation, torsades de pointes and sudden death with short courses of chloroquine or hydroxychloroquine as used in COVID-19: a systematic review.**  
   Jankelson Lior Heart rhythm 2020;:No page numbers.

Chloroquine and hydroxychloroquine are now being widely used as treatments for COVID-19. Both medications prolong the QT interval and accordingly may put patients at increased risk of torsades de pointes and sudden death. Published guidance documents vary in their recommendations for monitoring and managing these potential adverse effects. Accordingly, we set out to conduct a systematic review of the arrhythmogenic effect of short courses of chloroquine or hydroxychloroquine. We searched in MEDLINE and Embase, as well as grey literature up to April 17, 2020, on the risk of QT prolongation, torsades, ventricular arrhythmia, and sudden death with short-term chloroquine and hydroxychloroquine usage. This resulted in 390 unique records, of which fourteen were ultimately selected for qualitative synthesis and which included data on 1515 COVID-19 patients. Approximately 10% of COVID-19 patients treated with these drugs developed QT prolongation. We found evidence of ventricular arrhythmia in two COVID-19 patients out of a group of 28 treated with high-dose chloroquine. A limitation of these results is unclear follow-up and possible publication/reporting bias, but there is compelling evidence that chloroquine and hydroxychloroquine induce significant QT interval prolongation and potentially increase the risk of arrhythmia. Daily ECG monitoring and other risk mitigation strategies should be considered in order to prevent possible harms from what is currently an unproven therapy.

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1. **Recommendations for the measurement of the QT interval during the use of drugs for COVID-19 infection treatment. Updatable in accordance with the availability of new evidence.**  
   Asensio Enrique Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing 2020;:No page numbers.

COVID-19 infection has shown rapid growth worldwide, and different therapies have been proposed for treatment, in particular, the combination of immune response modulating drugs such as chloroquine and hydroxychloroquine (antimalarials) alone or in combination with azithromycin. Although the clinical evidence supporting their use is scarce, the off label use of these drugs has spread very quickly in face of the progression of the epidemic and the high mortality rate in susceptible populations. However, these medications can pathologically prolong the QT interval and lead to malignant ventricular arrhythmias such that organized guidance on QT evaluation and management strategies are important to reduce morbidity associated with the potential large-scale use.

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1. **Response to the editorial "COVID-19 in patients with cardiovascular diseases": Covid-19 treatment with hydroxychloroquine or chloroquine and azithromycin: A potential risk of Torsades de Pointes.**  
   Funck-Brentano Christian Archives of cardiovascular diseases 2020;113(5):367-368.

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1. **Response to: 'Antimalarial use and arrhythmias in COVID-19 and rheumatic patients: a matter of dose and inflammation?' by Erre et al**  
   Graef E.R. Annals of the rheumatic diseases 2020;:No page numbers.

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1. **Review: Hydroxychloroquine and Chloroquine for Treatment of SARS-CoV-2 (COVID-19).**  
   Pastick Katelyn A. Open forum infectious diseases 2020;7(4):ofaa130.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a rapidly emerging viral infection causing coronavirus disease 2019 (COVID-19). Hydroxychloroquine and chloroquine have garnered unprecedented attention as potential therapeutic agents against COVID-19 following several small clinical trials, uncontrolled case series, and public figure endorsements. While there is a growing body of scientific data, there is also concern for harm, particularly QTc prolongation and cardiac arrhythmias. Here, we perform a rapid narrative review and discuss the strengths and limitations of existing in vitro and clinical studies. We call for additional randomized controlled trial evidence prior to the widespread incorporation of hydroxychloroquine and chloroquine into national and international treatment guidelines.

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1. **Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19).**  
   Mercuro Nicholas J. JAMA cardiology 2020;:No page numbers.

ImportanceAdministration of hydroxychloroquine with or without azithromycin for the treatment of coronavirus disease 2019 (COVID-19)-associated pneumonia carries increased risk of corrected QT (QTc) prolongation and cardiac arrhythmias.ObjectiveTo characterize the risk and degree of QT prolongation in patients with COVID-19 in association with their use of hydroxychloroquine with or without concomitant azithromycin.Design, Setting, and ParticipantsThis was a cohort study performed at an academic tertiary care center in Boston, Massachusetts, of patients hospitalized with at least 1 positive COVID-19 nasopharyngeal polymerase chain reaction test result and clinical findings consistent with pneumonia who received at least 1 day of hydroxychloroquine from March 1, 2020, through April 7, 2020.Main Outcomes and MeasuresChange in QT interval after receiving hydroxychloroquine with or without azithromycin; occurrence of other potential adverse drug events.ResultsAmong 90 patients given hydroxychloroquine, 53 received concomitant azithromycin; 44 (48.9%) were female, and the mean (SD) body mass index was 31.5 (6.6). Hypertension (in 48 patients [53.3%]) and diabetes mellitus (in 26 patients [28.9%]) were the most common comorbid conditions. The overall median (interquartile range) baseline QTc was 455 (430-474) milliseconds (hydroxychloroquine, 473 [454-487] milliseconds vs hydroxychloroquine and azithromycin, 442 [427-461] milliseconds; P < .001). Those receiving concomitant azithromycin had a greater median (interquartile range) change in QT interval (23 [10-40] milliseconds) compared with those receiving hydroxychloroquine alone (5.5 [-15.5 to 34.25] milliseconds; P = .03). Seven patients (19%) who received hydroxychloroquine monotherapy developed prolonged QTc of 500 milliseconds or more, and 3 patients (3%) had a change in QTc of 60 milliseconds or more. Of those who received concomitant azithromycin, 11 of 53 (21%) had prolonged QTc of 500 milliseconds or more and 7 of 53 (13 %) had a change in QTc of 60 milliseconds or more. The likelihood of prolonged QTc was greater in those who received concomitant loop diuretics (adjusted odds ratio, 3.38 [95% CI, 1.03-11.08]) or had a baseline QTc of 450 milliseconds or more (adjusted odds ratio, 7.11 [95% CI, 1.75-28.87]). Ten patients had hydroxychloroquine discontinued early because of potential adverse drug events, including intractable nausea, hypoglycemia, and 1 case of torsades de pointes.Conclusions and RelevanceIn this cohort study, patients who received hydroxychloroquine for the treatment of pneumonia associated with COVID-19 were at high risk of QTc prolongation, and concurrent treatment with azithromycin was associated with greater changes in QTc. Clinicians should carefully weigh risks and benefits if considering hydroxychloroquine and azithromycin, with close monitoring of QTc and concomitant medication usage.

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1. **Safety signals for QT prolongation or Torsades de Pointes associated with azithromycin with or without chloroquine or hydroxychloroquine**  
   Sarayani A. Research in social & administrative pharmacy : RSAP 2020;:No page numbers.

BACKGROUND: Combinations of hydroxychloroquine (HCQ) and azithromycin have been promoted as treatments for COVID-19 based on small, uncontrolled clinical trials that have not assessed potential risks. Risks of treatment include QT segment prolongation, Torsades de Pointes (TdP), and death. This comparative pharmacovigilance analysis evaluated the risk of these events. <br/>METHOD(S): Data from the U.S. Food and Drug Administration's Adverse Event Reporting System (FAERS) (&gt;13 million total reports) were used. Queries extracted reports based on exposures of HCQ/chloroquine (CQ) alone, azithromycin alone, HCQ/CQ + azithromycin, amoxicillin alone, HCQ/CQ + amoxicillin alone. Amoxicillin served as a control. Events of interest included death and TdP/QT prolongation as well as accidents/injuries and depression as control events. Proportional Reporting Ratios (PRR) and 95% confidence intervals (CI) were calculated where a lower limit of the of 95% CI (Lower95CI) value of &gt;=2.0 is interpreted as a potential safety signal. <br/>RESULT(S): Lower95CIs for HCQ/CQ alone showed no potential safety signals for TdP/QT prolongation, death, or any of the control events included. The PRRs and 95% CIs for TdP/QT prolongation was 1.43 (1.29-2.59) with HCQ/CQ use alone and 4.10 (3.80-4.42) for azithromycin alone. For the combined HCQ/CQ + azithromycin group, the PRR and 95% CI was 3.77 (1.80-7.87). For the control of amoxicillin, there were no safety signals when used alone or in combination with HCQ/CQ. <br/>CONCLUSION(S): HCQ/CQ use was not associated with a safety signal in this analysis of FAERS data. However, azithromycin used alone was associated with TdP/QT prolongation events and should be used with caution.<br/>Copyright &#xa9; 2020 Elsevier Inc. All rights reserved.

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1. **The Effect of Chloroquine, Hydroxychloroquine and Azithromycin on the Corrected QT Interval in Patients with SARS-CoV-2 Infection**  
   Saleh M. Circulation. Arrhythmia and electrophysiology 2020;:No page numbers.

Background - The novel SARs-CoV-2 coronavirus is responsible for the global COVID-19 pandemic. Small studies have shown a potential benefit of chloroquine/hydroxychloroquine +/- azithromycin for the treatment of COVID-19. Use of these medications alone, or in combination, can lead to a prolongation of the QT interval, possibly increasing the risk of Torsade de pointes (TdP) and sudden cardiac death. Methods - Hospitalized patients treated with chloroquine/hydroxychloroquine +/- azithromycin from March 1st through the 23rd at three hospitals within the Northwell Health system were included in this prospective, observational study. Serial assessments of the QT interval were performed. The primary outcome was QT prolongation resulting in TdP. Secondary outcomes included QT prolongation, the need to prematurely discontinue any of the medications due to QT prolongation and arrhythmogenic death. Results - Two hundred one patients were treated for COVID-19 with chloroquine/hydroxychloroquine. Ten patients (5.0%) received chloroquine, 191 (95.0%) received hydroxychloroquine and 119 (59.2%) also received azithromycin. The primary outcome of TdP was not observed in the entire population. Baseline QTc intervals did not differ between patients treated with chloroquine/hydroxychloroquine (monotherapy group) vs. those treated with combination group (chloroquine/hydroxychloroquine and azithromycin) (440.6 +/- 24.9 ms vs. 439.9 +/- 24.7 ms, p =0.834). The maximum QTc during treatment was significantly longer in the combination group vs the monotherapy group (470.4 +/- 45.0 ms vs. 453.3 +/- 37.0 ms, p = 0.004). Seven patients (3.5%) required discontinuation of these medications due to QTc prolongation. No arrhythmogenic deaths were reported. Conclusions - In the largest reported cohort of COVID-19 patients to date treated with chloroquine/hydroxychloroquine {plus minus} azithromycin, no instances of TdP or arrhythmogenic death were reported. Although use of these medications resulted in QT prolongation, clinicians seldomly needed to discontinue therapy. Further study of the need for QT interval monitoring is needed before final recommendations can be made.

1. **Urgent Guidance for Navigating and Circumventing the QTc-Prolonging and Torsadogenic Potential of Possible Pharmacotherapies for Coronavirus Disease 19 (COVID-19).**  
   Giudicessi John R. Mayo Clinic proceedings 2020;:No page numbers.

As the coronavirus disease 19 (COVID-19) global pandemic rages across the globe, the race to prevent and treat this deadly disease has led to the "off-label" repurposing of drugs such as hydroxychloroquine and lopinavir/ritonavir, which have the potential for unwanted QT-interval prolongation and a risk of drug-induced sudden cardiac death. With the possibility that a considerable proportion of the world's population soon could receive COVID-19 pharmacotherapies with torsadogenic potential for therapy or postexposure prophylaxis, this document serves to help health care professionals mitigate the risk of drug-induced ventricular arrhythmias while minimizing risk of COVID-19 exposure to personnel and conserving the limited supply of personal protective equipment.

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1. **Ventricular arrhythmia risk due to chloroquine / hydroxychloroquine treatment for COVID-19: Should it be given**  
   Malviya A. Indian Heart Journal 2020;:No page numbers.

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1. **718 Hydroxychloroquine and cardiovascular events in patients with morphea: A report from the RADAR (Research on Adverse Drug events And Reports) program**  
   Zhao J. Journal of Investigative Dermatology 2019;139(5):No page numbers.

Hydroxychloroquine (HCQ) is used off-label for morphea, and has been associated with rare yet serious cardiovascular (CV) adverse events. For the first time, we characterize HCQ-associated CV risk (including conduction disorders and ischemic events) in morphea patients. Data from a medical record repository (&lt;6 million patients; Jan 2004 to Nov 2018; aged 18-89 years) were extracted using ICD-9 or 10 codes for those with morphea who had no CV event prior to HCQ exposure and had at least 2 months follow-up after initiation of HCQ. Separate CV risk calculations were performed for morphea patients on HCQ combined with a non-HCQ systemic therapy (methotrexate, prednisone or mycophenolate; N=65) and for those on a non-HCQ systemic therapy (N=431) compared to those morphea patients with no systemic therapy as a control (N=1866). Of 2,398 morphea patients, 38 had HCQ monotherapy (no combined systemic therapy) and were excluded from further analysis as the cohort had no incident CV events. However, patients on HCQ combined therapy had a significantly increased risk for incident CV events (RR: 2.07 CI: 1.33-3.22; p = 0.0013) compared to the control group and there was a significantly increased risk for the non-HCQ systemic therapy cohort compared to control (RR: 1.85 CI: 1.49-2.30; P &lt; 0.0001), with a number needed to harm of 9.86 for non-HCQ systemic therapy versus 7.86 for HCQ in combination with other systemic therapy. Although the findings from this study demonstrate a favorable cardiovascular safety profile for HCQ monotherapy in morphea patients, enhanced monitoring for CV events seems warranted when HCQ is not utilized as monotherapy in the management of morphea.<br/>Copyright &#xa9; 2019

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1. **A Case of Sarcoidosis Presenting as Refractory Arrhythmias: Quieting the Storm**  
   Aurora L. Journal of Cardiac Failure 2019;25(8):No page numbers.

Introduction: Sarcoidosis is a multisystem granulomatous disorder of unknown etiology. Cardiac sarcoidosis can manifest as conduction abnormality, ventricular tachycardia (VT), heart failure or sudden cardiac death. Although well studied in the literature, we present an uncommon case of arrhythmia as a presenting manifestation of this disease. Case: 45-year-old female with no significant past medical history presented with acute onset shortness of breath and palpitations. Initial transthoracic echocardiogram revealed an ejection fraction of 50%. Electrophysiology (EP) study showed a chemically inducible accelerated idioventricular rhythm with right bundle morphology. Left heart catheterization showed angiographically normal vessels and cardiac MRI showed no regional wall motion abnormalities or abnormal delayed enhancement. Patient presented to the hospital again due to recurrence of arrhythmia, found to be VT. Nuclear medicine whole body PET scan showed perfusion defects consistent with cardiac sarcoidosis. A mediastinal lymph node biopsy demonstrated focal non-granulomatous inflammation. Patient was initiated on anti-arrhythmics and underwent a single-chamber ICD placement. She continued to have episodes of wide QRS tachycardia, and was evaluated by Advanced Heart Failure for refractory arrhythmias. Decision-making: Patient was initially managed with Amiodarone and a beta-blocker. Due to unstable VT, she was taken to EP lab where a focal origin of the VT was successfully found in the basal anterolateral endocardial left ventricle and at the base of one of the papillary muscles. Ablations were performed in these areas with reduction in VT rate. Patient was also discovered to have complete atrioventricular block. Subsequently, she developed recurrence of arrhythmia and was admitted again for VT management. Patient was taken back to the EP lab for an endocardial and epicardial ablation. A focal VT source was found in the apical lateral left ventricle. Due to proximity of the phrenic nerve to the site, no ablations were performed. However, due to recurrence of arrhythmia, she was taken back to the lab for a third ablation in the epicardial area with resulting success. Antiarrhythmics were changed to Flecainide which has since suppressed her VT. Patient has been maintained on Methotrexate, Hydroxychloroquine, and Prednisone for continued sarcoid therapy. We are using periodic F-FDG PET imaging to monitor the severity of myocardial inflammation. Based on patient's clinical status and PET imaging, we have determined the time to wean immunosuppressant agents. <br/>Conclusion(s): Cardiac sarcoidosis affects at least 25% of sarcoidosis patients and accounts for substantial mortality and morbidity.Ventricular arrhythmias may be the presenting symptom of cardiac sarcoidosis and are challenging to treat. Risk stratification through proposed techniques such as advanced cardiac imaging and EP studies is integral in this population. Recognition of sarcoidosis as a possible etiology of arrhythmias through integration of clinical and imaging findings can lead to appropriate lifesaving treatments.<br/>Copyright &#xa9; 2019

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1. **Analysis of rituximab off-label use**  
   Gonzalez Vaquero D. European Journal of Hospital Pharmacy 2019;26:No page numbers.

Background Rituximab is a monoclonal antibody indicated in Spain in adults with non-Hodgkin's lymphoma, chronic lymphatic leukaemia, rheumatoid arthritis and granulomatosis with polyangiitis and microscopic polyangiitis. Purpose To evaluate the use of rituximab in a district hospital in off-label conditions which did not respond to corticosteroids or immunosuppressants treatment. Material and methods We carried out a retrospective observational study of the use of rituximab off-label from its inclusion in the pharmacotherapeutic guide of the hospital in 2009 until July 2018. Data collected: number of patients, sex, age, diagnosis, previous treatment with rituximab, concomitant treatment with rituximab, treatment schemes and adverse effects 6 months after the start of treatment. Digital clinical history and external consultations application were used. Statistical analysis was performed with SPSS version 24. Results Number of patients: 21. Sex: 11 (52.4%) males. Mean Age: 53.3 (21-80). Diagnostic groups: six patients (28.6%) developed glomerulonephritis, five (23.8%) lupus, five (23.8%) vasculitis for cryoglobulins and ANCA positive, three (14.3%) myositis and two (9.5%) pemphigus. Treatment prior to rituximab: all patients were treated with prednisone, 11 (52.4%) with mycophenolate mofetil, 10 (47.6%) with azathioprine, 10 (47.6%) with cyclosporine A, six (28.6%) with hydroxychloroquine, three (14.3%) methotrexate, two (9.5%) with tacrolimus, one (4.8%) with immunoglobulins and one (4.8%) with monoclonal antibodies. Concomitant treatment with rituximab: all patients had been treated with prednisone, five (23.8%) with hydroxychloroquine, five (23.8%) with azathioprine, four (19%) with mycophenolate mofetil and two (9.5%) with tacrolimus. Treatment schemes: eight (38.1%) patients received 15 day cycles with a fixed dose of 1000 mg on days 1 and 15. Ten patients (47.6%) with 500 mg weekly for 4 weeks and three patients (14.3%) received doses of 875 mg/m2 weekly for 4 weeks. Adverse reactions: 11 patients (52.4%) developed cytopaenia. The most frequent cytopaenia was anaemia: five patients 45.4%. Seven (33.3%) patients developed pneumonia or sepsis that required hospital admission. A case of atrial fibrillation was recorded. No reactions related to the perfusion of rituximab were recorded. Conclusion The use of rituximab off-label has increased in recent years. It is therefore necessary to develop protocols to unify the criteria for use, evaluating its effectiveness and safety profile to increase the quality of care.

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1. **ANTIMALARIAL AMINOQUINOLINES REDUCE THE BURDEN OF PERSISTENT ATRIAL FIBRILLATION**  
   Chidipi B. Heart Rhythm 2019;16(5):147-148.

Background: In the clinic, reducing the burden of persistent atrial fibrillation (AF) by pharmacological means is challenging. We tested the hypothesis that blocking the background, and the acetylcholine activated inward rectifier potassium currents (IK1, and IKACh) could be used clinically as an anti- persistent AF therapy. <br/>Objective(s): We explored how antimalarial 4-aminoquinolines block IK1, and IKACh, and if this block can decrease the burden of persistent AF Methods: We used conventional and automated patch clamp, as well as molecular modeling of the intracellular domains of Kir3.1 (IKACh molecular correlate) and of Kir2.1 (IK1 molecular correlate) to explore how the aminoquinolines chloroquine, hydroxychloroquine, primaquine and quinidine block IK1 and IKACh. Additionally, we tested, as a proof of concept, if oral chloroquine administration to a patient with persistent AF can decrease the arrhythmia burden, and we simulated the effects of chloroquine on persistent AF in a 3D model of the human atria. <br/>Result(s): Automated and conventional patch clamp showed that chloroquine was a stronger IK1 and IKACh blocker compared to hydroxychloroquine, primaquine and quinidine. Molecular modeling suggested that all aminoquinolines blocked the IK1 and IKACh channels by binding in a distinct pocket in the intracellular domain of Kir2.1 and Kir3.1, respectively. However, the binding orientation differed among the compounds. We investigated in a patient with persistent AF, the effects of chloroquine, the strongest IK1 and IKACh blocker in the group of drugs studied. Oral chloroquine administration for 14 days significantly decreased the burden of persistent AF. The mathematical simulations of persistent AF in a 3D model of human atria suggested that block of IK1 and IKACh prolonged the action potential duration, and increased the wavelength of rotors, leading to failure of reentrant excitation, and the subsequent termination of the arrhythmia. <br/>Conclusion(s): Blocking the IK1 and IKACh intracellular ion permeation pathways can be a therapeutic strategy targeted towards persistent AF. Understanding the structural mechanisms of how small molecules block ion channels can help in the rational design of new, and more effective antiarrhythmics.<br/>Copyright &#xa9; 2019. Published by Elsevier

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1. **Cardiovascular risk of synthetic, non-biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs).**  
   Mourouzis Iordanis S. Current vascular pharmacology 2019;:No page numbers.

Patients with rheumatoid diseases have an increased risk of CVD and CVD-related death compared with the general population. Both the traditional cardiovascular risk factors and systemic inflammation are contributors to this phenomenon. This review examines the available evidence about the effects of synthetic, non-biologic disease-modifying antirheumatic drugs (DMARDs) in CVD risk. This is an important issue for clinicians when deciding on individual treatment plans in patients with rheumatic diseases. Evidence suggests that synthetic, non-biologic DMARDs such as methotrexate, sulfosalazine, hydroxychloroquine, leflunomide and tofacitinib show decreased CVD morbidity and mortality. However, the strongest data in favor of a reduction in CVD events in rheumatoid patients are shown with methotrexate which has been the focus of most studies. Adequate proof for a favourable effect also exists for hydroxychlorokine. Larger, prospective studies and randomized clinical trials are needed to better characterize the effect of synthetic, non-biologic DMARDs on CVD outcomes in these patients. Design of future studies should include areas with lack of evidence, such as the risk for heart failure, arrhythmias and valvular heart disease. The clinically relevant question whether synthetic, non-biologic DMARDs are inferior to biologic DMARDs in terms of CVD outcomes still remains not adequately addressed.

1. **Causes of fetal third-degree atrioventricular block and use of hydroxychloroquine in pregnant women with Ro/La antibodies.**  
   Mollerach F. B Clinical rheumatology 2019;38(8):2211-2217.

INTRODUCTION/OBJECTIVESComplete congenital atrioventricular block (AVB) may be due to cardiac malformations or the presence of maternal antibodies (autoimmune AVB). Our objective was to estimate the prevalence of autoimmune AVB among all AVB in newborns treated at our hospital. Secondly, we estimated the prevalence of AVB among mothers with anti-Ro/La antibodies and examined the relationship of those fetal AVB with mother's use of hydroxychloroquine during pregnancy.METHODSRetrospective cohort in which we reviewed electronic medical records from years 2000 to 2014 of (a) all mothers with children born with third degree AVB and (b) all pregnant women with anti-Ro/La-positive antibodies.RESULTSTwenty-three AVBs were diagnosed. Ten (43.5%, 95% CI 23.2-65.5) were associated with maternal rheumatologic disease. The remaining 13 were associated with cardiac malformations. Sixty-two pregnancies in 47 mothers with Ro/La antibodies were identified; eight (12.9%, 95% CI 5.7-23.8) suffered AVB. Fourteen mothers consumed hydroxychloroquine during full pregnancy (one newborn (7.1%) suffered AVB) and 48 did not (7 newborns with AVB (14.6%); p = 0.5).CONCLUSIONSAll congenital AVB diagnosed at our hospital without cardiac malformations were associated with a maternal rheumatologic disease/antibodies. Therefore, if a AVB is diagnosed in a newborn without structural heart disease, the mother should be studied for an autoimmune disease. We found a high prevalence of AVB among mothers with anti-Ro/La antibodies. Although not statistically significant, AVBs in mothers with Ro/La antibodies were numerically more frequent in those not using hydroxychloroquine.Key Points• Although structural heart malformations were the predominant cause of third-degree AVB, autoimmune AVB was still a significant cause.• The distinction between structural or non-structural cause of AVB constitutes an essential issue since it determines the prognostic of these fetuses in terms of complications.• Although not statistically significant, AVBs in mothers with Ro/La antibodies were more frequent in those not using hydroxychloroquine.• If an AVB is diagnosed in a newborn without structural heart disease, the mother should be studied for an autoimmune disease.

1. **Complete heart block: A rare presentaton in rheumatoid arthrits**  
   Dataprasad G. Indian Journal of Rheumatology 2019;14(6):No page numbers.

Rheumatoid arthrits is a chronic infammatory disease of unknown etology characterized by infammatory polyarthrits with systemic involvement. Cardiac manifestatons involve pericardium, cardiomyopathy and rarely conducton defects. Here we report a rare presentaton of Rheumatoid arthrits as complete heart block which has incidence of &lt;0.1%. Case Report: A 44 year male with no signifcant past and family history presented with syncope, palpitatons and exertonal dyspnea of 1-month duraton. Pain and swelling of multple small joints of hands for 5 months. On examinaton, pulse rate was 35 beats/minute, BP was 110/70 mm of hg, respiratory rate was 16 cycles/minute. No abnormality detected on cardiovascular and respiratory system examinaton. Lef 2nd MCP and PIP joints were swollen and infamed. ECG showed complete heart block. Treated with Hydroxychloroquine, methotrexate and antinfammatory drugs. Permanent pacemaker was inserted and symptoms improved. <br/>Discussion(s): Cardiac manifestatons in Rheumatoid arthrits include cardiomyopathy, pericardial efusion, valvular involvement, coronary artery disease, and conducton defects. Conducton block manifests as RBBB, hemiblocks or AV blocks of variable degree like Complete heart block which is extremely rare. Mechanisms involved are 1) granulomatous invasion and fbrosis of conducton system,2) vasculits of the arterial supply of conducton system,3) hemorrhage into the rheumatoid nodule, 4)infammatory lesion extension from the aortc or mitral valve, 5) amyloid depositon. <br/>Conclusion(s): Rheumatoid arthrits involving the conducton system is atypical presentaton and manifestaton as complete heart block is extremely rare with an incidence of &lt;0.1%. only a few case reports are reported worldwide.

1. **Effect of Hydroxychloroquine on Atrial Fibrillation Recurrence**  
   ClinicalTrials.gov 2019;:NCT03592823.

Atrial fibrillation is the most common arrhythmia in clinic. It can lead to heart failure or stroke, and has a high disability rate and mortality rate. At present, although radiofrequency ablation can cure atrial fibrillation, the success rate is only 50~70%, and has a high recurrence rate. In recent decades, no effective new antiarrhythmic drugs have been introduced, but there are side effects in long‐term application of the existing antiarrhythmic drugs. Therefore, it is urgent to provide new and effective antiarrhythmic drugs. Autophagy level of atrial myocytes in atrial fibrillation patients was significantly higher than that in sinus rhythm. Hydrochloroquine (HCQ) is a hydroxychloroquine sulfate composed of 4‐ amino quinoline compounds. As an effective inhibitor for autophagy, HCQ could effectively prevent the increased autophagy level of atrial myocytes in atrial fibrillation rabbits, prevent atrial effective refractory period (AERP) shortening, and decrease the rate and duration of atrial fibrillation. At present, hydroxychloroquine is mainly used in the treatment of rheumatic immune system diseases and anti malaria. Because of its good safety and small side effects, HCQ has become an indispensable member of drugs in the combined treatment of rheumatoid arthritis and systemic lupus erythematosus patients. In recent years, studies have reported that hydroxychloroquine plays an important role in the prevention and treatment of cardiovascular diseases. Chloroquine could effectively shorten the action potential of atrial myocytes by blocking the inward rectifier potassium ion channel (Kir2.1) and reducing the inward potassium ion current Ik1. HCQ could also reduce 72% (P=0.002), and 70% for the risk of coronary heart disease, stroke, and transient ischemic disease. So the investigators speculate that HCQ may be a potential drug to block the occurrence of acute atrial fibrillation.

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1. **Efficacy of infliximab therapy in cardiac sarcoidosis: A single center case series**  
   Sinokrot O. American Journal of Respiratory and Critical Care Medicine 2019;199(9):No page numbers.

Rationale: Infliximab (IFX), a monoclonal antibody against tumor necrosis factor alpha (TNF-alpha) is used as third-line therapy in recalcitrant severe cardiac and extra-cardiac sarcoidosis. There is very limited literature on the use of IFX in cardiac sarcoidosis, specifically, its efficacy and its safety. <br/>Method(s): We reviewed 5 patients (between January 2016- January 2018) who met criteria for initiation of third line therapy for severe cardiac sarcoidosis. IFX therapy was initiated in these patients due to refractory dysrhythmias, moderate to severe cardiomyopathy, and evidence of persistent FDG uptake on PET, despite standard first- and second-line therapies. We compared the prednisone dose, the ejection fraction (EF), Cardiac MRI and/or PET-FDG changes, as well as arrhythmias before and after IFX therapy. <br/>Result(s): IFX was started in patients who had persistent worsening cardiac function despite the use of high dose steroids as well as a steroid-sparing agent. Second line agents used were methotrexate (4/5) and hydroxychloroquine (1/5). Patients were treated with IFX for a mean of 1.0 +/- 0.5 yrs. The mean daily prednisone dose 6 months after starting IFX was 10.0 +/- 5.0 mg versus 30.0 +/- 15.5 mg at the time of IFX initiation (p=0.002). The mean LVEF was 35.0% +/- 10.5% after IFX therapy versus 25.0% +/- 10.0% prior to therapy (p=0.30). On follow up cardiac PET and MRI scans, the mean cardiac involvement was 28.7% +/- 8.7% following IFX compared to 37.9% +/- 10.7% before infliximab therapy (p=0.001). 1/5 patient developed adverse events. <br/>Conclusion(s): This small case series suggests that IFX therapy is likely an effective third line agent for cardiac sarcoidosis that can lead to improved cardiac function and a reduction in steroid as well as cytotoxic medication doses. IFX therapy should be considered when cardiac sarcoidosis is recalcitrant to traditional first- and second-line therapies. Further randomized trials are needed to develop guidelines on the use and safety of IFX in cardiac sarcoidosis.

1. **Experience with biologic agents for the treatment of cardiac sarcoidosis in a U.S. Academic medical center**  
   Pillarisetty A. Annals of the Rheumatic Diseases 2019;78:1000-1001.

Background: Sarcoidosis is a multisystem granulomatous disease of unclear etiology characterized histologically by non-caseating granulomas. Lungs are the most common organs affected but sarcoidosis can affect almost any organ system. While clinically manifest cardiac involvement occurs in only about 5% of patients with sarcoidosis, a significant proportion have clinically silent disease. Symptomatic cardiac involvement portends a poorer prognosis with manifestations varying from heart failure and conduction abnormalities to ventricular arrhythmias including sudden death. Immunosuppression with corticosteroids and DMARDs such as methotrexate and mycophenolate mofetil has been the mainstay of treatment despite a paucity of data. There is a subset of patients that are either non-responders to these agents or in whom the side effect profile is prohibitive for their long term use. Biologic agents, mainly TNF alpha antagonists, have been used as salvage therapies in these patients. However, the evidence regarding their efficacy and safety is limited to a few case reports. In fact, there remains much apprehension regarding the use of TNF alpha antagonists in patients with systolic heart failure due to concerns that they can exacerbate heart failure. <br/>Objective(s): To study the efficacy and safety of using biologics for the treatment of cardiac sarcoidosis. <br/>Method(s): We conducted a retrospective and prospective observational study of all adult patients with cardiac sarcoidosis treated with biologics at an academic medical center in Washington D.C, USA between 2013 and 2018. <br/>Result(s): We identified 9 patients (3 men and 6 women) diagnosed with cardiac sarcoidosis at our institution. The mean age at diagnosis was 49.9 (SD 8.6). 1 patient was Caucasian and the rest (n=8) were African American. Lungs were the most common extra cardiac organ involved (n=7) followed by CNS (n=4), liver (n=4) and skin (n=3). 5 of the patients presented with systolic heart failure (EF&lt;50%), 3 with atrial and ventricular arrhythmias and 1 was found to have incidental abnormal myocardial uptake on PET imaging. 8 of the 9 patients had abnormal myocardial uptake on PET imaging. All but 1 patient had been initially treated with oral steroids (1 refused) and 7 of the 9 patients had also been given oral DMARDs; methotrexate (n=6), azathioprine (n=2), hydroxychloroquine (n=2) and mycophenolate mofetil (n=1). Biologics used were adalimumab (n=5), infliximab (n=3) and rituximab (n=1). The most common indication for biologics was progression of disease despite optimal doses of standard therapy, followed by intolerance or contraindication to standard therapy. 75% of the patients were noted to have marked clinical improvement with the addition of a biologic. 4 out of 9 patients had decreased myocardial uptake on PET following treatment with a biologic. One patient had no change on PET and 4 have not had repeat imaging done yet. None of the patients had worsening of left ventricular systolic function with the addition of a TNF alpha antagonist. There were no reported major infections or significant adverse events that were attributable to the use of biologics. <br/>Conclusion(s): Based on our small cohort, biologics (mainly TNF alpha antagonists) appear to be safe and efficacious as salvage therapy for cardiac sarcoidosis. However, there is a need for prospective studies to further validate these findings as well as to identify the subset of patients that would benefit from early initiation of these therapies.

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1. **Fetal dysrhythmias.**  
   Carvalho Julene S. Best practice & research. Clinical obstetrics & gynaecology 2019;58:28-41.

Fetal dysrhythmias are common abnormalities, usually manifesting as irregular rhythms. Although most irregularities are benign and caused by isolated atrial ectopics, in a few cases, rhythm irregularity may indicate partial atrioventricular block, which has different etiological and prognostic implications. We provide a flowchart for the initial management of irregular rhythm to help select cases requiring urgent specialist referral. Tachycardias and bradycardias are less frequent, can lead to hemodynamic compromise, and may require in utero therapy. Pharmacological treatment of tachycardia depends on the type (supraventricular tachycardia or atrial flutter) and presence of hydrops, with digoxin, flecainide, and sotalol being commonly used. An ongoing randomized trial may best inform about their efficacy. Bradycardia due to blocked bigeminy normally resolves spontaneously, but if it is due to established complete heart block, there is no effective treatment. Ongoing research suggests hydroxychloroquine may reduce the risk of autoimmune atrioventricular block. Sinus bradycardia (rate <3rd centile) may be a prenatal marker for long-QT syndrome.

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1. **Hypoxia induced supraventricular tachycardia, resolved with continuous positive airway pressure titration**  
   Ramaniuk A. Sleep 2019;42:No page numbers.

Introduction: Arrhythmogenesis in obstructive sleep apnea in a known but under-recognized phenomenon, which may be due to autonomic nervous system imbalance triggered by a combination of apnea and hypoxemia, as well as cardiac remodeling. This case demonstrates a dose-dependent reduction in atrial arrhythmia with increasing continuous positive airway pressure (CPAP) in the setting of moderate sleep apnea, AHI 17.8. Report of Case: A 74-year-old female presents for sleep apnea evaluation. Past history of excessive daytime sleepiness and restless leg syndrome, asthma, hypertension, lupus. Vital signs blood pressure 140/80 saturation, HR72, 94% on room air weight 212 pounds, BMI 42.82 pounds per inches. Cardiovascular exam shows an apical impulse on the left fifth intercostal space midclavicular line, normal rate and rhythm without murmurs no pedal edema. Current medications include hydrochlorothiazide 25 mg, enalapril 10 mg, albuterol HFA, hydroxychloroquine 200 mg. During PSG and CPAP titration, multiple atrial arrhythmias were noted during REM sleep with associated hypoxia. Patient was noted to have a total of 53 desaturation events, with 13 being less than 80%. The lowest SaO2% reached 67.0%. AHI was noted to be 17.8 with resolution to &lt; 5 on 11cm/h20. Mean heart rate during REM elevated to 139 bmp. Following titration of pressures up to 11 cm/H20, not only did the apnea and hypoxia index normalize, the patient no longer experienced episodes of SVT. Unfortunately, after PSG completion, patient ultimately refused to tolerate PAP therapy due to mask intolerance and claustrophobia. <br/>Conclusion(s): Appropriate titration of CPAP not only reduced OH/OA respiratory events and decreased AHI, but increases baseline saturation and normalization of heart rate. This case highlights a possible future clinical patter. Criteria of a successful titration may not be limited to supine AHI reduction, but a more complex evaluation of baseline SaO2 and normalization of heart rate. With more evidence, further assessment and re-evaluation of the gold standard of a successful titration may be warranted. Furthermore, patient compliance with PAP therapy may be emphasized to serve a long term cardio-protective role.

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1. **INFLIXIMAB STABILIZES EJECTION FRACTION AND REDUCES VENTRICULAR TACHYCARDIA IN REFRACTORY CARDIAC SARCOIDOSIS**  
   Kowlgi G.N. Heart Rhythm 2019;16(5):32.

Background: Cardiac sarcoidosis (CS) may cause heart block, ventricular tachycardia (VT) or heart failure. Scarce data exist to guide the use of steroid-sparing agents to treat CS, including infliximab (IFX), a monoclonal antibody against tumor necrosis factor-alpha used in rheumatologic disorders. <br/>Objective(s): We hypothesized that IFX would reduce VT and stabilize left ventricular ejection fraction (LVEF) in patients (pts) with refractory CS. <br/>Method(s): Clinical, imaging, and arrhythmia data were collected on 27 pts with symptomatic CS who failed at least one immunosuppressant and were treated with IFX at 6 international centers. VT was defined as clinical sustained VT or VT requiring defibrillator shock or anti-tachycardia pacing. <br/>Result(s): All pts (n=27) met Heart Rhythm Consensus diagnostic criteria. Median age (interquartile range) was 54 (45-59) years and 70% were male. Pts presented with complete heart block (41%), VT (37%), and premature ventricular contractions (44%). All pts except one were treated initially with steroids and/or steroid-sparing agent (methotrexate 70%; azathioprine 25% or hydroxychloroquine 10%) with median number of failed immunosuppressants prior to IFX = 2. All pts had fluorodeoxyglucose (FDG) uptake on baseline PET. Median duration of IFX therapy was 21 (12.5 - 35.5) months. There was a ten-fold reduction in VT after IFX initiation (37.0% to 3.7%; p=0.03). PET at 25 (14-33) months showed decreased uptake in 74% pts. Median baseline EF was 49 (35-55) vs. 49 (44-55) at follow-up (p=0.49). <br/>Conclusion(s): IFX decreased inflammation on FDG-PET, reduced VT burden and stabilized LVEF in majority of pts with medically-refractory CS. [Figure presented]<br/>Copyright &#xa9; 2019. Published by Elsevier

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1. **Monoclonal gammopathy of clinical significance : about a case of nodular pulmonary amyloidosis**  
   Verstraete G. Clinical Lymphoma, Myeloma and Leukemia 2019;19(10):No page numbers.

Amyloid proteins can infiltrate virtually all organs. Diagnosis is usually difficult owing to its diverse clinical presentation. Involvement of the lung is relatively common, but rarely symptomatic, and most commonly observed in localized (primary) forms of amyloidosis. We report here a case of nodular pulmonary amyloidosis that evolved over a 10-year period. A 61 year-old woman was referred for a suspicion of pulmonary amyloidosis. She has been diagnosed at the age of 30 with rheumatoid arthritis (RA) that required for years, hydroxychloroquine. In 2008, a chest x-ray described lung and pleural calcifications that were attributed to RA. A small IgG lambda monoclonal component was noted in 2013. The patient remained substantially asymptomatic until December 2014, when she developed tachycardia with paroxystic atrial fibrillation. Echocardiography was normal. The association of cardiopulmonary symptoms along with a clinical history of autoimmune disease and the presence of a monoclonal gammopathy raised the suspicion of amyloidosis. Progressively, she presented a worsening of dyspnea (NYHA grade 2). The cardiac work-up failed to identify any abnormality pointing out cardiac amyloidosis with cardiac biomarkers remaining in the normal range. Respiratory function test highlighted a mixed defect along with signs of impaired CO diffusion. The light chain lambda M-component was measured at 40.8 mg/l (N &lt;26.3 mg/l), with a normal kappa/lambda ratio. Multiple myeloma was ruled out. FDG-18 pet-scan confirmed the presence of multiple sub-pleural and parenchymatous hypermetabolic nodules. Biopsies of a sub-pleural nodule and peri-umbilical fat aspiration were not contributive. Transthoracic CT-guided biopsy identified foci of amorphous eosinophilic material, positive for TTF1 and cytokeratine-7 by immunostaining, consistent with the diagnosis of pulmonary nodular amyloidosis, AL lambda subtype. So far, the patient did not receive any specific treatment, as suggested in the literature, and her medical condition remains stable. Standard bortezomib-based chemotherapy will be proposed in case of worsening of her respiratory situation. Nodular pulmonary amyloidosis is an extremely rare condition that can be asymptomatic and misdiagnosed for years. It is usually diagnosed incidentally on chest x-rays. In most cases, it is localized, and association to systemic amyloidosis is uncommon. Differential diagnosis includes primary or metastatic neoplasms and granulomatous diseases. Management depends on the severity of symptoms. Treatment is usually not required. Keywords: amyloidosis MGUS Tracks: Other Plasma Cell Disorders and Amyloidosis<br/>Copyright &#xa9; 2019

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1. **Neonatal autoimmune mediated congenital heart block two case reports**  
   Sfyril K. Journal of Perinatal Medicine 2019;47:No page numbers.

Objective Congenital heart block (CHB) has an incidence of 1/15.000-20.000 births. Maternal risk factors include transplacental transfer of anti-nuclear antibodies to the fetus, metabolic diseases, medications, and viral infections. This transfer, may occur from 11 weeks of gestation, and represents the most common cause, known as autoimmune mediated CHB (ACHB). These autoantibodies attach to and subsequently harm the cardiomyocytes and conduction tissue in susceptible fetuses. We report 2 cases of neonates, who manifested CHB, born to asymptomatic mothers with positive ANA-antibodies. Case 1 A 48-year-old primigravida following IVF was referred to our centre at 20+5 weeks of gestation age (GA), for fetal Echocardiography (ECHO), due to fetal bradycardia, noticed during routine obstetric ultrasound. ECHO findings, included systolic dysfunction of both ventricles, and complete CHB 2:1 with a ventricular rate of 70 bpm. Mother, who had been completely asymptomatic, underwent further work-up which revealed positive anti-SSA but negative anti-SSB antibodies. She was treated with low molecular weight heparin and oral dexamethasone 4mg/day. At 32+2 weeks, Doppler ultrasound revealed absence of end-diastolic flow velocity in the umbilical artery, severe fetal bradycardia, and symmetrical IUGR. A female neonate weighing 1320gr (&lt;2nd centile) was born by Caesarean section (CS), with an Apgar score of 71 and 85. On admission to the NICU the neonate was intubated for respiratory distress. A dose of surfactant was administered and umbilical catheters were placed. The newborn was transferred to the reference center for congenital heart diseases with a heart rate of 65-70 bpm. Case 2 A 40 year old (gravida: 5) was referred to the emergency department of our hospital because of fetal bradycardia (70-80 bpm) diagnosed on obstetric ultrasound at 20 weeks of gestation. She had a medical history of high titers, positive of Anti-ENA(++), Anti-Ro(++), and ANA(++) antibodies, without any clinical symptoms. During pregnancy medications included acetylsalicylic acid, hydroxychloroquine, and prednisolone. Fetal ECHO showed CHB; 2nd degree AV block and aortic stenosis hypoplasia, echogenic intracardiac focus, ventricular septal defect but no evidence of fetal distress. She was followed up by ultrasound scans on a weekly basis for the evaluation of fetal heart rate. At 38+6 weeks of gestation, CS was performed and a male neonate with birth weight of 2610 g (2nd centile), and an Apgar of 81 and 95, was born. At NICU, the newborn was intubated for respiratory distress and showed a heart rate of 50 bpm. Isoprenaline 0.02 g/kg/min was administered via UAC and the newborn was transferred to the reference center for congenital heart diseases for pacemaker placement. Conclusion ACHB is undeniably a severe, potentially life-threatening disorder strictly defined as the presence of 2 key mandatory features (maternal anti-Ro/La auto-antibodies and a diagnosis of AV block in utero or postnatally). This helps differentiate ACHB from other non-autoimmune CHB which consists of different entities with an unknown and probably heterogeneous etiology.

1. **Prenatal diagnosis and management of congenital complete heart block.**  
   Pruetz Jay D. Birth defects research 2019;111(8):380-388.

Congenital complete heart block (CCHB) is a life-threatening medical condition in the unborn fetus with insufficiently validated prenatal interventions. Maternal administration of medications aimed at decreasing the immune response in the fetus and beta-agonists intended to increase fetal cardiac output have shown only marginal benefits. Anti-inflammatory therapies cannot reverse CCHB, but may decrease myocarditis and improve heart function. Advances in prenatal diagnosis and use of strict surveillance protocols for delivery timing have demonstrated small improvements in morbidity and mortality. Ambulatory surveillance programs and wearable fetal heart rate monitors may afford early identification of evolving fetal heart block allowing for emergent treatment. There is also preliminary data suggesting a roll for prevention of CCHB with hydroxychloroquine, but the efficacy and safety is still being studied. To date, intrauterine fetal pacing has not been successful due to the high-risk invasive placement techniques and potential problems with lead dislodgement. The development of a fully implantable micropacemaker via a minimally invasive approach has the potential to pace fetal patients with CCHB and thus delay delivery and allow fetal hydrops to resolve. The challenge remains to establish accepted prenatal interventions capable of successfully managing CCHB in utero until postnatal pacemaker placement is successfully achieved.

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1. **Risk of coronary artery disease and stroke in patients with systemic lupus erythematosus using Japanese health insurance database**  
   Sakai R. Annals of the Rheumatic Diseases 2019;78:1739-1740.

Background: Patients with systemic lupus erythematosus (SLE) have higher risk of coronary artery disease (CAD) and stroke than the general population 1-2. Because these comorbidities influence on patients' vital prognosis and quality of life, it is essential for rheumatologists to manage them appropriately. Considering differences in life style and ethnicity, it is of great interest and needed to investigate risk of these comorbidities in Asia. However, to date, such evidence is scarce. <br/>Objective(s): To estimate incidence rate (IR) and identify risk factors of CAD and stroke in patients with SLE using a Japanese health insurance database. <br/>Method(s): This retrospective longitudinal population-based study was conducted using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan). We defined individuals as SLE cases if they met all of the following: 1) had at least one ICD10 code (M321 or M329); 2) had at least one prescription of oral corticosteroids (CS), methylprednisolone (mPSL) pulse therapy, immunosuppressive drugs (IS) (azathioprine, mizoribine, tacrolimus, mycophenolate mofetil, cyclophosphamide, methotrexate), biologics (belimumab, rituximab) or hydroxychloroquine between April 2008 and July 2017; 3) were 16 years old or over. The start of observation was defined by the first month in which cases met all of the above criteria. Patients were followed until the earliest of date of first CAD event or stroke, date of loss of follow-up, or the end of follow-up (June 2018). CAD and stroke were defined as follows: for CAD, at least one ICD10 code (I20.x or I21.x or I23-24.x) and either percutaneous coronary intervention, coronary artery bypass procedure, or thrombolytic agents during hospitalization: for stroke, at least one ICD10 code (I60-62.x or I63-64.x) and either cerebrovascular procedures, thrombolytic agents, or antiplatelet drugs during hospitalization. Patients were excluded if they had a previous diagnosis of CAD or stroke and were prescribed antiplatelet drugs or anticoagulants during the first 3 months. We defined baseline characteristics using the data from the first 3 months, and calculated IR and adjusted hazard ratio (HR) of risk factors for CAD or stroke after adjusting for baseline characteristics using a Cox proportional hazard model. <br/>Result(s): In this study, 19,138 cases were included. The median age was 53 years and 81.3% were female. Median observation period was 3.1 years. IR [95% CI]/1,000 patient-years (PY) of CAD or stroke was 1.41 [1.11-1.77] and 4.10 [3.56-4.70], respectively. IR of any CAD or stroke was increased age-dependently (2.06 [1.47-2.80] for 16-39 years-old, 5.07 [4.36-5.86] for 40-69, 13.0 [10.9-15.5] for 70-). Adjusted HR [95% CI] was 1.37 [95% CI, 1.27-1.47] for age by decade, 3.34 [1.78-6.28] for CS use, 1.46 [1.16-1.84] for presence of hypertension (HT), 1.38 [1.04-1.85] for diabetes mellitus (DM), 1.73 [1.25-2.38] for chronic kidney disease (CKD), and 1.95 [1.15-3.32] for atrial fibrillation (AF). <br/>Conclusion(s): This is the first study investigating the risk of CAD or stroke in Japanese patients with SLE using a large health insurance database. Older age, use of CS, and presence of HT, DM, CKD, and AF were identified as significant risk factors of these comorbidities.

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1. **The superimposed myocarditis in arrhythmogenic right ventricular cardiomyopathy: The role in the course of the disease and the results of treatment**  
   Yulia Alexandrovna Lutokhina Y.A. European Journal of Heart Failure 2019;21:457.

Purpose: to study the role of myocarditis in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC), and to evaluate the results of its treatment. <br/>Method(s): 54 patients (38.7+/-14.1 y., 42.6% men) with ARVC according to Revised Task Force Criteria 2010 were evaluated (34 patients with defnite, 18-with borderline, 2 with possible diagnosis). Follow-up period 21 [6; 60] months. All patients underwent ECG, 24h-Holter monitoring, echocardiography, DNA-diagnostic, blood tests for detection of anti-heart antibodies (AHA) and DNA of viruses. Also were performed cardiac MRI (n=49), signal-averaged ECG (n=18), endomyocardial biopsy (n= 2), autopsy (n=2). <br/>Result(s): myocarditis was diagnosed in 38 (70.4%) patients, 8 of whom were virus-positive (2 by myocardium, 6 by blood). Immunosuppressive therapy (IST) was conducted in 25 patients and included hydroxychloroquine (n=22, 200 mg/day), steroids (n=7, 16 [8; 24] mg/day), azathioprine (n=2, 150 mg/day). Patients with myocarditis who received and not received IST were compared. Initially, patients receiving IST had a longer term of disease, higher titers of AHA and a larger end diastolic volume of the left ventricle (LV) by MRI. Patients who received IST, had significantly lower mortality in comparison with patients with myocarditis without treatment (4.0 vs 30.8%, p=0.03). Only patients with myocarditis treated with IST demonstrated significant positive dynamics in PVs number (11,7 [2,6; 37] vs 0,8 [0,01; 4.5] thousand/day., p&lt;0.001); nonsustained ventricular tachycardia (VT, 57.9 vs 26.3%, p=0.034); sustained VT (SVT, 31.6 vs 0%, p=0.014); their LV ejection fraction (EF) remained stable (52.1+/-14.8 vs 52.4+/-13.5%, p=0.58). In patients with myocarditis without IST, there was a tendency to EF reduction (64,3+/-8,8 vs 57,2+/-9,4, p=0,058). Comparison of patients with isolated ARVC and ARVC plus myocarditis revealed no differences in structural and functional parameters (severity of arrhythmias, EF of both ventricles, heart chambers size, functional class of CHF, etc.), in the effectiveness of radiofrequency ablation and in the frequency of adverse outcomes. The absence of differences is regarded as the result of effective IST. However, myocarditis was significantly less common in patients with the most typical form of ARVD (SVT without significant CHF; with mutations in the PKP2 gene) than in patients with latent arrhythmic form (without SVT, with mutations in the DSG, SCN5A, FLNC genes) and with biventricular HF (mutations in DSP, DES genes). <br/>Conclusion(s): the frequency of superimposed myocarditis in patients with ARVC exceeds 70%. Myocarditis in ARVC could be primary (including viral) or secondary (autoimmune). Regardless to etiology, myocarditis in ARVC should be actively diagnosed and treated, because patients with myocarditis not receiving IST have significantly worse effectiveness of antiarrhythmic therapy and outcomes in comparison with patients with ARVD and myocarditis, received IST.

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1. **Toxicokinetics of hydroxychloroquine following a massive overdose**  
   de Olano J. American Journal of Emergency Medicine 2019;37(12):2264.

Background: We report a patient with a massive hydroxychloroquine overdose manifested by profound hypokalemia and ventricular dysrhythmias and describe hydroxychloroquine toxicokinetics. Case report: A 20-year-old woman (60 kg) presented 1 h after ingesting 36 g of hydroxychloroquine. Vital signs were: BP, 66 mmHg/palpation; heart rate, 115/min; respirations 18/min; oxygen saturation, 100% on room air. She was immediately given intravenous fluids and intubated. Infusions of diazepam and epinephrine were started. Activated charcoal was administered. Her initial serum potassium of 5.3 mEq/L decreased to 2.1 mEq/L 1 h later. The presenting electrocardiogram (ECG) showed sinus tachycardia at 119 beats/min with a QRS duration of 146 ms, and a QT interval of 400 ms (Bazett's QTc 563 ms). She had four episodes of ventricular tachydysrhythmias requiring cardioversion, electrolyte repletion, and lidocaine infusion. Her blood hydroxychloroquine concentration peaked at 28,000 ng/mL (therapeutic range 500-2000 ng/mL). Serial concentrations demonstrated apparent first-order elimination with a half-life of 11.6 h. She was extubated on hospital day three and had a full recovery. <br/>Conclusion(s): We present a massive hydroxychloroquine overdose treated with early intubation, activated charcoal, epinephrine, high dose diazepam, aggressive electrolyte repletion, and lidocaine. The apparent 11.6 hour half-life of hydroxychloroquine was shorter than previously described.<br/>Copyright &#xa9; 2019 Elsevier Inc.

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1. **10x genomics-based single-cell rna-seq and low input RNA-seq identify a transcriptional landscape supporting interferon in the pathogenesis of autoimmune-associated congenital heart block**  
   Suryawanshi H. Arthritis and Rheumatology 2018;70:1034.

Background/Purpose: Towards understanding the molecular mechanisms that link maternal anti-Ro antibodies to the development of conduction system disease in a second trimester fetus, single cell (scRNA-seq) and bulk RNA-seq were applied to a fetal heart dying with complete congenital heart block (CHB) and a gestational age-matched healthy heart from an elective termination. <br/>Method(s): The CHB heart was obtained from a 20-week fetus identified to have complete block at 19 weeks. The mother (35 y/o Asian with SS on no hydroxychloroquine) declined dexamethasone or IVIG and elected to terminate, thus no exposure to maternal medications confounded interpretation of findings. Both hearts were obtained under identical conditions. Freshly collected single-cell suspensions were generated using a Langendorff preparation with cannulation and perfusion of the aorta with collagenase and trypsin enzymes. Two approaches were taken to mine the transcriptome in the resulting cell suspensions: agnostic evaluation applying 10X Genomics platform-based scRNA-seq and low input RNA-seq of flow sorted cells upon leukocytes (DAPI negative, CD45+) and fibroblasts (DAPI negative, CD45-, podoplanin-positive). <br/>Result(s): For scRNA-seq, we obtained 2,693 and 5,408 high-quality scRNA-seq profiles from the control and CHB hearts, respectively. We applied a graph-based clustering method and identified 13 and 14 major clusters of cells from the control and CHB hearts, respectively, as visualized by t-distributed stochastic neighbor embedding (t-SNE). Differential gene expression analysis guided by established lineage markers revealed four cardiomyocyte clusters (CM1-CM4), three fibroblast clusters (FB1-FB3), endothelial cells (EC), erythroblasts (EB), macrophages (MAC), dendritic cells (DC), Tcells (TC) and B cells (BC). Ranked by abundance, the control heart exhibited CM&gt;FB&gt;EC&gt;MAC&gt;DC&gt;EB, BC, TC; the CHB heart exhibited CM&gt;FB&gt;EC, MAC&gt;TC, BC, EB. The CHB heart also contained natural killer cells (NK) and mast cells (MC, lowest abundance). Given the high abundance of MACs among the immune cells (control:108;CHB:606) and the consistent identification of MACs on histologic analysis of CHB hearts, differential expression analysis demonstrated overexpression of interferon-induced genes (4-fold or greater, i.e. log2(CHB-control)&gt;2) in CHB MACs. In CHB, most cell types expressed high levels of ISG1, IFITM1 and IFITM3, whereas in the control only IFITM3 showed widespread expression. For SIGLEC1, expression was restricted to MACs and was expressed by 18% of CHB MACs and only 6% of control MACs. While the transcriptome using low input RNA-seq of anti-CD45 flow-sorted CHB leukocytes did not allow granular analysis of leukocyte subpopulations, expression of SIGLEC1 and interferon-related genes were increased in CHB versus control. Applying 10X Genomics, proliferating fibroblasts expressed MKI67 and TOP2A in CHB but not control fibroblasts. <br/>Conclusion(s): This unprecedented opportunity to obtain CHB tissue absent any exposure to maternal medications support scRNA-seq's utility to survey landscape and heterogeneity not possible with low input RNA-seq of flow-sorted cells. IFNand SIGLEC1-positive macrophages may contribute to fibrosis.

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1. **A rare case of hydroxychloroquine toxicity successfully treated with intralipid emulsion therapy**  
   Berkel M.V. Critical Care Medicine 2018;46:431.

Learning Objectives: Hydroxychloroquine (HCQ) is a 4-aminoquinolone derivative, used for malaria and inflammatory autoimmune disorders. Through sodium and potassium channel blockade, HCQ toxicity can lead to hypokalemia, QTS and QT prolongation, and torsade de pointes. Additionally vasodilation and negative inotropic effects contribute to hypotension. <br/>Method(s): We present a 46 year old female with a reported ingestion of four 200 mg HCQ tablets, approximately 30 minutes prior to arrival. She had a history of depression, but denied suicidal ideation. Initial vitals included mild hypotension with a blood pressure of 92/63 mmHg, and sinus tachycardia at 103 bpm. A glascow coma score of 15 was maintained throughout her admission. Activated charcoal 50g orally and ondansetron 4mg intravenous (IV) were given shortly after arrival. Approximately 50 minutes after ondansetron administration, frequent episodes of ventricular tachycardia and torsade de pointes were seen, which were successfully terminated with sodium bicarbonate 50mEq IV and magnesium sulfate 4g IV. An electrocardiogram immediately after termination showed a heart rate of 85 bpm with frequent premature ventricular complexes, a corrected QT of 837 msec and a QRS of 92 msec. Hypotension persisted after fluid boluses, therefore intralipid emulsion (ILE) therapy 0.1 ml/kg/hr and midazolam 0.5mg/hr were initiated. These were continued for 12 hours and no additional dysrhythmias were seen. Mild hypokalemia (3.2 mmol/L) was treated and other labs were within normal limits except for serum ethanol of 280 mg/dL; a HCQ level was not obtained. <br/>Result(s): HCQ overdoses are rarely reported but can have serious clinical consequences. This novel case report highlights the unpredictable nature of HCQ toxic ingestions given the severe cardiovascular toxicity seen in this case despite the seemingly small dose ingested. Additionally, a drug interaction with the additive QT prolonging effects of ondansetron may have contributed to ventricular arrhythmias in this case. Cardiovascular benefits with both ILE and high dose benzodiazepines, specifically diazepam, have been previously reported. ILE therapy and midazolam, combined with magnesium and sodium bicarbonate were successful in this case for treating torsade de pointes.

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1. **A rare combination of two genetic cardiomyopathy (arrhythmogenic right ventricular dysplasia and left ventricular noncompaction) and the role of myocarditis in disease progression**  
   Olga Blagova O.V. European Journal of Heart Failure 2018;20:208.

Background: First identified the phenotype of dilated cardiomyopathy (DCM) should be considered as a syndrome that requires expanded nosological diagnosis. Simultaneous presence of sustained ventricular tachycardia (SVT) increases the probability of the genetic nature of the disease. <br/>Purpose(s): to evaluate the features of the clinical picture, laboratory and instrumental diagnostics and the effectiveness of complex treatment in a patient with a high risk of sudden cardiac death. <br/>Method(s): There was a female patient 34 years. From 23 years (after a respiratory infection) - chest pains, shortness of breath. Coronary arteries are intact. In 2013 she survived syncope, in Holter-ECG she had 2048 PVBs / day, episode of SVT (1 minute). MRI was performed, and a cardioverter-defibrillator (ISD) was implanted. Follow up is 50 months. <br/>Result(s): ECG showed the low QRS voltage and negative T waves in leads V2-V6. EchoCG revealed LV EDD 6.2 cm, RV EDD 4.0 cm, LVEF 35%, LV myocardial noncompaction (NCM). Late ventricular potentials were detected. MRI sowed NCM of LV, thickening of the epicardial fat on the anterior wall of the right ventricle (RV), RV EDV 133 ml/m2, EF 41%, LV EDV 115 ml/m2, EF 25%, hypo / dyskinesia of the anterior wall, subepicardial gadolinium enhancement in the early and late phase in the LV, intraventricular septum and the free walls of the RV. The level of all anti-heart antibodies was high (1:160-1:320). The reasons for statement of a possible diagnosis of myocarditis in this case were the connection the onset of symptoms with viral infection, high titers of anti-heart antibodies, early and late subepicardial gadolinium enhancement by MRI. The endomyocardial biopsy of RV was performed: subendocardial lipomatosis (about 10%), separation of myocardium by fibrous septa, lymphocytic infiltrates (more than 14 cells), vasculitis without viral genome. DNA diagnosis revealed a splicing mutation in the gene desmoplakin (DSP). Arrithmogenic right ventricular dysplasia (ARVD), LV NCM and myocarditis were diagnosed. Immunosuppressive therapy (hydroxychloroquine, prednisone, azathioprine) was prescribed, LV EF stabilized at 40%. The appropriate shock of the ICD for VT (HR of 210 / min.) with transformation in ventricular fibrillation was recorded twice. For this reason, sotalol was replaced with amiodarone. <br/>Conclusion(s): In a young patient with arrhythmogenic syncope and DCM syndrome was diagnosed combination of ARVD (3 major and 2 minor criteria, definite diagnosis) and NCM with the biopsy proved virus-negative chronic myocarditis. The DCM as a syndrome can have multiple causes, and the combination of myocarditis and primary cardiomyopathy is not rare. NCM can be observed in patients with typical desmosome proteins mutations. The use of immunosuppressive therapy led to the stabilization of heart failure, however, recurrent ventricular arrhythmias a greater degree determined by the presence of primary cardiomyopathy.

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1. **Association of hydroxychloroquine use and incident atrial fibrillation in rheumatoid arthritis: A retrospective study**  
   Gupta A. Arthritis and Rheumatology 2018;70:2370-2371.

Background/Purpose: Hydroxychloroquine (HCQ) is a derivative of quinidine, a class 1 a anti-arrhythmic agent used to prevent ventricular arrhythmias and recurrent atrial fibrillation (AFib). AFib occurs more commonly in patients with rheumatoid arthritis (RA) compared to the general population. HCQ is commonly used to treat mild RA. This study examines the association of HCQ use and AFib or ventricular arrhythmias in RA. <br/>Method(s): A retrospective cohort of adult RA (ICD10: M05 and M06) patients at a tertiary academic rheumatology practice from Dec 1,2014 to May 30,2017 excluding patients with prevalent AFib was constructed. Patients were categorized as HCQ users versus nonusers. Primary outcome was incident AFib adjudicated by electronic health record (EHR) review and EKG confirmation. AFib events occurring in the first year of observation were considered prevalent AFib to allow for a run-in period and exclude prevalent cases more reliably. Secondary outcome was incident ventricular arrhythmias- a composite of ventricular tachycardia (VT), ventricular fibrillation (VF), torsades and sudden cardiac death (SCD) adjudicated similarly. Multivariate regression analysis was performed to estimate the association between HCQ exposure and development of incident AFib, after adjusting for relevant confounders, including demographics (age, sex, ethnicity), AFib-related co-morbidities (BMI, smoking, alcohol use, chronic obstructive pulmonary disease, obstructive sleep apnea, hypertension, coronary artery disease, heart failure, diabetes, cerebrovascular accident and transient ischemic attack, peripheral vascular disease, thyroid disorder, chronic kidney disease and liver dysfunction), anti-arrhythmic medication use (beta-blockers, calcium channel blockers, flecainide, digoxin, amiodarone), and autoimmune serologies. Sub-group analysis was performed on patients age &gt;65yrs (given higher risk of AFib). <br/>Result(s): Our study included 5697 patients with RA, including 1304 HCQ users. During the observation period, 28 incident AFib events occurred in HCQ users and 54 in non-users. Unadjusted odds ratio (OR) was calculated at 1.76 (95% CI 1.11-2.80, p=0.02), and multivariable logistic regression analysis showed an OR of 2.07 (95% CI 1.30-3.30, p=0.002) for incident AFib. Three incident ventricular arrhythmias occurred in HCQ users and 7 in non-users, all were VT, with OR of 1.44 (95% CI 0.37-5.59, p=0.59). In the age&gt;65 yrs sub-group analysis, OR was 1.99 (95% CI 1.18-3.38, p=0.01). <br/>Conclusion(s): In this exploratory study, HCQ use was associated with a 2 times higher risk of AFib in RA patients. These preliminary results need to be confirmed in larger studies given HCQ's otherwise favorable effect on cardiovascular disease risk profile in multiple previous studies.

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1. **Association of hydroxychloroquine use and incident atrial fibrillation in systemic lupus erythematosus: A retrospective study**  
   Gupta A. Arthritis and Rheumatology 2018;70:2999-3000.

Background/Purpose: Hydroxychloroquine (HCQ) is a derivative of quinidine, a class 1a anti-arrhythmic agent used to prevent ventricular arrhythmias and recurrent atrial fibrillation (AFib). AFib occurs more commonly in patients with systemic lupus erythematosus (SLE) compared to the general population. HCQ is a cornerstone treatment in SLE. This study examines the association of HCQ use and AFib or ventricular arrhythmias in SLE. <br/>Method(s): A retrospective cohort of adult SLE (ICD 10: M32) patients at a tertiary academic rheumatology practice from Dec 1,2014 to May 30,2017 excluding patients with prevalent AFib was constructed. Patients were categorized as HCQ users versus non-users. Primary outcome was incident AFib adjudicated by electronic health record (EHR) review and EKG confirmation. AFib events occurring in the first year of observation were considered prevalent AFib to allow for a run-in period and exclude prevalent cases more reliably. Secondary outcome was incident ventricular arrhythmias- a composite of ventricular tachycardia (VT), ventricular fibrillation (VF), torsades, and sudden cardiac death (SCD) adjudicated similarly. Multivariate regression analysis was performed to estimate the association between HCQ exposure and development of incident AFib, after adjusting for relevant confounders, including demographics (age, sex, ethnicity), AFib-related co-morbidities (BMI, smoking, alcohol use, chronic obstructive pulmonary disease, obstructive sleep apnea, hypertension, coronary artery disease, heart failure, diabetes, cerebrovascular accident and transient ischemic attack, peripheral vascular disease, thyroid disorder, chronic kidney disease and liver dysfunction), anti-arrhythmic medication use (beta-blockers, calcium channel blockers, flecainide, digoxin, amiodarone), and autoimmune serologies. Sub-group analysis was performed on patients age &gt;65yrs (given higher risk of AFib). <br/>Result(s): Our study included 1646 patients with SLE including 754 HCQ users. During the observation period, 5 AFib events occurred in HCQ users and 18 in non-users. Unadjusted odds ratio (OR) was calculated at 0.22 (95% CI 0.08-0.60, p=0.003), and multivariable logistic regression analysis showed an OR of 0.33 (95% CI 0.12-0.91, p=0.03) for incident AFib. Six incident ventricular arrhythmia events (2 VT, 3 torsades, 1 SCD) occurred in HCQ users and 3 (2 VT, 1 SCD) occurred in non-users with OR of 2.49 (95% CI 0.62-9.9, p=0.2). In the age&gt;65 yrs sub-group analysis, OR was 0.4 (95% CI 0.13-1.25, p=0.11). <br/>Conclusion(s): In this exploratory study, HCQ use was associated with a 67% reduced risk of incident AFib in SLE. In light of the cardiovascular risk benefits of HCQ and its close relation to anti-arrhythmic medication quinidine, if our preliminary results are confirmed in larger studies, our findings may be used as rationale for a randomized study of HCQ's protective role against AFib in high-risk patients with SLE. (Table Presented) .

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1. **Autoimmune induced heart block**  
   Kandalaft O. Journal of the American College of Cardiology 2018;71(11):No page numbers.

Background: Rheumatoid arthritis (RA) is a very common autoimmune disease, affecting around 1% of the general population. Although not always clinically apparent, it can manifest in the form of cardiovascular pathology in 50% of affected patients<sup>(1)</sup>. Case: A 67 year old female with a history of mitral regurgitation, aortic stenosis and active RA, on etanercept and hydroxychloroquine, was admitted with chest pain. She was found to be in complete atrioventricular block and had a pacemaker placed. An echocardiogram showed worsened mitral and aortic regurgitation, and both valves were surgically replaced with acquisition of myocardial biopsies. Histological findings showed infltrative rheumatoid nodules within the myocardium, revealing necrobiotic nodules with central fibrinoid degeneration, explaining the patient's rapidly deteriorating condition. Decision-making: Cardiovascular disorders in patient with RA usually present in the form of ischemic heart disease<sup>(1)</sup>; atrioventricular block is exceedingly rare, with 0.1% of patients experiencing this complication. One study describes multiple cases of RA patients presenting with AV blockage, where histopathology showed a "characteristic finding [of a] granuloma in or near the AV node", as well as infltration with histiocytes, similarly to our patient<sup>(2)</sup>. Pathogenesis is described as an extension of the infammatory infltrate, leading to formation of intracardiac rheumatoid nodules that can interfere with the conduction pathway. <br/>Conclusion(s): In our case, the patient's complete heart block was due to the formation of a rheumatoid nodule in the myocardium. Although rare, patients with active, severe RA, who present with acute cardiac decompensation, should be investigated for an intracardiac infltration.

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1. **Cardiac Manifestations in Systemic Lupus Erythematosus: A Case Report and Review of the Literature.**  
   Kreps Alexandra American journal of medical case reports 2018;6(9):180-183.

BackgroundSystemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with a wide range of clinical features and variable clinical course. SLE tends to affect women during childbearing years and is characterized by multi-organ involvement. Cardiac complications in SLE, which have been described to occur in about 50% of the cases, contributes to significant morbidity and mortality in this population. We describe a patient with SLE and established lupus nephritis who subsequently developed cardiac manifestations including valvular abnormalities, arrythmia and end stage heart failure. The clinical features, work up and management will be discussed.Case presentationA 35 year-old African American woman diagnosed with SLE in her twenties presented to our hospital for evaluation of shortness of breath. After SLE diagnosis, the patient had been prescribed hydrochloroquine and low dose steroids for joint and skin manifestations. Four years after initial presentation, she developed biopsy proven lupus nephritis for which standard induction therapy was administered. She was placed on maintenance immunosuppression with stable renal function. On admission, the patient's symptoms included dyspnea on exertion, chest pain, palpitations, and a non-productive cough. Initial evaluation identified atrial fibrillation and new onset of heart failure given elevated brain natriuretic peptide (BNP) levels and left ventricular ejection fraction (EF) of 15% by echocardiogram. Cardiac catheterization revealed global hypokinesis and non-obstructive coronary artery disease (CAD). The patient was deemed not a suitable candidate for cardiac transplant and was offered a life vest as bridging to an implantable cardioverter (ICD). Twenty-four months after discharge, the patient continued to be managed medically and has not had any subsequent hospitalizations.ConclusionCardiac complications, reported in about 50% of SLE patients, are associated with high morbidity and mortality. Pericarditis is the most common, however conduction defects, valvular damage and heart failure are also observed among SLE patients. The pathogenesis of cardiac involvement seems to be multifactorial. The management of heart failure in SLE entails medical therapy and implantable device use. Further research is needed to explore new options to arrest the development and progression of cardiac disease among lupus patients.

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1. **Diffuse alveolar hemorrhage necessitating extracorporeal membrane oxygenation rescue therapy**  
   Beck E. American Journal of Respiratory and Critical Care Medicine 2018;197:No page numbers.

Introduction Pulmonary hemorrhage is a rare and life-threatening complication of systemic lupus erythematosus (SLE). Diffuse alveolar hemorrhage (DAH) in SLE is thought to be secondary to capillaritis and bland hemorrhage and usually responds to high-dose corticosteroids with or without other immunosuppressive agents. Here, we present a case of severe, refractory SLErelated DAH requiring rescue extracorporeal membrane oxygenation (ECMO). Case Presentation A 52 year-old woman with SLE complicated by nephritis was admitted to the ICU for hypoxemic respiratory failure related to hemoptysis necessitating endotracheal intubation and mechanical ventilation. Bronchoscopic findings confirmed DAH. High-dose steroids were added to her regimen of mycophenolate mofetil and hydroxychloroquine. She continued to have progressive hemoptysis with impaired oxygenation and a second bronchoscopy was performed with instillation of topical thrombin and epinephrine into the LUL where active bleeding was previously seen. Hemostasis was confirmed visually. Preparations were made for instituting plasmapheresis given rapid progression of her disease activity in the setting of optimal medical management. Placement of a hemodialysis catheter was complicated by ventricular arrhythmia with cardiac arrest. She underwent CPR with restoration of cardiac function but subsequent hemodynamic collapse and copious bloody secretions with progressive refractory hypoxemia despite FiO<sub>2</sub> 1.0 and PEEP 15 cm H<sub>2</sub>O. The ECMO team was mobilized and VA ECMO was initiated for hemodynamic and respiratory support. While undergoing ECMO, she received cyclophosphamide, plasmapheresis and transfusion support due to oozing from catheter sites while on systemic anticoagulation. Her cardiopulmonary status improved over the following 6 days; ECMO lines were removed and she was extubated on hospital day 7. Her hospital course was prolonged and complicated by progressive renal failure necessitating hemodialysis, GI bleeding, and recurrent episodes of respiratory failure related to recurrent DAH and opportunistic infections. She was discharged to a long term acute facility after 2.5 months. Discussion Pulmonary hemorrhage occurs in 0.5 - 5.4% of lupus patients with a &gt;50% mortality; higher for those requiring mechanical ventilation. First-line treatment involves high doses of corticosteroids followed by a second immunosuppressive agent. Severe, refractory cases may require mechanical ventilation and consideration of plasma exchange or other toxic intensive therapies such as cyclophosphamide or rituximab. Although controversial, ECMO is indicated in potentially reversible severe acute cardiac or respiratory failure unresponsive to conventional therapy. Uncontrolled active bleeding is a relative contraindication due to need for systemic anticoagulation. When instituted in the setting of active hemorrhage, careful attention to and adjustments in anticoagulation may be necessary.

1. **Electrocardiographic disturbances in children with systemic lupus erythematosus**  
   AlTwajery M. International Journal of Pediatrics and Adolescent Medicine 2018;5(4):127-130.

Background: Conduction disturbances other than heart block related to neonatal lupus are rarely explored and reported in children with systemic lupus erythematosus (SLE). <br/>Objective(s): To report the electrocardiographic (ECG) abnormalities in children with SLE and assess whether anti-Ro/SSA antibodies and hydroxychloroquine are associated with the rhythm disturbances. <br/>Method(s): This cross-sectional retrospective study comprised patients with SLE who had regular follow-up in the Pediatric Lupus Clinic at King Faisal Specialist Hospital and Research Center-Riyadh. All enrolled patients were evaluated with regard to demographics, age at disease onset, disease duration, clinical and laboratory variables including autoantibodies, disease activity using SLEDAI disease activity index, and medications. An expert pediatric cardiologist reviewed the ECG findings of all enrolled patients independently without knowing the clinical status of the patients. <br/>Result(s): A total of 41 (35 females, 6 males) unselected patients with SLE with a mean age of 12.8 (2.5) years and mean follow-up duration of 4 (3) years completed the evaluation. The most frequent manifestations were renal disease (65.8%), followed by musculoskeletal (46.3%), hematological (41.5%), and cardiac involvement (19.5%). Thirty-two had active disease (SLEDAI &gt;4), and the mean of SLEDAI was 9.2 (6.2). ECG abnormalities were seen in 12 patients (29.3%); these changes included ST-T changes (9.8%), right bundle branch block (7.3%), 4 prolonged QT interval (9.8%), and low QRS voltage (2.4%). Thirty-seven (90.3%) patients were on hydroxychloroquine, and 9 patients (22%) had positive anti-Ro/SSA antibodies. ECG abnormalities were associated significantly with anti-Ro/SSA antibodies (P &lt;.05) and a low platelet count (P &lt;.5) but had no association with other autoantibodies, hydroxychloroquine, or SLEDAI score. <br/>Conclusion(s): Children with SLE with anti-Ro/SSA antibodies are probably prone to heart conduction abnormalities. However, the heart rate and QT interval were affected by hydroxychloroquine. A larger prospective study is required to allow more definitive conclusions.<br/>Copyright &#xa9; 2018 King Faisal Specialist Hospital & Research Centre (General Organization), Saudi Arabia

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1. **Hydroxychloroquine poisoning and the potential for cardiotoxicity**  
   Kim T. Journal of Medical Toxicology 2018;14(1):32-33.

Background: Current management of hydroxychloroquine overdose ex-trapolates from the existing chloroquine literature given the chemical similarities of the two drugs, as well as from a few sparse case reports. It remains unclear, however, whether hydroxychloroquine causes similar cardiotoxicity as chloroquine in overdose. Research Question: How commonly does hydroxychloroquine poisoning result in QRS and QTc prolongation, arrhythmias, or death? Methods: All hydroxychloroquine cases reported to our regional poison center (RPC) were retrospectively queried over a nine-year period (June 2008-September 2017). All cases with a history of hydroxychloroquine exposure with follow-up were included. Demographic data (age, sex, coingestants, unintentional versus intentional), electrocardiographic results (QRS and QTc intervals), arrhythmias, and deaths were analyzed by two trained and monitored abstractors. <br/>Result(s): A total of 165 hydroxychloroquine cases were identified. Kappa was 1.0. Of these, 81 (49%) were managed at home and 84 (51%) in the emergen-cy department Average age was 29 years (range 9 months-91 years) and 45 patients were &lt;5 years. Majority were female: 118 females (72%) and 47 males (28%). Coingestants were reported in 71 (43%) cases. In 41 (25%) patients, the cause was unintentional and in 115 (70%), intentional. In 9 (5%) patients, the cause was unknown. In 69 of 84 cases seen at a hospital, an EKG was recommended and 58 had EKGs on follow-up. QRS intervals ranged from 66 to 120 ms. A QRS interval greater than 100 ms was recorded in 12 patients (7% of all cases). QTc intervals ranged from 388 to 644 ms. In 12 patients (7% of all cases), a QTc greater than 450 ms, but less than 500 ms was reported. In 13 patients (8% of all cases), a QTc above 500 ms was documented. None developed arrhythmias or died. <br/>Discussion(s): Despite 7-8% of patients having QRS or QTc prolongation, none developed arrhythmias or died. Limitations included reporting bias, missing data, coingestants, and patients lost to follow-up. <br/>Conclusion(s): Hydroxychloroquine may cause EKG abnormalities, and further studies are needed directly comparing hydroxychloroquine to chloro-quine to better understand the development of cardiotoxicity in overdose.

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1. **Long QT syndrome secondary to drug interaction between hydroxychloroquine and amiodarone**  
   Miranda-Aquino T. Revista Mexicana de Cardiologia 2018;29(2):98-101.

A 67-year-old female patient with a diagnosis of heart failure with preserved ejection fraction secondary to severe mitral regurgitation in treatment with metoprolol, spironolactone, and digoxin. She was diagnosed systemic lupus erythematosus (SLE) because of the presence of arthritis, alopecia, thrombocytopenia, direct positive Coombs +++, positive ANAs 1:1,280 and positive lupus anticoagulant. The rheumatology service indicated hydroxychloroquine 200 mg every 24 hours. She presented atrial fibrillation, and amiodarone was initiated. Two weeks later the patient was admitted because of presyncope, electrocardiogram showed sinus bradycardia with long QT interval. A temporary pacemaker was placed, and hydroxychloroquine and amiodarone suspended. Twenty-four hours later, a new electrocardiogram was taken showing pacemaker rhythm with reduction of the QT interval. After 72 hours the temporary pacemaker was removed and on the fifth day the patient was discharged with an electrocardiogram in sinus rhythm with a corrected QT (Bazett) of 456 miliseconds. The hydroxychloroquine was reinitiated following discharge. She presented another episode of atrial fibrillation, and was treated with amiodarone, hydroxychloroquine was suspended previously, and she did not present prolongation of QT interval. The long QT syndrome was present when amiodarone and hydroxychloroquine interacted.<br/>Copyright &#xa9; 2018 Asociacion Nacional de Cardiologos de Mexico. All rights reserved.

1. **Lupus myocarditis presenting as acute cardiogenic shock: A rare presentation**  
   Rathi A. American Journal of Respiratory and Critical Care Medicine 2018;197:No page numbers.

Cardiac manifestations in Systemic lupus erythematosus (SLE) is common and have reported to be higher than 50%. The most common cardiac complications include pericarditis, endocarditis, pulmonary hypertension, and coronary involvement. SLE presenting with overt myocarditis causing cardiogenic shock may be rare however can be fatal.We present a case of a 23 year old female with history of SLE (on prednisone, mycophenolate mofetil (MMF) and plaquenil) and lupus nephritis who presented with complaints of headaches, nausea, vomiting, decreased oral intake and fever. She was noted to be hypotensive and bradycardic on presentation. Initial labs were remarkable for WBC of 12K, SCr of 1.6. C3 and C4 were noted to be low, 22 and 2 respectively. CRP and ESR were elevated. ANA was positive (1:320) and dsDNA was negative. Bedside ECHO revealed biventricular dilatation with severely depressed systolic function. Patient was started on norepinephrine, epinephrine and vasopressin for presumed cardiogenic shock likely from SLE flare. Patient received 3 days of pulse dose steroids followed by maintenance steroid regimen. She was continued on her home regimen of MMF and plaquenil. Repeat ECHO after 3 days showed improvement in LV function and almost normal function of the RV. The patient's kidney and liver function improved with improvement in C3 and C4. Lupus myocarditis is rare, reported in approximately 9% of patients in clinical studies however during post mortem studies subclinical myocarditis was reported to be present in majority of the cases. Most common presenting symptoms are consistent with congestive heart failure, dyspnea, palpitations, non-exertional chest pain and arrhythmia. Lupus Myocarditis presenting with severe Left Ventricular dysfunction is reported in about 2% percent of the cases. Diagnosis is usually based on clinical suspicion and ECHO findings however endomyocardial biopsy remains gold standard despite being invasive. Despite prompt treatment, lupus myocarditis carries varying success rates with mortality upto 8% in first 5 years. (Figure Presented).

1. **Multiple embolic strokes as a result of Libman-Sacks endocarditis associated with lupus and secondary antiphospholipid antibody syndrome: a case report.**  
   Arnautovic Jelena Z. European heart journal. Case reports 2018;2(3):yty094.

BackgroundLibman-Sacks endocarditis (LSE) is an infrequently recognized pathogenesis of embolic cerebrovascular disease. Patients often have asymptomatic valvular dysfunction which if not recognized promptly, can lead to serious complications such as heart failure, arrhythmias, cerebroembolic phenomena with increased neurocognitive disability, and even death. It can be associated with systemic lupus erythematosus and/or antiphospholipid antibody syndrome (APLS).Case summaryPreviously very healthy and active, 49-year-old Caucasian female with past medical history of mild lupus, for which she stopped treatment 10 year ago, saw a primary care physician complaining of intermittent double vision of 2 months duration. Urgent brain magnetic resonance imaging revealed multiple embolic infarcts of the brain stem. Further comprehensive work-up led to diagnosis of mitral LSE and APLS. After 2 months of systemic anticoagulation with warfarin and immunosuppressive therapy with hydroxychloroquine sulfate, repeat imaging demonstrated resolution of the mitral valve vegetation with no clinical recurrence of thromboembolic events at 6 months.DiscussionMild, often silent, autoimmune disease as described in our case can lead to significant cerebrovascular disease. Patients who present with cryptogenic strokes with high suspicion of underlying autoimmune disease should be worked up thoroughly for possible valvular heart disease associated with lupus, APLS, or both. Acquisition of transoesophageal images proved superior to transthoracic approach and it should be implemented in these subsets of patients. With this case report, we highlight the importance of early recognition of cardiac manifestations, amelioration of risk factors, as well as close follow-up of lupus or APLS patients, as crucial steps in reducing their morbidity and mortality along with preventing recurrence or progression of cerebrovascular disease.

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1. **Myocarditis in a patient with nephrotic syndrome**  
   Finet F. Acta Clinica Belgica: International Journal of Clinical and Laboratory Medicine 2018;73:28-29.

Introduction: Although pericarditis is the most frequent manifestation of systemic lupus erythematosus (SLE), all other cardiac structures may be involved. We report the case of a young woman who developed myocarditis as the first sign of SLE. Case report: A 31-year-old woman was admitted in the intensive care unit for the management of hypoxic hepatitis revealing acute heart failure (HF) that required vasopressor and inotropic support. The occurrence of lymphocytic exsudative ascites, thrombocytopenia and acute kidney injury associated with impure nephrotic syndrome (microscopic hematuria) raised the possibility of a systemic disease. The patient also described polyarthralgia, photosensitivity, oral ulcers and Raynaud's phenomenon evolving for several weeks. She complained of diplopia explained by vertical gaze palsy of vascular origin, and also presented paralysis of the right external popliteal sciatic nerve. Further laboratory analysis showed decreased C3 and C4 complement and the presence of antinuclear antibodies (titer: 1/640) with anti-DNA and anti-SSA, leading to the diagnosis of SLE. Cardiac initial work-up showed slightly elevated troponins levels (1.67 ng/ml) contrasting with severe and diffuse impairment of left ventricular systolic function associated with moderate mitral regurgitation and pulmonary arterial hypertension on transthoracic echocardiography. Renal biopsy was performed and showed mixed proliferative and membranous (class III and V) lupus nephritis (LN). Secondary antiphospholipid syndrome and cryoglobulinemia were ruled out. According to the Euro-Lupus protocol, high-dose methylprednisolone and cyclophosphamide were administrated followed by maintenance with azathioprine, low-dose corticosteroids and hydroxychloroquine. At 6 months of follow-up, complete remission of LN, normalization of the left ventricular systolic function, and regression of signs of HF and neurologic symptoms were noted. <br/>Conclusion(s): Myocarditis can be the inaugural sign of SLE in more than half of patients and requires urgent clinical attention because of the risk of arrhythmias, dilated cardiomyopathy and HF. Diagnosis relies on high troponins levels (observed in some but not all patients with myocarditis), abnormalities on echocardiography and cardiac magnetic resonance imaging, endomyocardial biopsy being not routinely used. The prevalence of lupus myocarditis is estimated to be about 9%. Treatment includes high-dose corticosteroids with or without other immunosuppressive agents in addition to standard cardiac management. Despite severe initial presentation of LM, cardiac recovery generally remains good.

1. **Plasma exchange for patients with arrhythmias and dilated cardiomyopathy due to myocarditis**  
   Kulikova V. Journal of Clinical Apheresis 2018;33(2):157-158.

Purpose We report the clinical efficiency of plasma exchange (PE) in patients with arrhythmias and inflammatory dilated cardiomyopathy (iDCM) due to myocarditis. It was used either with immunosuppression drugs or without them Methods 20 patients (15 female, mean age 61,5+/-10,1 years) with arrhythmias (premature atrial contractions (PACs) (n=3), premature ventricular contractions (PVCs) (n=8) both more than 3000 per day and atrial fibrillation (AF) (n=9)) resistant to antiarrhythmic drugs (AADs) and 11 patients with iDCM (10 male, mean age 43,7+/-12,3 years, left ventricular end-diastolic diameter (LVEDD) 6,5+/- 0,6 cm, left ventricular end-diastolic volume (LVEDV) 188,5+/-31,0 ml, left ventricular ejection fraction (LVEF) 31,9+/-7,8%, NYHA functional class 3 [2;3]) underwent a single volume PE filled with 0.9% sodium chloride. All the patients had a high prevalence of at least two auto-antibodies (AABs) directed against cardiac nuclear antigens, endothelial, cardiomyocytes, conduction and smooth muscle cells. Patients underwent evaluation including heart CT scan, MRI, endomyocardial biopsy (EMB), myocardial perfusion scan, and coronary angiography to diagnose myocarditis. Clinical and echocardiographic parameters of iDCM patients were assessed at baseline, with a 4.6+/-2.5 month follow-up. We also evaluated a 6-minute walk test (6MWT) distance and AABs level at baseline and a 6.0+/-1.0 and 5.5+/-2.0 month follow-up respectively. Patients with arrhythmias underwent clinical evaluation and Holter monitoring at baseline, with a 6.9+/-1.3 month and 13.6+/-3.3 month follow-up. 8 patients with arrhythmias and 3 iDCM patients were treated by immunosuppressive drugs (hydroxychloroquine, azathioprine or methylprednisolone) before PE. 12 patients with arrhythmias and 6 iDCM patients got it after PE. The mean dose of methylprednisolone was 8 [4; 16]/8 [8; 17.25] mg per day in each group Results AABs level significantly decreased just after PE and during the follow-up in both groups (p&lt;0.05). 8 iDCM patients had significant improvement in LVEF (31.9+/-7.8% vs. 40.0+/-7.9%) (p&lt;0.05), left atrial volume (109.3+/-38.1 vs. 87.9+/-24.3 ml (p&lt;0.05), 6MWT distance (423.5+/-49.7 vs. 507.5+/-81.9 m) (p&lt;0.05), LVEDV (188.5+/-31.0 vs. 174.7+/-29.2 ml), LVEDD (6.5+/-0.6 vs. 6.3+/-0.5 cm). 5 patients with absolute LVEF improvement &gt;10% were classified as responders. 3 iDCM non-responder patients were characterized by lower QRS voltage (correlation ratio 0.54, p=0.085). One of them underwent heart transplantation. 55% (n=11) patients with arrhythmias were classified as responders. They achieved a decrease of PAVs and PVCs or AF frequency&gt;75% relative to baseline. In five patients ineffective AADs have become effective again. AADs were.

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1. **Pulmonary embolism at patient taking NOACs for atrial fibrillation: Why anticoagulation therapy was not rather effective?**  
   Gulnoza Dussekeyeva G. European Journal of Heart Failure 2018;20:539.

82-year-old male was consulted to the cardiology because of clinics of heart failure (severe symmetric edema on the legs, dyspnea). He had history of hypertension, permanent atrial fibrillation for more than 10 years. Coronary angiography 1 year ago showed no significant stenosis of coronary arteries. He was using rivaroxaban 20 mg daily for prevention of thromboembolism regularly for 6 months. On clinical examination, percussion sound was blunted on right lung upper lobe from third to fifth ribs, vesicular breathing on this side was weaken. He was admitted chest-X-ray. Chest-X-ray showed peripheral wedge of airspace opacity and right lung upper lobe infarction. Patient's hemodynamics was stable. Probability of pulmonary embolism was estimated by Wells criteria and Geneva score. It was moderate, that is why we analyzed D-dimer. The indicator was upgraded. After that we multidetector computed tomography (MDCT) was made. MDCT showed thromboembolism of sub segmental branch of right pulmonary artery with right lung upper lobe infarction. Pulmonary embolism was verified and patient was given rivaroxaban dosage regimen using in the case of pulmonary embolism (15 mg 2 times a day 3 weeks, then 20 mg for this patient permanently).We investigated is there any other factors predisposing pulmonary embolism in the case of this patient, expect of atrial fibrillation. We find that this patient has thrombocytopenia, higher level of lupus anticoagulant and positive antiphospholipid antibodies. Antiphospholipid syndrome was diagnosed and patient was admitted specific therapy (Hydroxychloroquine 200 mg per day).

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1. **Two case reports of neonatal autoantibody-associated congenital heart block.**  
   Li Xiaoxia Medicine 2018;97(45):e13185.

RATIONALENeonatal lupus erythematosus (NLE) is an infrequent disease caused by transplacental maternal autoantibodies. The most common effects of NLE include cutaneous involvement and congenital heart block (CHB), although it might involve multiple organs, such as the liver, lungs, blood, and nervous or digestive systems. Izmirly PM1 and Tonello et al recently reported cutaneous manifestations of neonatal lupus and risk of subsequent CHB. The most serious complication of NLE is complete atrioventricular (AV) block.PATIENT CONCERNSWe experienced 2 cases of NLE that were diagnosed in the past year in our Neonatal Intensive Care Unit. These cases showed 2 different clinical spectrums (CHB, multisystemic effects). One case was a 32-week pregnant woman with combined liver damage and fever, and her fetus was premature due to bradycardia and pericardial effusion. The second case was a young pregnant woman who had systemic lupus erythematosus for 2 years and had been taking methylprednisolone and hydroxychloroquine for a long time since her illness. When prenatal testing at 28 weeks of pregnancy showed that the fetus had CHB, the mother began taking dexamethasone.DIAGNOSISThe first case was diagnosed as NLE with CHB after birth, while the second was diagnosed as NLE with CHB, ductus arteriosus, and atrial septal defect when she was born at 34 weeks.INTERVENTIONSBoth of 2 cases were treated with steroids, intravenous immunoglobulin, and a diuretic. But the second case was treated with isoprenaline in addition to the above.OUTCOMESBoth of the infants was followed up and found to be clinically normal. During the clinic follow-up of the first case, the 8-month-old infant was still asymptomatic with normal growth and development. Her heart rate fluctuated from 40 to 90 beats/minute.LESSONSAutoimmune CHB is a severe, potentially life-threatening disorder associated with passive transfer of maternal anti-Sjogren's syndrome A/Ro and anti-Sjogren's syndrome B/La autoantibodies. Mothers who are positive for these autoantibodies are recommended to have serial echocardiography and obstetric ultrasonography from the early second trimester. Newborns should be delivered at an early stage of gestation if there is evidence of pericardial effusion, ascites, increasing ventricular ectopy, reduced ventricular shortening fraction, or AV valve regurgitation. Aggressive medical management after birth should be coupled with pacemaker implantation in infants who do not respond to medical therapies alone.

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1. **'Too young to have a broken heart': Spontaneous coronary artery dissection causing st elevation myocardial infarction in a young adult**  
   Tiongson M.D.A. Journal of the Hong Kong College of Cardiology 2017;25(1):35.

Synopsis: ST-elevation myocardial infarction (STEMI) rarely occurs among patients 18 to 34 years old. Spontaneous coronary artery dissection (SCAD) is a rare cause of STEMI and is frequently described among patients in peripartum period. SCAD has a high mortality rate if not recognized and treated immediately. We present a case of SCAD presenting as STEMI in a 19-year-old nonpregnant patient. Case: A 19-year-old female with chronic kidney disease, complained of sudden onset substernal chest pain. Physical examination showed a BP of 140/90 mmHg, HR of 112 bpm, with note of rales, pedal edema, and cold clammy extremities. Electrocardiogram showed ST-elevation in leads V3 to V6. Cardiac troponin was elevated and echocardiography revealed left ventricular segmental hypokinesia and depressed systolic function. Patient was diagnosed with acute anterolateral wall STEMI. Coronary angiogram revealed total occlusion of the mid-segment of the left anterior descending artery (LAD), while the rest of the coronary arteries were strikingly normal. After initial balloon angioplasty and stenting of the mid LAD, coronary artery dissection was noted at the distal LAD. A stent was successfully deployed, achieving TIMI flow grade III with no residual stenosis. She remained stable and was discharged improved. of renal vein thrombosis. Despite the resistance of an IgM nephropathy to steroids, the patient responded well to Hydrocortisone and was later shifted to oral Prednisone. The nephrotic syndrome and the activity of SLE were successfully treated with Enalapril and Atorvastatin; and Hydrochloroquine and Prednisone, respectively. The presence of renal vein thrombosis warrants vigilant search for underlying complicated diseases, which greatly affects treatment strategies. <br/>Discussion(s): STEMI rarely happens in the young adults. Moreover, literature highlights the rarity of STEMI caused by SCAD. SCAD usually occurs among young pregnant patients without risk factors for atherosclerosis. We highlighted the significance of suspecting SCAD among young patients who present with STEMI and prompt treatment with revascularization in clinical situations such as this case. <br/>Conclusion(s): SCAD remains to be a rare cause of STEMI. However, SCAD should be considered among young individuals with STEMI. Treatment is primarily medical unless there is persistent chest pain and/or ischemic ECG changes, hemodynamic instability, or unstable arrhythmia, where revascularization is necessary.

1. **Electrocardiogram abnormalities related to antimalarials in SLE**  
   McGhie T. Journal of Rheumatology 2017;44(6):902.

Objectives: Antimalarial drugs, hydroxychloroquine (HCQ) and chloroquine CQ) are routinely used in the treatment of systemic lupus erythematosus SLE) for a myriad of benefits. Cardiotoxicity is a rare but serious complication of antimalarials with several case reports documenting potential conduction disturbances and chamber enlargement on electrocardiogram ECG). Our objective was to study whether treatment with antimalarials is associated with ECG abnormalities in patients with SLE. <br/>Method(s): We studied prospectively collected data from the University of Toronto Lupus Cohort. Patients' 1st routine 12-lead resting supine ECG was analyzed using the Minnesota Code by a single cardiologist blinded to identifying data. Demographics, disease activity, damage, medications and laboratory data were assessed. For the purpose of this study, structural ECG abnormalities were defined as: left ventricular hypertrophy (LVH) or atrial enlargement; conduction ECG abnormalities were defined as: arrhythmias including prolonged QTc, left bundle branch block (LBBB) and right bundle branch block (RBBB). First, normal and abnormal ECG patients were identified and described, associations between cumulative antimalarial doses and ECG abnormalities (structural or conduction) were assessed using logistic regression analysis after adjusting for baseline patient characteristics. Second, a nested case control study (1:3 matching) based on gender, ECG testing years, SLE duration at ECG, and hypertension was conducted. <br/>Result(s): For the 453 patients included in the analysis, 393 patients were treated with antimalarial. Mean age at ECG was 49.2 +/- 13.7 years, SLE duration at ECG was 19.7 +/- 10.4 years and the median cumulative antimalarial dose was 1048 grams before ECG. 58 (12.8%) showed structural abnormalities, 71 (15.7%) conduction abnormalities and 118 (26.0%) structural or conduction abnormalities. The multivariable analysis found the following statistically significant (p &lt; 0.05) predictors of structural ECG abnormalities: SLE duration at ECG (OR: 1.04 95% CI: 1.01-1.07), hypertension before ECG (OR: 2.92 95% CI: 1.32-6.48); and cumulative antimalarial dose higher than median dose prior to ECG (OR: 2.08 95% CI: 1.12-3.87). SLE duration (OR: 1.04 95% CI: 1.01-1.08) and hypertension OR: 9.17 95% CI: 1.16-72.29) predicted ECG conduction abnormalities. There was no association of antimalarial dose with ECG conduction abnormalities OR: 0.84 95% CI: 0.51-1.40). The nested case control analysis (58 cases:159 controls) confirmed the relationship between structural ECG abnormalities and a higher than median cumulative antimalarial dose prior to ECG (OR: 2.14 95% CI: 1.07-4.29). <br/>Conclusion(s): Higher cumulative antimalarial doses are associated with structural ECG abnormalities.

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1. **Electrocardiogram abnormalities related to antimalarials in systemic lupus erythematosus**  
   McGhie T. Arthritis and Rheumatology 2017;69:No page numbers.

Background/Purpose: Anti-malarials (AM), such as hydroxychloroquine (HCQ) and chloroquine (CQ), have long been used for the treatment of systemic lupus erythematosus (SLE). However, despite their general safety, both drugs have the potential to cause serious toxicity. These drugs have significant lysosomal affinity and induce the prominent development of autophagic vacuoles in several tissues. Cardiotoxicity with potential conduction/structural abnormalities on electrocardiogram (ECG) have been reported with AM. We aimed to study whether cumulative AM is associated with ECG abnormalities. <br/>Method(s): A standard resting supine ECG was performed on consecutive patients attending the Lupus Clinic since 2012. ECGs were analyzed and tracings were coded by a single cardiologist blinded to identifying data and previous AM exposure on the basis of the Minnesota criteria. ECG abnormalities were grouped into structural [left ventricular hypertrophy or atrial enlargement] and conduction abnormalities [prolonged corrected QT interval (QTc), short PR interval, left bundle branch block (LBBB), right bundle branch block (RBBB) and atrioventricular block (AVB), bradycardia, tachycardia, premature atrial complex, ectopic atrial rhythm, atrial fibrillation, premature ventricular complex and ventricular bigeminy]. Clinical and laboratory variables from the baseline (corresponds to the ECG visit) were studied as potential factors associated with ECG abnormalities. Associations between cumulative AM [calculated after equating 3.0 mg of CQ with 6.5 mg of HCQ] and ECG abnormalities (structural or conduction) were assessed using logistic regression analysis (after adjusting for baseline patient characteristics) and in a nested case control study (1:3) [matching for sex, SLE duration at ECG within 5 years, ECG testing year within 5 years and hypertension status]. <br/>Result(s): Of 453 patients treated with AM, the median cumulative AM was 1207 grams at ECG. The mean age at ECG was 49.2 +/- 13.8 years and SLE duration was 19.8 +/- 10.4 years. CQ or HCQ had been used by 409 (90.3%) before the ECG. Conduction abnormalities were more prevalent than structural abnormalities, 71 (15.7%) vs. 58 (12.8%). AM cumulative dose did not show a statistical significant association with ECG structural abnormalities, (OR 1.82, p=0.07) while it was protective for conduction ECG abnormalities (OR 0.42, p=0.006) (table 1). The nested case control analysis also found that AM cumulative dose is protective against conduction ECG abnormalities (OR 0.36; 95% CI: 0.17-0.75; p=0.007). SLE duration was a risk factor for both structural and conduction ECG abnormalities. <br/>Conclusion(s): This study suggests an association between cumulative AM dose above the median (1207 g) and structural ECG abnormalities. More importantly, cumulative AM decreases the odds of ECG conduction abnormalities. (Table Presented).

1. **Heart failure-is it lupus myocarditis or peripartum cardiomyopathy?**  
   Malhotra G. American Journal of Respiratory and Critical Care Medicine 2017;195:No page numbers.

Introduction: SLE has myriad manifestations with a highly variable course. Cardiac manifestations are protean with myocarditis being usually subclinical and rarely presenting with left ventricular dysfunction. Case presentation: A 38 year old female with history of SLE presented with pleuritic chest pain and shortness of breath a week after undergoing urgent cesarean section at 30 weeks gestation because of pre-eclampsia. She had fever and sub-sternal non-radiating chest pain which improved on sitting up and worsened on lying down. She did not have any cough, orthopnea, paroxysmal nocturnal dyspnea, or hemoptysis. No history of prolonged immobilization, new skin rash, recent chest trauma or recurrence of musculoskeletal complaints. She denied use of cigarettes, alcohol or illicit drugs. She had a fever of 102.8degreeF, mild respiratory distress and decreased breath sounds in the left hemithorax. Chest xray revealed a posterior left lower lobe consolidation with small left pleural effusion and cardiomegaly. Pulmonary embolism was ruled out. Transthoracic echocardiogram showed ejection fraction (EF) of 60-65% with a small pericardial effusion without hemodynamic compromise. Laboratory examination revealed elevated ESR &gt;140, C-reactive protein 271, complement C3 - 126 and C4 - 26, elevated anti-DNA, negative lupus anticoagulant and antiphospholipid antibodies but positive anti-Smith and anti-SSA antibodies. She was started on antibiotics and prednisone 60 mg along with hydroxychloroquine. Her clinical condition worsened and repeat echocardiogram revealed a drop in EF to 20-25% with an increase in size of pericardial effusion but without tamponade. She eventually went into acute respiratory failure and cardiogenic shock requiring intubation and vasopressor support. Chest x-ray showed moderate left pleural effusion and pulmonary edema. Pulse dose steroids were started and her condition improved significantly within 48 hours. This was accompanied by improvement in EF to 45-50% and decrease in pericardial effusion. An endomyocardial biopsy confirmed the diagnosis of lupus myocarditis with lymphocytic infiltration. She was eventually discharged home on prednisone. <br/>Discussion(s): Myocardial involvement is not uncommon in SLE however symptomatic myocarditis is seen in up to 9% of cases only. It can be complicated by arrhythmias, dilated cardiomyopathy and heart failure. It is important to differentiate myocarditis from peripartum cardiomyopathy. Endomyocardial biopsy is the gold standard for diagnosis. However it has low sensitivity and specificity as the myocardial involvement is patchy. The 2010 Heart Failure Society recommends that endomyocardial biopsy be considered for patients with acute deterioration of heart function of unknown origin that is not responding to medical treatment.

1. **High maternal expression of SIGLEC1 on monocytes as a surrogate marker of a type I interferon signature is a risk factor for the development of autoimmune congenital heart block.**  
   Lisney Anna R. Annals of the rheumatic diseases 2017;76(8):1476-1480.

OBJECTIVESAutoimmune congenital heart block (CHB) is associated with placental transcytosis of maternal autoantibodies directed against Ro/SS-A and La/SS-B. However, only about 2% of children born to mothers with the respective antibodies are affected, indicating that further risk factors exist, which are not yet fully understood. In this study, we investigated whether a maternal type I interferon (IFN) signature represents a risk factor for the development of CHB.METHODSBlood samples, clinical data and serological parameters from 9 women with CHB pregnancies, 14 pregnant women with antibodies against Ro/SS-A but without a CHB complication and another 30 healthy pregnant women as controls were studied. SIGLEC1 expression was measured by flow cytometry and was correlated to plasma IFN-α levels measured by ELISA, and IFN-γ-induced protein 10 (IP-10) levels measured by Bio-Plex technique.RESULTSMothers of affected children had a significantly higher expression of SIGLEC1 (p=0.0034) and IFN-α (p=0.014), but not of IP-10 (p=0.14, all MWU) compared to mothers of unaffected children. SIGLEC1 and IFN-α expression were reduced by hydroxychloroquine and oral glucocorticoids.CONCLUSIONSHigh expression of SIGLEC1 in pregnant women with autoantibodies against Ro/SS-A indicates an enhanced risk for CHB development, and these women may benefit especially from IFN-α directed therapy, for example with hydroxychloroquine.

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1. **Hydroxychloroquine overdose presenting as acquired qt interval prolongation and torsade de pointes**  
   Ndukwu I. Journal of the American College of Cardiology 2017;69(11):2340.

Background: Hydroxychloroquine (HCQ) is an aminoquinoline derivative used as an anti-inflammatory agent in lupus. It is a highly lipophilic substance with a large volume of distribution which blocks sodium channel function. Although rare, life-threatening cardiac conduction disturbances can occur within hours after ingestion. We report a case of HCQ overdose which presented as acquired QT prolongation and quickly developed into torsade de pointes. Case: A 20-year-old woman with lupus and depression was admitted in a comatose condition following an intentional ingestion of 60 grams of HCQ. Physical exam revealed normal vital signs and a Glasgow Coma Scale (GCS) of 4/15. The rest of her exam was unremarkable. Her initial labs were significant for marked hypokalemia and hypocalcemia as well as toxic serum levels of HCQ. Her admission ECG showed a prolonged corrected QT interval of 600mec. She underwent gastric decontamination in the emergency department but shortly after admission, she developed frequent ventricular ectopic activity leading to runs of torsade de pointes. Decision-Making: She was given intravenous magnesium, calcium and potassium followed by an amiodarone infusion. Despite this, she remained hemodynamically unstable and continued to have runs of torsades. Consequently, intravenous lipid emulsion (ILE) was initiated in an effort to sequester lipophilic HCQ away from cardiac myocytes. Stabilization of hemodynamic parameters and conversion to sinus rhythm occurred within minutes after initiation of ILE therapy. A follow-up ECG showed normalization of her QT interval. <br/>Conclusion(s): HCQ poisoning is rare but serious because of its rapid progression to life-threatening conditions such as ventricular dysrhythmias. Early ILE administration should be considered as it may improve myocardial stability by extending the "lipid sink" effect of ILE and normalizing electrolyte concentrations.

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1. **Inducible ventricular tachycardia and dilated cardiomyopathy as cardiac manifestations of systemic myositis**  
   Ho J. Acta Cardiologica 2017;72(5):577-578.

Objectives: Polymyositis is a systemic idiopathic inflammatory myopathy with a prevalence of 2 in 100,000 people in North America. It is associated with congestive heart failure, left ventricular diastolic dysfunction, and cardiac arrhythmias. However, ventricular tachycardia has not been previously reported as a cardiac manifestation of polymyositis. We report a case of ventricular tachycardia with atypical findings on cardiac magnetic resonance (CMR) imaging in a patient with systemic myositis. Methods/results: A 35-year-old previously healthy woman presented with a 3-4 month history of progressive dyspnoea on exertion, palpitations, and proximal muscle weakness. Her electrocardiogram (ECG) revealed wide complex tachycardia consistent with ventricular tachycardia that was managed with synchronised DC cardioversion (Figure 1(B)). Transthoracic echocardiography confirmed a markedly dilated left ventricle, severe global left ventricular hypokinesis with an EF of 25-30%, and moderate impairment of right ventricular systolic function. CMR confirmed moderate-to-severe biventricular systolic dysfunction. Following administration of gadolinium on delayed enhancement imaging, there was full-thickness involvement of the basal to mid-anterior wall with less than 50% involvement of the basal anterior septum, anterolateral, and lateral wall (Figure 1(A)). She complained of worsening proximal muscle weakness with persistently elevated creatine kinase (CK), 11 kg weight loss over two months, dysphagia with solids, facial rash, and alopecia. On examination, she had 4/5 strength on neck flexion, shoulder abduction, elbow extension and flexion, and 3/5 on hip flexion. Although the CMR was suggestive of an ischaemic aetiology, her coronary angiogram demonstrated no flow-limiting epicardial coronary artery stenoses. An electrophysiology study reproduced easily inducible sustained monomorphic ventricular tachycardia (Figure 1(C)). She received a dual-chamber implantable cardioverter-defibrillator and was started on amiodarone. Figure 1. (A) Cardiac magnetic resonance imaging demonstrating full-thickness involvement of the basal to mid anterior wall with less than 50% involvement of the basal anterior septum, anterolateral, and lateral wall suggestive of underlying ischemia (arrows). (B) 12-lead ECG demonstrating clinical monomorphic ventricular tachycardia. (C) Ventricular tachycardia induced with triple ventricular extra-stimuli at the right ventricular apex. Electromyography was consistent with myositis but could not differentiate between SLE and polymyositis. After two courses of IVIG and steroid treatment, she had mild improvement of her proximal weakness but her CK remained elevated. She was subsequently maintained on prednisone, hydroxychloroquine, and azathioprine. <br/>Conclusion(s): This case illustrates a patient with systemic myositis secondary to mixed connective tissue disease, leading to atypical and life-threatening cardiac manifestations and CMR findings. This is the first report in the literature of this presentation with both imaging and electrophysiologic findings.

1. **Infliximab decreases FDG uptake on cardiac PET in refractory cardiac sarcoidosis**  
   Kowlgi N.G. Circulation 2017;136:No page numbers.

Introduction: Cardiac sarcoidosis (CS) is characterized by granulomatous inflammation and fibrosis that may cause heart block, ventricular arrhythmias or heart failure. Corticosteroids are the mainstay of CS management, however their benefits are counterbalanced by side effects. Scarce data exists to guide the use of steroid-sparing agents to treat CS. Hypothesis: We hypothesized that treatment of refractory CS with the chimeric monoclonal antibody against tumor necrosis factor-alpha infliximab (IFX) would stabilize or decrease cardiac inflammation measured by fluorodeoxyglucose positron emission tomography (FDG-PET). <br/>Method(s): Clinical, medication, and imaging data were collected on five patients with CS who were treated with IFX. <br/>Result(s): All patients (n=5) met Heart Rhythm Consensus diagnostic criteria with all patients having positive tissue biopsy. Median age was 41 (range: 23-56 years). Patients presented with complete AV block (n=2), ventricular tachycardia (n=2), and symptomatic premature ventricular contractions (n=1). All patients were initially treated with steroids and a steroid-sparing agent (methotrexate n = 4; hydroxychloroquine n = 2, and azathioprine n = 1). All patients showed FDG uptake on baseline PET prior to IFX. IFX was added to the medical regimen for a mean duration of 20 +/- 18.8 months (10-32 months). On follow-up PET at 17.6 months (range: 7-34 months), 4 of 5 patients showed decreased FDG uptake (Figure) and 1 patient had no change. Three had improved LV ejection fraction (EF). Mean EF improved from 43.2% +/- 38.3% to 50.7 +/- 21.6 % at follow-up (p = 0.15). No patients had sustained VT while on IFX. <br/>Conclusion(s): Addition of infliximab to medical therapy decreased inflammation on FDG-PET in 4 of 5 patients with refractory CS. Further data is needed to evaluate the efficacy and safety of steroid-sparing agents in CS.

1. **Neonatal lupus erythematosus presenting with heart block and pneumonitis: A difficult case**  
   Aguiar F. Pediatric Rheumatology 2017;15:No page numbers.

Introduction: Neonatal lupus erythemathosus (NLE) is a rare autoimmune condition of neonates related to the transplacental passage of maternal autoantibodies (anti-SSA/Ro, SSB/La and rarely anti-U1RNP) to the foetus after the 16th week of gestation leading to lesions in target organs. The most common findings include skin lesions and/or congenital heart block, but hepatobiliary disease and haematological abnormalities can also occur. Other systemic features as pneumonitis have been occasionally documented. <br/>Objective(s): Our aim is to describe a case of Acute Lupus Pneumonitis in a newborn with NLE. <br/>Method(s): A boy born to a 35-year-old mother with systemic lupus erythemathosus with positivity for anti-SSA and anti-SSB, and a previous child with NLE with congenital heart block who died at the age of two due to myocarditis. The pregnancy was surveilled, the mother was treated with prednisolone and hydroxychloroquine and a prenatal diagnosis of heart block was made. The mother received dexamethasone and salbutamol but refused endovenous immunoglobulin and plasmapheresis. <br/>Result(s): The child was born during the 36th week of gestation, by cesarean, with an Apgar 1'/5'of 9/10, complete heart block was confirmed and he was admitted to the Department of Neonatology. 24 hours after birth a temporary pacemaker was inserted, which was only replaced by a definitive pacemaker when the patient was 14 days old due to concurrent sepsis. Empiric antibiotic intravenous therapy with meropenem and vancomycin was started. At D22 he developed hypoxemic acute respiratory failure requiring mechanical ventilation, with chest radiographs showing diffuse bilateral cotton-like infiltrates. In the following 48 hours there was clinical worsening, despite the broad-spectrum antibiotics, absence of fever and progressive normalization of leukocyte count and C-reactive protein level. At this time pediatric rheumatology evaluation was requested. The neonate had a history of transitory rough skin rash on chest and back after birth; thrombocytopenia probably in the context of neonatal sepsis whithout other hematologic abnormalities; hepatomegaly without elevation of liver enzymes. The immunology panel showed positivity for antinuclear antibodies at titer 1/320 (speckled pattern), positivity for antibody anti-SSA and also anti-dsDNA, with absence of anti-SSB, anti-RNP. The clinical picture was interpreted as NLE-related pneumonitis and the patient received intravenous methylprednisolone pulses (30 mg/kg/day) on 3 consecutive days, followed by oral prednisolone in progressively lower doses, with excellent clinical and imagiological response: after the second pulse he started to ventilate spontaneously and after 7 days supplementary oxygen was no longer needed. <br/>Conclusion(s): This case represented a challenge as pulmonary manifestations presented in a neonate with NLE with congenital heart block that was being treated for neonatal sepsis. Besides the rarity of NLE-related pneumonitis, treatment with corticosteroids had a lot of risks, especially in this patient. However, the imagiological and immunological findings and the fact that there was a good response to corticotherapy and not to broad spectrum antibiotics made this diagnosis the most probable, with a successful outcome.

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1. **No histologic evidence of foetal cardiotoxicity following exposure to maternal hydroxychloroquine.**  
   Friedman Deborah Clinical and experimental rheumatology 2017;35(5):857-859.

It is currently recommended that hydroxychloroquine (HCQ) be maintained during pregnancy in patients with systemic lupus erythematosus. Recent data suggest that this Toll-like receptor inhibitor may also reduce the recurrence rate of anti-SSA/Ro associated congenital heart block (CHB). This case report describes a unique situation in which a CHB-afflicted, HCQ-exposed pregnancy was electively terminated. The heart did not reveal any characteristic features of cardiotoxicity, providing further evidence supporting the safety of foetal exposure to HCQ.

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1. **Obstetric and perinatal outcome in anti-Ro/SSA-positive pregnant women: a prospective cohort study.**  
   Martínez-Sánchez Nuria Immunologic research 2017;65(2):487-494.

Anti-Ro/SS-A is one specific type of antinuclear antibodies. They are in the majority of cases associated with primary Sjögren syndrome (SS) but also in Systemic Lupus Erythematosus (SLE), rheumatoid arthritis (RA), and in healthy people. During pregnancy, they are mainly associated to congenital heart block (CHB) and neonatal lupus (NL). The aim of this study was to compare the rate of maternal and fetal complications between a series of anti-Ro/SS-A positive pregnant women prospectively followed. Forty-two anti-Ro/SSA antibodies positive pregnant women that were referred to our hospital between 2011 and 2015. Data about pregnancy follow-up and outcomes were prospectively recorded from electronic databases. Data included demographic characteristics of the patients and their diseases (type, treatments, profile of anti-Ro/SSA, and antiphospholipid antibodies), pregnancy complications (CHB, preeclampsia, preterm delivery), ultrasound examinations and conditions, and mode of delivery. Maternal age was 35.22 ± 3.42 years and most of them were either SLE (n = 16, 40%) or Sjögren syndrome (n = 15, 37.5%). The rest of them were asymptomatic carriers (n = 8; 20%), and there was only one case of rheumatoid arthritis (n = 1; 2.5%). The incidence of anti-Ro52 and anti-Ro60 positive was n = 13, 82.4% and n = 16, 100%, respectively. Anti-La/SSB antibodies were present in n = 17, 48,6% of the patients. Half of the patients were taking hydroxycloroquine (n = 18, 45%). Seven pregnancies were complicated by fetal anti-Ro-related cardiac disease (17.9%) including four cases (57.1%) of second-degree heart block, two cases of third degree heart block (28.6%) and one case (14.3%) of intense and diffuse hyperechogenicity in atrioventricular valves without heart block. Gestational age at diagnosis of these conditions was 23.2 ± 3.5 weeks. One of the 18 patients having hydroxychloroquine (5.6%) compared with the six of them in women not having this medication (6/22, 27.3%) (p = 0.10). Concerning about Doppler evaluation, the Z score of umbilical pulsatility index (PI) was significantly higher in the SLE patients (p = 0.02). There were no cases of preeclampsia. Labor was induced in 21 cases (52.5%) and cesarean section rate was 45%. Gestational age at birth was 39 (37-40) weeks, and the general prematurity rate was 20% (n = 8). Birthweight was 2985 g (2425-3185 g) and 2850 (12.25-52.50) centiles for gestational age. The rate of small for gestational age (SGA) infants was 31.3% for SLE patients (5/16), 13.3% for Sjögren syndrome (2/15), and 12.5% for asymptomatic women (1/8). The rate of neonatal acidosis (pH < 7.20) was 20% (8/34) and it was higher in the SLE cases (6/15, 40%) when delivered after 38 weeks. The main pregnancy complication associated to anti-Ro/SS-A antibodies is CHB. The prevalence of CHB in patients taking hydroxychloriquine is lower without distinguishing between high or low risk patients. Preterm delivery occurs in anti-Ro/SS-A patients at the same rate as in the general population if no complications such as CHB or intrauterine growth restriction (IUGR) occur. The SGA rate also is higher probably because of SLE not because anti-Ro/SS-A antibodies. Finally, the finding of high umbilical artery PI will allow to predict fetus at risk of adverse pregnancy outcomes.HIGHLIGHTS•Anti-Ro/SS-A and anti-La/SS-B are clinically very relevant during pregnancy mainly because of their association to congenital heart block and neonatal lupus. •In our cohort, the prevalence of congenital heart block detected in patients taking hydroxycloroquine is much lower than in patients not taking it without distinguishing between high and low risk patients. •High umbilical artery pulsatility index in Doppler scans studies has been detected in our anti-Ro/SSA population (basely in SLE patients) demonstrated this measurement as a predictor of SGA and adverse pregnancy outcomes in general population such as cesarean section for fetal distress. The small for gestational age rate is higher probably because of SLE not because anti-Ro/SS-A •Preterm delivery happens in anti-Ro/SS-A patients at the same rate as in the general population if no complications such as congenital heart block or intrauterine growth restriction occur.

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1. **Progress in the pathogenesis and treatment of cardiac manifestations of neonatal lupus.**  
   Izmirly Peter Current opinion in rheumatology 2017;29(5):467-472.

PURPOSE OF REVIEWTo provide new insights into pathogenesis, prevention and management of cardiac manifestations of neonatal lupus (cardiac neonatal lupus) and issues pertinent to all anti-SSA/Ro positive individuals of childbearing age.RECENT FINDINGSAntibody specificity with high risk for cardiac neonatal lupus remains elusive, but high titers of Ro60, Ro52 or Ro52p200 antibodies appear to be required. Varying antibody specificities to the p200 region of Ro52 can induce first-degree block in a rodent model. In consideration of the contribution of macrophages to inflammation and fibrosis in cardiac neonatal lupus, hydroxychloroquine (HCQ) is being considered as preventive therapy. Cord blood biomarkers support the association of fetal reactive inflammatory and fibrotic components with the development and morbidity of cardiac neonatal lupus. Data from U.S. and French registries do not provide evidence that the prompt use of fluorinated steroids in cases of isolated block significantly alters fetal/neonatal morbidity or mortality.SUMMARYThe search for a high-risk cardiac neonatal lupus antibody profile remains, but high-titer antibodies to Ro60 and R052 are a consistent finding, and this may guide the need for fetal echocardiographic surveillance. The uniform use of fluorinated steroids to prevent progression of cardiac neonatal lupus or reduce mortality does not appear justified. HCQ, based on diminishing an inflammatory component of cardiac neonatal lupus, is under consideration as a potential preventive approach.

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1. **Treatment of cardiac sarcoidosis with steroids and steroid-sparing immunosuppressants: Findings from the cardiac sarcoidosis consortium registry**  
   Kron J. Heart Rhythm 2017;14(5):No page numbers.

Background: Cardiac sarcoidosis (CS) can lead to lifethreatening arrhythmias and heart failure. Steroids are the primary therapy, but utilization and efficacy of alternate immunosuppressive agents has not been systematically studied. <br/>Objective(s): We sought to describe the usage of corticosteroids and alternate immunosuppressants in a large cohort of CS patients. <br/>Method(s): The Cardiac Sarcoidosis Consortium is a prospective, multicenter, international registry that includes demographic, clinical, medication, and imaging data. We evaluated immunosuppression therapy on 318 CS patients at the time of enrollment in the registry. <br/>Result(s): The mean age is 55.3+/-11.3 (range 22.5-82.5), 178 (56%) are male, and mean left ventricular ejection fraction is 47.2 +/-14.5. Eighty-eight (27.7%) of patients are on an antiarrhythmic drug, 42 (13.2%) are on a beta blocker, and 198 (62.3%) have an implantable cardiac defibrillator (ICD). Of 318 patients, 85 (26.7%) are on steroids only, 72 (22.6%) are on steroids and steroid-sparing medications, 31 (9.7%) are on steroid-sparing agents only, and 130 (40.9%) are not on immunosuppression. Of patients on prednisone and steroidsparing agent, 44 (64.7%) are on methotrexate, 14 (20.6%) are on mycophenolate mofetil, 8 (11.8%) are on hydroxychloroquine, 7 (10.3%) are on azathioprine, 4 (5.9%) are on infliximab, 2 (2.9%) are on tacrolimus) and 1 (1.5%) is on sirolimus. Of patients only on a steroid-sparing agent, 22 (71.0%) are on methotrexate, 9 (29.0%) are on hydroxychloroquine, 4 (12.9%) are on mycophenolate mofetil, 1 (3.2%) is on infliximab and 1 (3.2%) is on tacrolimus. The mean daily dose of prednisone for patients on steroids alone was 25.6+/-24.3 mg versus 20.2+/-16.3 mg for patient on steroids plus steroid sparing-agent (p=0.12). The number of appropriate ICD shocks with the past year was 0.4 +/- 1.2 for patient on steroids alone, 0.2 +/- 0.8 for patients on steroids and steroid-sparing agents, 0.5 +/- 2.0 for patients on steroid-sparing agents alone, and 0.1 +/- 0.7 for patients not on immunosuppression (p=0.19). <br/>Conclusion(s): More than half of CS patients receiving immunosuppression therapy are on steroid-sparing agents, either in conjunction with steroids or alone. Further research is needed to define the best immunosuppression strategy for CS.

1. **Wide heterogeneity in treatment protocols and inappropiate use of prednisolone for anti-RO/LA associated-congenital heart block: A systematic review of 492 cases**  
   Erden A. Annals of the Rheumatic Diseases 2017;76:1215-1216.

Background: Congenital heart block (CHB) risk is 1-2% in case of maternal anti SSA/Ro and/or anti SSB/La antibody positivity. CHB have significant mortality (20-30%) and available therapeutic options' efficacy is contradictory. <br/>Objective(s): To review the literature regarding different treatment modalities for CHB. <br/>Method(s): We performed a systematic review (August 2015) on Pubmed, using the following MeSH terms: "neonatal lupus", "congenital heart block"; results were restricted to human studies and English language . 1125 articles were assessed in abstract form and, after employing exclusion criteria, 267 original articles/case reports were evaluated in full text. Finally, 199 studies were included, reporting on a total of 492 CHB patients. All administered treatments were assessed on a patient-by-patient basis. <br/>Result(s): A total of 243 cases reported data for CHB treatment: glucocorticoids (GCs) in 106 (43.6%) cases, intravenous immunoglobulin (IVIG) in 14 (5.7%) cases, and hydroxychloroquine in 5 (2.0%) cases. 21 patients received plasmapheresis treatment . 134 (55.1%) cases received no treatment. Both GCs and IVIG were mostly used in cases with complete atrioventricular (AV) block (74.1% and 61.5% of cases, respectively). Different types of GCs were used: Dexamethasone in 54 (58.6%) patients, prednisolone in 27 (29.3%) and betamethasone in 11 (11.9%) patients (total 92 patients with available data). Dosing schemes and regimens were also widely heterogeneous, with fifteen different regimens used by different centres (Table). Regarding IVIG treatment, six different algorithms were used. Similarly, five different plasmapheresis protocols were used. <br/>Conclusion(s): There is no consensus in the treatment of CHB. Drug selection and dosing regimens have wide heterogeneity. More than half cases received no treatment. Of note, prednisolone has often been used, despite its inability to cross the placenta.

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1. **Xanthoma-like Skin Changes in an Elderly Woman with a Normal Lipid Profile.**  
   Nockowski Piotr Acta dermatovenerologica Croatica : ADC 2017;25(2):167-169.

Dear Editor, An 83-year-old woman developed yellow-brownish infiltrates, nodules, and tumors mimicking xanthomas, mostly involving the periorbital and chest area within three months (Figure 1). She had no abnormalities in serum cholesterol or triglycerides levels. A detailed laboratory analysis revealed the presence of mild monoclonal gammopathy with a presence of immunoglobulin G (IgG) kappa light chains; however, according to hematologist consultation, it did not require medical intervention. Imaging assessment and ultrasound examination did not show any specific involvement of internal organs. The skin biopsy demonstrated necrobiotic areas alternated with foci of xanthogranulomatous infiltration throughout the reticular dermis with extension into subcutaneous tissue. The granulomatous infiltrate was composed of epithelioid, foamy histiocytes in addition to conspicuous giant cells of the Touton type and foreign body type, as well as variable numbers of lymphocytes, plasma cells, and neutrophiles. Lipid vacuoles were seen within the foci of necrobiosis and xanthogranulomatous infiltration (Figure 2). Two months after first admission to our department, the first signs of necrosis within the lesions were noted, and massive necrosis of skin lesions occurred after the following 5 months (Figure 1). Based on the clinical manifestation and histological and laboratory findings, the diagnosis of necrobiotic xanthogranuloma (NXG) was established. In our patient, the extremely late onset of the disease, its very aggressive course, and the absence of malignant hematological disorder were remarkable. The general condition improved after local treatment and a low dose of prednisone. However, patient anamnesis revealed myocardial infarction in the past, congestive heart failure, and atrial fibrillation. Eventually, the patient died due to acute heart failure before alkylating agents could be administered; we consider the patient's death to have been unrelated to NXG. NXG is a rare, chronic granulomatous disorder which was first described in 1980 by Kossard and Winkelmann (1). Currently, less than one hundred fifty cases of this syndrome have been reported in the literature worldwide (2,3). The disease occurs during adulthood, slightly more frequently in women, and usually after the age of 60 years, although the youngest reported patient was 17 years old (3). The disease initially manifests as xanthoma-like eruptions of yellowish or red-orange papules and nodules that coalesce into indurated plaques (4). The size of the lesions typically increases over time or with the next recurrences. In comparison to hyperlipemic and normolipemic xanthomas, the lesions are firmer, more prominent, and more polymorphic (3) with superficial telangiectasias, sometimes erythematous and/or violaceous borders, and atrophy (5). Ulcerations of the lesions were observed in about 50% of patients and tended to be extensive and progressive (4). Skin lesions of NXG can occur anywhere on the body. However, about two-thirds of patients had periorbital involvement, particularly on the upper and/or lower eyelids or elsewhere on the face. The second most commonly affected site was the trunk, predominantly the chest (3-6). However, many skin lesions first appear on the trunk or extremities and subsequently involve the periorbital area (4). More than one body area was affected in about 90% of the published cases (3,4). In individual cases, the occurrence of NXG was noted within scars, after trauma, or in a previously X-ray irradiated area (5). Lesions may be asymptomatic; however, over half of patients asked reported various symptoms, predominantly itching but also burning, tenderness, and even pain (4,5). Periorbital skin lesions are often accompanied by ophthalmic manifestations, mainly scleritis, choroiditis, or conjunctivitis (3), and with complications such as blepharoptosis, restricted ocular motility, and proptosis (4,5). Extracutaneous lesions are most commonly seen in the respiratory tract, including the lungs and larynx, followed by the myocardium, oral cavity, skeletal muscles, kidneys, ovaries, intestine, and other sites (5,6). Extracutaneous involvement was reported in less than 20% of cases (3), but its frequency seems to have increased in recent years (5). Regarding laboratory abnormalities, the majority of patients with NXG (70% and up to 90% depending on the studied population) have a monoclonal gammopathy (more often IgG-kappa than IgG-lambda). Elevated erythrocyte sedimentation rate, anemia, leukopenia, low C1 and C4 levels, and cryoglobulinemia are also frequently present (3-6). Incisional biopsy is recommended to confirm the diagnosis of NXG, but correlations between the clinical presentation and specific histopathologic findings have been poorly characterized so far. The histopathology shows an inflammatory infiltrate composed of macrophages, foam cells, plasma cells, and other inflammatory cells as well as Touton and foreign body-type giant cells in the dermis and subcutaneous tissue. Necrobiosis is usually present, and nodular lymphoid aggregates are common. Cholesterol clefts or asteroid bodies are rare or absent. The epidermis may be atrophic or normal. Special stains are not helpful in establishing the diagnosis of NXG, but immunohistochemistry for CD68 is positive while it is always for CD1a and PS100 negative, like in non-X histiocytosis (4,5). In patients without a known myeloproliferative disorder, bone marrow biopsy may reveal atypical or increased plasma cells and, very rarely, true multiple myeloma (5). As mentioned above, NXG can be a manifestation of multiple myeloma. However, chronic lymphocyte leukemia, B-cell lymphoma, and other lymphoproliferative diseases have also been reported in patients with NXG (3). Remarkably, hematological disorders may emerge many years before or after the onset of skin lesions (even up to 11 years) (4). According to available literature data, the course of the disease is usually chronic and slowly progressive, and the prognosis is relatively good in the absence of co-occurrence of malignant hematological disorders ([5-7). Aside from hyperlipemic and normolipemic xanthomas, the differential diagnosis of NXG includes multifocal necrobiosis lipoidica, granuloma annulare, foreign-body granuloma, juvenile xanthogranuloma, rheumatoid nodules, and amyloidosis (4). In 5 cases from the literature, xanthoma and NXG were present at the same time (3). Despite several hypotheses, the etiopathogenesis of NXG remains unknown (3,4,8). For that reason and due to the rarity of the disease, the optimal therapy has not been not defined. Frequently, chlorambucil or melphalan have been used alone or in combination with prednisone (4). Treatment may result in remission of symptoms on the skin, but it does not provide a permanent cure (8). There are also single reports of the successful use of thalidomide, lenalidomide, cyclophosphamide, dexamethasone, interferon 2a and 2b, plasmapheresis and hydroxychloroquine, azathioprine, infliximab, and autologous bone marrow transplantation (3). Methotrexate seems to be ineffective (9). Local therapy, including local steroids, laser CO2, or radiotherapy, results in partial improvement (3,4). Skin lesions which relapsed or were unresponsive to treatment could be excised surgically and the defects resurfaced with skin grafts. [2].

1. **Zoonotic aortitis presenting with pseudoaneurysm of the ascending aorta and complicated by endocarditis of the aortic bioprosthesis**  
   Graca Santos L. European Heart Journal Cardiovascular Imaging 2017;18:No page numbers.

Introduction: Mycotic pseudoaneurysm of the thoracic aorta, usually secondary to infective endocarditis (IE) or aortic valve surgery, is a rare but potentially fulminant condition since it may progress to rupture and death unless early diagnosis is achieved and appropriate treatment rapidly initiated. Description of the problem, procedures, techniques and/or equipment used: A 75-year-old male, with recent aortic valve replacement (Edwards Perimount n&lt;=23 bioprosthesis), presents with 2 week history of fatigue, weight loss and fever. Empirical antibiotherapy was started after blood samples for microbiology and serology were collected. The transesophageal echocardiogram (TEE) performed, after inconclusive transthoracic echocardiogram, was not suggestive of ongoing IE. To exclude possible occult solid tumor, he underwent thoracoabdominal angiography computed tomography (CT) which revealed contrast-filled structures adjacent to the non-coronary and right coronary cusps, and a hypodense structure measuring 48mm of transverse diameter adjacent to the anterior wall of the ascending aorta. For better assessment, TEE was repeated, confirming this finding and also suggesting aortic annulus abscess (not present in the previous exam). Magnetic resonance angiography confirmed these findings, revealing two pseudoaneurysms, one measuring 28x13x25mm in the dependency of the non-coronary cusp, and another one, bilobed, measuring 42x20x39mm, in the dependency of the right coronary cusp. It also showed a T2-hyperintensive 45mm diameter collection suggestive of an abscess, anterior to the ascending thoracic aorta. Questions, problems or possible differential diagnosis: Regarding the aortic abcess and pseudoaneurysms, it is important to evaluate its probable aetiology (surgical trauma, aortitis or ongoing IE) and its implications. Regarding the patient's management, the need and timing of surgical repair must be discussed and, in the scenario of possible infectious phenomenon, the suitability of antibiotic therapy has to be considered. Answers and discussion Blood cultures were negative and serology was compatible with both acute Q fever and disseminated Lyme disease (later confirmed by Westernblot). Given this information and the fact that the first TEE already revealed no signs of IE, the diagnosis of infective aortitis of the ascending aorta with retrograde contiguous dissemination was suggested. Doxycycline, hydroxychloroquine and levofloxacin were started and the patient referred to cardiac surgery. While waiting for surgery, he developed an extensive right brain infarction with CT scan suggesting embolic cause, probably septic since no atrial fibrillation episodes were present on telemetry. The patient did not recover completely and entered a rehabilitation programme, and surgery was postponed. Conclusions and implications for clinical practice: To our best knowledge, we report the first case of aortitis featuring pseudoaneurysms of the ascending aorta with extension of the infection to the aortic annulus, in the scenario of both Lyme disease and acute Q fever. This case emphasizes the critical relevance of prompt diagnosis and adequate treatment, paying attention not only to the valvular apparatus but also to the adjacent structures since they may be as well affected by the infectious process. It is important not to delay surgery, regardless of the risk, in order to avoid complications and mortality (Figure presented).

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1. **Bacterial meningitis secondary to postoperative thigh abscess: A case report**  
   O'Connor Emmett R. Journal of Neurosurgical Anesthesiology 2016;28(2):No page numbers.

Background: Central nervous system dysfunction in patients with systemic lupus erythematosus is highly variable. A literature review found no cases of meningitis disseminated from a postoperative hip wound abscess. Case Report: B.H. is a 59-year-old woman who presented to the emergency department with fever and confusion. She resides in a nursing home. She presented with a temperature of 102.4 and was confused with some posturing of her hands. CT of head showed no acute bleeding. Magnetic resonance imaging revealed no acute findings. Lumbar puncture was not possible in the initial phase of her care as her INR was 3.4. There is no report of cough, nausea, or vomiting per the nursing home. No immediate family was present to interview. The patient was obtunded and could not give an accurate history. Chart review uncovered an open reduction internal fixation of her left hip 2 months before this admission. Documents from the nursing home revealed a significant history, including but not limited to systemic lupus erythematosus, atrial fibrillation, cerebral vascular accident without deficits, mitral valve repair. Her medications included plaquenil, cellcept, and coumadin. Laboratory data showed and INR of 3.4, C-reactive protein level 343, white blood cell count 9.8, and creatinine of 3.3. Upon physical examination a warm, erythematous area over her left lateral thigh was noted. CT scan revealed an abscess. Given her immune compromised state and neurological examination, it was decided to treat for potential meningitis. She was given dexamethasone followed by vancomycin, rocephin, and acyclovir. She was admitted to the intensive care unit for fluid resuscitation, neuromonitoring, and supportive care while correcting her INR with fresh frozen plasma. An EEG was performed upon admission and showed encephalopathy of indeterminate cause. The following day a lumbar puncture was performed which revealed yellow hazy fluid. Total protein count 382, glucose 33, total nucleated cells 1119, red blood cells 69. Gram stain showed Gram-positive cocci in pairs. The other tests for fungal and viral causes were negative and the acyclovir was stopped. Streptococcus pneumoniae cultures returned from the abscess and blood were susceptible to rocephin. The vancomycin was stopped. Her mental status improved dramatically over the next several days, and her creatinine returned to baseline. She made a remarkable recovery over the course of her hospitalization. <br/>Discussion(s): As neurointensivists, our responsibility to patient care is to consider the entire spectrum of disease processes. Although this patient appeared as many do with central nervous system sequela of severe sepsis, she suffers from immunosuppression and therefore requires a complete workup to include a radiographic imaging, and EEG and if warranted sampling of the cerebral spinal fluid. Immunocompromised patients are at increased risk for meningitis over the general population. Her presentation was complicated by the obvious source of infection in her leg and could have explained her symptoms, but without full workup the management could have been minimized to debridement, fluids and an incomplete antibiotic course, causing increased morbidity and potentially death.

1. **Clinical implications of persistent sinus tachycardia in systemic lupus erythematous: A retrospective study**  
   Bhusal S. Arthritis and Rheumatology 2016;68:2270.

Background/Purpose: Resting Sinus Tachycardia (ST) is found in approximately 50 % of patients with SLE. Unexplained episodes of intermittent ST could be a manifestation of disease activity. Approximately 13-15 % of patients, however, continue to have unexplained ST that persists beyond the duration of disease flare. The significance of this finding is still under investigation, but may be associated with physical deconditioning, higher SLEDAI scores or occult serositis. We conducted a retrospective study to further elucidate its clinical significance. <br/>Method(s): SLE was defined as patients fulfilling SLICC 2012 criteria. Persistent ST was defined as unexplained resting heart rate &gt; 90 bpm in &gt; 50 % of all outpatient visits; a minimum of 8 outpatient visits were required such that transient episodes of tachycardia were excluded. Also excluded were tachycardia episodes with potential explanation e.g. acute illness, severe pain, fever, acute anemia, hyperthyroidism, pregnancy and history of cardiac arrhythmias. A retrospective chart review was performed in patients with a diagnosis of SLE between January 2000 and December 2015. Patients meeting SLICC 2012 criteria and &gt; 8 outpatient visits were dichotomized into groups with or without persistent ST. Multiple variables were compared: demographics; individual components of SLICC 2012 criteria at the first and the latest follow-up; laboratory tests including ENA, APL, ESR/CRP, anemia and nephritis class; pulmonary, cardiac and renal components of SLICC damage index; comorbidities including APS, hypertension, hyperlipidemia and history of deep vein thrombosis; and, hydroxychloroquine, angiotensin converting enzyme inhibitor and beta blocker use. Fisher's exact test was used and two sided p value &lt; 0.05 considered significant. <br/>Result(s): Charts of 375 patients were reviewed. 106 met inclusion criteria. 17 (16%) had persistent ST. At the time of statistical analysis, complete data was available in 16 patients with persistent ST and 61 patients without. The mean duration of follow up was 6.4 and 7.3 years respectively. Persistent ST was found to be associated with the following in univariate analysis: serositis at presentation (44% vs 14% P 0.017), proteinuria &gt; 500 mg/24 hour at the latest follow up (63% vs 33% P 0.044) and anti-histone antibodies (75% vs 42% P 0.026). Quantitative analysis of maximal proteinuria revealed an association of persistent ST with any proteinuria &gt; 500 mg/24 hr (63% vs 31% P 0.02) as well as nephrotic proteinuria &gt; 3 gm/24 hr (44% vs 18% P 0.045). In addition, class 5 nephritis was more common (25% vs 5% P 0.031) in this group. Other variables trending towards significance include: active urinary sediment/&gt; 5 RBCs/hpf at latest follow up (50% vs 23% P 0.059), anti-DNA antibodies (75% vs 46% P 0.0504) and APS (25% vs 8% P 0.08). <br/>Conclusion(s): Unexplained persistent ST could be a meaningful clinical sign in SLE. Early in natural history, this may imply the presence of incipient serositis while later on, of an ongoing proteinuric renal disease. A novel finding of high prevalence of anti-histone antibodies in this subgroup needs further scrutiny to discern its significance.

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1. **Cohort of pregnant women with RO/LA antibodies: Risk of fetal third degree atrioventricular block and use of hydroxychloroquine**  
   Mollerach F.B. Arthritis and Rheumatology 2016;68:3237-3240.

Background/Purpose: Third degree atrioventricular block(AVB), a rare congenital complication, duplicate-triplicate frequency up to 2% when Ro/La maternal antibodies are present. Incidence rises to 17-20% in mothers with a previous child with AVB. Maternal consumption of hydroxychloroquine seems to reduce this risk. The purpose was to evaluate the incidence of fetal AVB and its relationship with the consumption of hydroxychloroquine in women with Ro/La antibodies whose pregnancies have been followed at our hospital. <br/>Method(s): We reviewed the electronic medical records from years 2000 to 2014 of a) all pregnant women with known Ro/La antibodies, b) all pregnant women with hydroxychloroquine consumption in the pharmacy registry and c) all mothers of children younger than 2 years old with AVB and/or pacemaker placement. <br/>Result(s): 62 pregnancies in 47 mothers with Ro/La antibodies were identified. Pregnant women who had consumed hydroxychloroquine during all the pregnancy (n=14) were compared with those who had not(n=48). Demographic characteristics are shown in table 1. One newborn (7.1%) suffered a AVB in the hydroxychloroquine group versus 7 newborn in the group without hydroxychloroquine (14.6%)(p=0.5). None of the mothers had more than one pregnancy with AVB. AVB was detected at a median gestational age of 20 weeks and they were all intrauterine (table 2). Between 2000 and 2014, 23 AVB were diagnosed on children younger than 2 years old, 10 of them were associated with the presence of antibodies and/or a maternal rheumatologic disease. 3 of these children (30%) required the collocation of a pacemaker before 2 years of age and 2 children (20%) died before a pacemaker could be implanted. The other 13 (10 followed up for more than 2 years) congenital AVB were associated to congenital structural heart disease and 100% required a pacemaker implantation (p&lt;0.001 versus AVB without structural heart disease)(table 2). <br/>Conclusion(s): A high incidence of AVB in patients with Ro/La antibodies in our hospital was observed (12.9 %), perhaps due to derivation bias. Although AVB was more frequent in mothers without hydroxychloroquine (14.6% versus 7.1%), the difference was not statistically significant. All congenital AVB diagnosed at our hospital without structural heart disease were associated with a rheumatic disease or presence of maternal antibodies. (Table Presented).

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1. **Early treatment with intravenous lipid emulsion in a potentially lethal hydroxychloroquine intoxication.**  
   Ten Broeke R. The Netherlands journal of medicine 2016;74(5):210-214.

This case report describes the possible benefit of intravenous lipid emulsion in two patients surviving a severe intoxication with hydroxychloroquine in a dose that was previously considered to be lethal. The first case involves a 25-year-old female who ingested 17.5 grams of hydroxychloroquine, approximately one hour before presentation. An ECG showed QRS widening and the lab results showed hypokalaemia. She became unconscious, and developed hypotension and eventually apnoea. After intubation, supportive care consisted of norepinephrine and supplementation of potassium. Moreover, sodium bicarbonate and intravenous lipid emulsion were started to prevent cardiac toxicity. After these interventions, haemodynamic stability was established within a few hours. Although cardiomyopathy was confirmed, the patient recovered after two weeks. The second case concerns a 25-year-old male who took 5 grams of hydroxychloroquine. At presentation, two hours after intake, he showed QTc prolongation and hypokalaemia. The patient was treated with the usual supportive care and, although presentation to hospital was later, with intravenous lipid emulsion. Also this patient recovered. In conclusion, these cases show the benefit of supplemental intravenous lipid emulsion to prevent cardiac toxicity after a severe intoxication with hydroxychloroquine.

1. **Endosomal Toll-like receptors in clinically overt and silent autoimmunity.**  
   Clancy Robert M. Immunological reviews 2016;269(1):76-84.

Toll-like receptors (TLRs), first identified as pattern recognition receptors, are now recognized to serve as a key interface between innate and adaptive immunity. Systemic lupus erythematosus (SLE) is characterized by both continuous and cyclic stimulation of the innate and adaptive immune system by endogenous nucleic acids released from apoptotic or necrotic cells. TLR7 and TLR9 function as innate sensors of viral infection as their ligands are ssRNA and dsDNA, respectively. Recognition of self nucleic acids by endosomal TLRs in B cells and pDCs is thought to be an important step in the pathogenesis of SLE, generating anti-nuclear antibodies and producing type I IFN. In this review, we take a specific look at how TLR7, non-coding RNA, and SSA/Ro60 can contribute to clinical autoimmunity and organ damage in the context of neonatal lupus (NL). Although 15 times less common than SLE, NL provides a unique opportunity to study two different aspects of autoimmunity: passively acquired tissue injury in a developing fetus and clinical progression of disease in an asymptomatic mother found to have anti-Ro60 autoantibodies only after identification of heart block/rash in a child. Finally, we discuss hydroxychloroquine (HCQ) use by asymptomatic subjects which may forestall the clinical expression of autoimmunity.

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1. **Insulin autoimmune syndrome in patients with rheumatoid arthritis and lipoic acid intake**  
   Lio S. Endocrine Reviews 2016;37(2):No page numbers.

Hypoglycemia is a common medical problem in diabetic patients. Although rarely, it can occur in non-diabetic patients with autoimmune diseases who take lipoic acid (LA), a nutritional supplement used for sport and fitness, sometimes used in peripheral neuropathies. LA it contains sulfhydryl groups and in genetically predisposed individuals can induce severe but reversible hypoglicemia caused by insulin autoimmune syndrome (IAS), a very rare syndrome with high insulin serum levels and anti-insulinantibodies (AIA) in patients without prior insulin exogenous exposure. IAS by LA has been described in Asian, with strong association with HLADRB1\*04:06, but is rare in non-Asian patients and in which an association with HLA-DRB1\*04:03 has been reported.A 68-year-old Italian woman was hospitalized for recurrent episodes of impaired consciousness, diaphoresis and non diabetic spontaneous, symptomatic, both fasting and postprandial hypoglycemia with sweating, tremors, instability with at home glycemic values down to 39. The symptoms resolved with food ingestion and/or glucose.His past medical history was significant for rheumatoid artritis by then years. Hypertensive cardiomiopathy, a year ago, only one episode of atrial fibrillation with proper electrical cardioversion, colecistectomy. No history of thyroid disease. No drug allergies. Here medications include prednisone at very low doses, hydroxychloroquine, colecalciferole, NSAIDs, paracetamol; bisoprolol, amlodipine, ASA, pantoprazole. Also, for right hip pain, a nutrional supplement containing LA (300-600 mg/day) for 3 weeks was administered. Preprandial insuline and C-peptide levels were high (52.3 mg/mL and 9.6 ng/mL, respectively); AIA were also elevated (48.65 U/mL). GH, IGF-I, urinary metanephrines, Cortisol, ACTH, TSH, TPOAb were normal. Fasting glucose was repeatedly low (up to 52 mg/dL) and glicemic stick down to 39; HbA1c was normal. A chest X-ray showed absence of abnormality features. A ultrasound abdomen did not detect suspicious lesions for neoplasia. HLA typing demonstrated the presence of HLA DRB1\*04:03. Oral or iv glucose was administered for 12 h and started the therapy with prednisone 12.5 mg/day gradually tapering. The LA it was discontinued after the hospitalization. At three months follow-up the patient remained asymptomatic; blood glucose levels were normal; insulin and anti-insulin antibodies decreased but slowly (41.2 mU/mL and 45.49 U/mL, respectively) In conclusion, 1. IAS, although rare, should be considered in the differential diagnosis of hypoglycemia in patients with autoimmune diseases taking drugs with sulfhydryl groups such as LA. 2. It may also be important to avoid, in the cases of doubtful diagnosis, an excess of diagnostic tests often very expensive and sometimes of unnecessary surgeries. 3. In susceptibility to IAS the HLA difference between Asians and non-Asians is confirmed.

1. **Late onset lupus-a case report**  
   Ribeiro F. European Geriatric Medicine 2016;7:No page numbers.

Introduction: Systemic lupus erythemtous (SLE) is a multissystemic autoimmune disease, traditionally considered a disease of young women. However several reports have described SLE in elderly populations, with a 9% development after the age of 50 in the Euro- Lupus cohort. Case presentation: 71- year old woman with chronic heart failure class II (NYHA), atrial fibrillation, hypertension and dyslipidemia treated with furosemide, valsartan+ hydrochlorothiazide, lercanidipine, diltiazem, synvastatin and rivaroxaban, admitted with an acute decompensated heart failure. X-ray: increased cardiothoracic index. Echocardiogram: large pericardial effusion without evidence of hemodynamic compromise, tricuspid regurgitation and right ventricular dysfunction. During the hospitalization she manifested biphasic Raynaud, that she had been presenting for 7 years, and nonerosive arthritis. She reported a history of arthritis at 12 and 4 years before, treated with corticosteroids and occasional painless oral ulceration. Additional study: sedimentation rate 56 mm, positive antinuclear antibodies (1/320), anti-dsDNA (62 UI/mL), anti-SSA/Ro (17 U/mL) and C3 consumption. Serologic tests for syphilis and virus and neoplastic markers were negative. Thoraco-abdomino-pelvic CT: small pericardial effusion and small pleural effusion. The diagnosis of systemic lupus erythematosus was made and she began treatment with hydroxychloroquine with good response. <br/>Conclusion(s): The low prevalence of SLE in the elderly and its nonspecific symptoms make the diagnosis difficult and may reflect senescence of the immune system. Due to all the potential differential diagnosis and the consequences of polymedication, it also gets misor undiagnosed. As early diagnosis and treatment is necessary for these patients, careful attention needs to be paid to symptoms and laboratory findings.

1. **Life Threatening Severe QTc Prolongation in Patient with Systemic Lupus Erythematosus due to Hydroxychloroquine.**  
   O'Laughlin John P. Case reports in cardiology 2016;2016:4626279.

We present a case of a syncopal episode resulting from significant QT interval prolongation in a patient on hydroxychloroquine for the treatment of systemic lupus erythematosus and end stage renal disease. The patient had been treated with hydroxychloroquine for two years prior to presentation. After thorough workup for secondary causes of QT interval prolongation hydroxychloroquine was discontinued and the patient's QT interval shortened. The patient was treated with mexiletine to prevent sudden ventricular arrhythmias, which was unique compared to other documented cases in which lidocaine was used. The patient was noted to have mild prolongation of the QT interval on electrocardiogram prior to initiation of hydroxychloroquine therapy which was exacerbated by its use and may have been caused due to toxicity from underlying renal failure.

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1. **Myocardial Biopsy In "Idiopathic» Atrial Fibrillation And Other Arrhythmias: Nosological Diagnosis, Clinical And Morphological Parallels, And Treatment.**  
   Blagova O. V Journal of atrial fibrillation 2016;9(1):1414.

BACKGROUNDThe nosological nature of "idiopathic" arrhythmias and the effect of etiotropic and pathogenetic treatment are often unknown.METHODS AND RESULTS19 patients (42.6±11.3 years, 9 women) with atrial fibrillation (n = 16), supraventricular (n = 10) and ventricular (n = 4) premature beats, supraventricular (n = 2) and ventricular tachycardia (n = 1), left bundle branch block (n= 2), AV block (n = 2) without structural heart changes. Viruses were identified (polymerase chain reaction, PCR) along with measurement of anti-heart antibodies (AHA) and endomyocardial biopsy (EMB). EMB allowed to establish diagnosis in all patients: infectious-immune myocarditis (n = 11, parvovirus-positive in 1),parvovirus-positive endomyocarditis (n = 1),systemic (n = 2) and myocardial (n = 1) vasculitis,Fabry's disease (n = 1), arrhythmogenic right ventricular dysplasia (n = 1),unspecified genetic cardiomyopathy (n = 2, herpes virus 6 one positive). Level of AHA had the greatest significance for myocarditis diagnostics. All patients with myocarditis/vasculitis had background therapy: acyclovir (n = 10), IV immunoglobulin (n = 2), meloxicam (n = 12), hydroxychloroquine (n = 15), steroids (n = 14, 31.1±12.5 mg/day), azathioprine 150 mg/day (n = 2). Median follow-up was 4 years. Treatment significantly reduced the rate of arrhythmias (8 [5;8] to 3 [1.25;7.75] points); disappearance of bundle branch block was noted.CONCLUSIONEMB allowed to diagnose immune-mediated inflammatory diseases in 78.9% patients with 'idiopathic' arrhythmias and genetic diseases in 21.1%. Background therapy of myocarditis improved the antiarrhythmic efficiency, and allowed the best premed for interventional treatment.

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1. **Quinine and the ABCs of Long QT: A Patient's Misfortune with Arthritis, (Alcoholic) Beverages, and Cramps.**  
   Sheehan Elyce T. Journal of general internal medicine 2016;31(10):1254-1257.

A 91-year-old woman presented to the emergency department by ambulance after her family found her minimally responsive. Telemetry monitoring demonstrated episodes of non-sustained polymorphic ventricular tachycardia (PMVT) associated with significantly prolonged repolarization. Her medical history revealed that she was taking quinine or a derivative in three different forms: hydroxychloroquine, quinine sulfate (for leg cramps), and her gin mixed with tonic water (containing quinine). The present case is illustrative of classic etiologies and findings of acquired long QT syndrome, and serves as an important reminder for providers to take a complete medication history, including use of duplicative and alternative medicines and type of alcohol consumption.

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1. **Targeting downstream transcription factors and epigenetic modifications following Toll-like receptor 7/8 ligation to forestall tissue injury in anti-Ro60 associated heart block.**  
   Clancy Robert M. Journal of autoimmunity 2016;67:36-45.

Based on the consistent demonstration of fibrosis of the atrioventricular node surrounded by macrophages and multinucleated giant cells in anti-Ro antibody exposed fetuses dying with heart block, this study focuses on macrophage signaling stimulated by ssRNA associated with the Ro60 protein and the impact of antagonizing innate cell drivers such as TLR7/8. Transcriptome and epigenetic modifications which affect transcription factors, NF-κB and STAT1, were selected to evaluate the phenotype of macrophages in which TLR7/8 was ligated following treatment with either anti-Ro60/Ro60/hY3 RNA immune complexes or transfection with hY3. Based on microarray, TNF and IL6 were among the most highly upregulated genes in both stimulated conditions, each of which was significantly inhibited by preincubation with hydroxychloroquine (HCQ). In contrast, following stimulation of macrophages with either TNF-α or IFN-α, which do not signal through TLR, the resultant gene expression was refractory to HCQ. Ligation of TLR7/8 resulted in increased histone methylation as measured by increased H3K4me2, a requirement for binding of NF-κB at certain promoters, specifically the kB1 region in the TNF promoter (ChIP-qPCR), which was significantly decreased by HCQ. In summary, these results support that the HCQ-sensitive phenotype of hY3 stimulated macrophages reflects the bifurcation of TLR downstream signals involving NF-κB and STAT 1 pathways and for the former dimethylation of H3K4. Accordingly, HCQ may act more as a preventive measure in downregulating the initial production of IFN-α or TNF-α and not affect the resultant autocoid stimulation reflected in TNF-α and IFN-α responsive genes. The beneficial scope of antimalarials in the prevention of organ damage, inclusive of heart block in an anti-Ro offspring or more broadly SLE, may include in part, a mechanism targeting TLR-dependent epigenetic modification.

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1. **The prevention, screening, and treatment of congenital heart block from neonatal lupus: A survey of provider practices**  
   Clowse M.E.B. Lupus Science and Medicine 2016;3:No page numbers.

Background There are presently no official guidelines about theprevention, screening, and treatment of congenital heart block(CHB) due to maternal Ro antibodies. The objective of this studywas to survey an international sample of providers to determinetheir current practices. Materials and methods A survey was designed by the organisingcommittee of the 9th International Conference of Reproduction,Pregnancy and Rheumatic Diseases. It was sent to 330 peoplewho were prior or current attendees of the conference or authorsof recent publications or abstracts at ACR 2012, 2013, or 2014on rheumatic diseases and pregnancy. Missing demographic information led to exclusion from analysis (n = 11).Results There were 48 respondents. Most (55%) follow &gt;15pregnancies in rheumatic patients per year, and 33% were practicing rheumatologists for &gt;15 years. Most were university-basedphysicians (88%) and from North America (42%) or Europe(42%).Screening In anti-Ro/SSA positive women, 80% recommendedserial fetal ECHOs, with most starting at gestational week 16(59%) and stopping at week 28 (25%), although the time to stopvaried widely. For women without a prior infant with neonatallupus, respondents recommend every other week (44%) orweekly (28%) fetal ECHOs. For women with a prior infant withneonatal lupus, 80% recommend weekly fetal ECHOs.Prevention Hydroxychloroquine was recommended by 67% ofrespondents to prevent CHB and most would start pre-pregnancy(62%).Treatment Respondents were asked about medications for varying degrees of CHB in a 20-week pregnant, anti-Ro and La positive SLE patient. Respondents recommended dexamethasone(53%) or HCQ (43%) for 1st degree HB; dexamethasone (88%)for 2nd degree HB; and dexamethasone (55%), IVIg (33%), orno therapy (27%) for complete HB. When dexamethasone wasstarted for 2nd degree CHB, 58% would stop dexamethasone ifit progressed to complete heart block, 47% would stop if heartblock disappeared, and 24% would stop if the 2nd degree CHBremained.Conclusions Despite the absence of official guidelines, manyphysicians with a clinical focus on pregnancy and rheumatic disease have developed similar patterns in the screening, prevention,and treatment of CHB. These include serial fetal ECHOs, preventive HCQ, and treatment of early heart block with dexamethasone. These practices are not uniform, however, and have notbeen formally tested in prospective trials. The next step in thisfield must include testing of these approaches to identify themost cost effective and efficacious plan for these pregnancies.

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1. **Can you teach an old dog new tricks? The antimalarial hydroxychloroquine shows promise in cardiac rate control through actions at the sino-atrial node**  
   Capel R.A. Heart 2015;101:No page numbers.

Hydroxychloroquine (HCQ) has been clinically prescribed since the early 1950s. Used as a prophylactic antimalarial and in chronic immune conditions, it has a good safety profile. Capitalising on a fortuitous clinical observation, we investigated the effects of HCQ on cardiac rate control. Application of HCQ to spontaneously-beating mouse atrial preparations revealed a dosedependent rate decrease (9 +/- 3% at 3 muM, 15 +/- 2% at 10 muM) which did not occur in the presence of funny current (I(f)) inhibitor ZD7288 (1 muM). 1 muM HCQ significantly reduced spontaneous beating rate in isolated guinea pig sino-atrial node myocytes. Voltage clamp studies revealed a significant, dosedependent I(f) inhibition (19 +/- 2% at 3 muM, 32 +/- 7% at 10 muM). Consistent with channel block, I(f) inhibition reduced maximal conductance without affecting voltage of half-activation. L-type calcium and delayed rectifier potassium currents were also significantly reduced. We performed mathematical safety modelling using methods described in. Modelling results for a maximum free therapeutic concentration of 1 mM indicated that the balance of potassium and calcium current inhibitions observed would not be expected to lengthen ventricular action potentials and placed HCQ in the 'low risk' category for Torsade de Pointes arrhythmia. HCQ is capable of reducing cardiac beating rate by effects on I(f). Given the excellent cardiac safety record of HCQ and safety profile modelling, it has potential as a rate-liming agent. Further work will be required in order to assess any potential cardiac benefits of HCQ in disease populations.

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1. **Controversies in the Management of Isolated Congenital Atrioventricular Block.**  
   DeNoble Anna E. Obstetrical & gynecological survey 2015;70(8):518-523.

Congenital atrioventricular block (CAVB) affects approximately 2% of fetuses of mothers with anti-Ro or anti-La antibodies, regardless of maternal rheumatologic symptoms. Anti-Ro and anti-La antibodies are antinuclear antibodies commonly found in autoimmune diseases. Congenital atrioventricular block is associated with a relatively high fetal morbidity and mortality, particularly more advanced degrees of block. There is significant controversy surrounding surveillance of anti-Ro/La-positive pregnancies and treatment of fetuses diagnosed with CAVB. Studies of dexamethasone in the treatment of CAVB have yielded conflicting results, with most suggesting only a limited potential benefit in first- and seconddegree CAVB and in cases complicated by fetal hydrops. Larger prospective studies are needed to further evaluate the efficacy of intravenous immunoglobulin in the treatment of CAVB and of intravenous immunoglobulin and hydroxychloroquine in the prevention of CAVB in fetuses of at-risk mothers. Surveillance and treatment regimens should be determined on a case-by-case basis, taking into consideration the degree of CAVB, costs, and potential adverse effects of treatment.

1. **Cost-effectiveness of screening and treatment of congenital complete heart block in mothers with positive SSA/RO-SSB/LA autoantibodies**  
   Kropf P.A. Journal of the American Society of Echocardiography 2015;28(6):No page numbers.

Background: Congenital complete heart block (CCHB) is a rare complication of maternal positive autoantibody serology that may have devastating consequences to the fetus. There is no consensus on the most cost effective method for screening, treatment and prevention of CCHB. <br/>Objective(s): Design a cost-effectiveness model to assess the hypothesis that screening for and treating CCHB is more cost-effective than not screening. <br/>Method(s): A decision tree model from the payer perspective was constructed to estimate the medical costs and outcomes of 4 CCHB screening and treatment strategies from pregnancy through the first 3 years of life: no fetal screening or treatment (reference strategy), weekly screening fetal echocardiography between 18 and 30 weeks gestation+/- hydroxychloroquine prophylaxis, and every 2 week screening fetal echocardiography between 18 and 30 weeks gestation. Analysis was also stratified by risk for developing CCHB including those at standard risk and those at higher risk including mothers with a previously affected child and those with hypothyroidism. Effectiveness of screening and treatment was estimated using aggregates of published outcomes data. Costs were estimated using Medicare reimbursement tables. <br/>Result(s): All methods were cost effective for high risk groups and for all antibody positive mothers combined. When standard risk mothers were analyzed alone the results were not cost effective. The costs per episode of heart block prevented are summarized in the following table. (Table presented) <br/>Conclusion(s): Screening and treating for CCHB is cost effective in high risk groups. Further strategies are needed to improve cost-effective screening for patients at standard risk for developing fetal complete heart block.

1. **Determinants of survival of fetuses with autoimmune congenital heart block and factors associated with neonatal and late-onset dilated cardiomyopathy: 214 cases from the french registry of neonatal lupus**  
   Levesque K. Annals of the Rheumatic Diseases 2015;74:102-103.

Background: Neonatal lupus syndrome (NLS) includes congenital heart block (CHB) and cardiomyopathies. Its optimal management is debated. <br/>Objective(s): We analyzed the mortality and morbidity of CHB, with special focus on risk factors. <br/>Method(s): This was a retrospective study of the French national registry of NLS. Inclusion criteria were high-degree CHB associated with maternal anti-SSA/SSB antibodies. <br/>Result(s): 214 CHB were included (202 in utero cases and 12 neonatal cases). These 214 fetuses or children were born to 195 mothers anti-SSA (99.5%) and/or anti-SSB antibodies (60%) positive. 51 mothers (26.2%) fulfilled the classification criteria for an autoimmune disease: systemic lupus erythematosus (n=23), Sjogren syndrome (n=14), undifferentiated connective tissue disease (n=7), or other autoimmune disease (n=7). The factors associated with feto-neonatal deaths (15.7%) were hydrops (p&lt;0.001; HR: 12.4 [95%CI: 4.7-32.7]) and prematurity (p=0.002; HR: 17.1 [95%CI: 2.8- 103.1]). During a median follow-up of 7 years [birth to 36.1 years], 148 of 187 surviving children (79.1%) had a pacemaker, 35 (18.8%, one missing data) had dilated cardiomyopathy (DCM), and 22 (11.8%) died. DCM was neonatal (n=13) or late-onset (n=22, diagnosed at a median age of 15.2 months [3.6 months-22.8 years]). Factors associated with neonatal DCM were maternal treatment with hydroxychloroquine, in utero cardiomegaly, in utero DCM, and hydrops. By contrast, only non-white race origin and significant in utero valvulopathy were associated with late-onset DCM. On multivariate analysis, only in utero DCM was associated with neonatal DCM (p=0.0001; HR 15.99 [95%CI: 3.93-65.01]), whereas non-white race origin was associated with late-onset DCM (p=0.0147; HR 3.65 [95%CI: 1.28-10.0]). For children who survived the neonatal period (n=179), the risk of death during follow-up was 7.8%. On multivariate analysis, the only factor associated with late mortality was postnatal DCM (neonatal and late-onset DCM) (p&lt;0.0001; HR 36.48 [95% CI 8.11-164.13]). The probability of survival at 10 years of age for a child with CHB born alive was 87.1%: 23.1% in the presence of neonatal DCM, 53.9% for those who developed a late-onset DCM requiring treatment versus 98.6% in those without DCM. Fluorinated steroid in utero treatment was not associated with CHB regression, survival or absence of late-onset DCM. <br/>Conclusion(s): The factors associated with late-onset DCM differ completely from those associated with neonatal DCM. Our findings do not support the use of fluorinated steroids for CHB.

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1. **End Stage Renal Disease (ESRD) in patients with rheumatoid arthritis**  
   Paudyal S. Arthritis and Rheumatology 2015;67:No page numbers.

Background/Purpose: Substantial progress has been made in the treatment of rheumatoid arthritis (RA) and life expectancy has increased. As the population of patients with RA continues to age, they may be more likely to suffer from diseases of aging, including ESRD. However, the characteristics of patients with RA and ESRD, treatment patterns for RA in the setting of ESRD and the impact of RA on mortality in ESRD have not been previously been examined. The purpose of this study was to determine the prevalence of ESRD and reasons for dialysis in RA, treatment modalities for RA in the setting of ESRD and five year cardiovascular mortality in patients with RA and ESRD compared to those with ESRD without RA. <br/>Method(s): Retrospective cohort study of adult ESRD patients with RA without HIV in the United States Renal Data System (USRDS) beginning in calendar year 2011. Medicare Part D beneficiary data was used to determine filled prescriptions for medications that might be used to treat RA including corticosteroids, DMARDs and biologics. Cox proportional hazard models were estimated to determine five year cardiovascular-related mortality in patients with RA compared to all others with ESRD without RA. <br/>Result(s): There were 28,589 patients with RA and ESRD in 2011. Based on population estimates of the frequency of RA in adults in the United States, approximately 2% of adult patients with RA have ESRD. Patients with ESRD and RA are more likely to be female, to have hypertension, diabetes, atrial fibrillation and cardiovascular events (p&lt;0.01 for all) than those with ESRD without RA. Hypertensive renal disease (30%) and type II diabetes (25%) are the most common causes of ESRD in RA; amyloidosis, vasculitis and analgesic nephropathy are uncommon, accounting for less than 5% of all cases. More than half of ESRD patients with RA had a filled prescription for a medication for RA treatment; most commonly prednisone (42% of all prescriptions). Ten percent of all filled prescriptions were for hydroxychloroquine; 2.63% for leflunomide and 1.39% for sulfasalazine. Biologics were a rare class of filled prescription therapies (etanercept 1.59%;adalimumab 1.07%; golimumab, infliximab, anakinra and abatacept each comprised &lt;1% of total filled prescriptions in this population). After adjustment for covariates, compared to patients without RA with ESRD, five year cardiovascular mortality in patients with RA and ESRD was significantly increased (HR 1.42 (95%CI 1.38-1.47). <br/>Conclusion(s): ESRD is infrequent in patients with RA but has a significant impact on cardiovascular mortality. Similar to the general ESRD population, hypertension and diabetes mellitus are the most common causes of dialysis. Prednisone and hydroxychloroquine are the most frequent prescriptions filled that could be used to treat RA; use of biologics appears uncommon in this population. Further prospective studies of the impact of ESRD on outcomes in RA and optimal treatments for RA in the setting of ESRD are needed.

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1. **Hydroxychloroquine reduces heart rate by modulating the hyperpolarization-activated current If: Novel electrophysiological insights and therapeutic potential.**  
   Capel Rebecca A. Heart rhythm 2015;12(10):2186-2194.

BACKGROUNDBradycardic agents are of interest for the treatment of ischemic heart disease and heart failure, as heart rate is an important determinant of myocardial oxygen consumption.OBJECTIVESThe purpose of this study was to investigate the propensity of hydroxychloroquine (HCQ) to cause bradycardia.METHODSWe assessed the effects of HCQ on (1) cardiac beating rate in vitro (mice); (2) the "funny" current (If) in isolated guinea pig sinoatrial node (SAN) myocytes (1, 3, 10 µM); (3) heart rate and blood pressure in vivo by acute bolus injection (rat, dose range 1-30 mg/kg), (4) blood pressure and ventricular function during feeding (mouse, 100 mg/kg/d for 2 wk, tail cuff plethysmography, anesthetized echocardiography).RESULTSIn mouse atria, spontaneous beating rate was significantly (P < .05) reduced (by 9% ± 3% and 15% ± 2% at 3 and 10 µM HCQ, n = 7). In guinea pig isolated SAN cells, HCQ conferred a significant reduction in spontaneous action potential firing rate (17% ± 6%, 1 μM dose) and a dose-dependent reduction in If (13% ± 3% at 1 µM; 19% ± 2% at 3 µM). Effects were also observed on L-type calcium ion current (ICaL) (12% ± 4% reduction) and rapid delayed rectifier potassium current (IKr) (35% ± 4%) at 3 µM. Intravenous HCQ decreased heart rate in anesthetized rats (14.3% ± 1.1% at 15mg/kg; n = 6) without significantly reducing mean arterial blood pressure. In vivo feeding studies in mice showed no significant change in systolic blood pressure nor left ventricular function.CONCLUSIONSWe have shown that HCQ acts as a bradycardic agent in SAN cells, in atrial preparations, and in vivo. HCQ slows the rate of spontaneous action potential firing in the SAN through multichannel inhibition, including that of If.

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1. **Novel Therapies for Myocardial Irritability following Extreme Hydroxychloroquine Toxicity.**  
   McBeth Paul B. Case reports in emergency medicine 2015;2015:692948.

Introduction. Hydroxychloroquine (HCQ) overdose is rare and potentially deadly when consumed in large doses. Management of severe HCQ toxicity is limited and infrequently reported. This report presents the case of a massive ingestion of HCQ. Case Report. A 23-year-old female presents following an intentional ingestion of approximately 40 g of HCQ. Within six hours after ingestion, she developed severe hemodynamic instability resulting from myocardial irritability with frequent ventricular ectopic activity leading to runs of polymorphic ventricular tachycardia (PMVT) and ventricular fibrillation (VF) requiring multiple defibrillations. Additional treatments included intravenous diazepam, epinephrine, norepinephrine, sodium bicarbonate, and magnesium sulfate. Despite the ongoing hemodynamic instability, the patient was also treated with Intralipid (ILE) and received hemodialysis. Improvements in her hemodynamics were observed after 18 hours. She survived her massive overdose of HCQ. Conclusion. HCQ poisoning is rare but serious because of its rapid progression to life-threatening symptoms. Hemodynamic support, gastric decontamination, electrolyte monitoring and replacement, and management of arrhythmias are the mainstays of treatment. The combined role of dialysis and ILE in the setting of massive HCQ overdose may improve outcomes.

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1. **Phase II trial of autophagy inhibition using hydroxychloroquine (HCQ) with FOLFOX/bevacizumab in the First-line treatment of advanced colorectal cancer**  
   Loaiza-Bonilla A. Journal of Clinical Oncology 2015;33(15):No page numbers.

Background: We have shown that autophagy, the regulated dissolution of cellular elements to maintain survival in adverse environmental conditions, is a determinant of resistance to chemotherapy in colorectal cancer models, and is reversed by chloroquine (Selvakumaran M, et al. Clin Cancer Res, 2013). A Phase I runin demonstrated that full doses of mFOLFOX6/bevacizumab were tolerated with HCQ 600mg PO twice daily. <br/>Method(s): We report a Phase II trial in previouslyuntreated patients with metastatic colorectal cancer. Patients were treated every two weeks with 5FU (400mg/m<sup>2</sup> bolus, then 2400 mg/m<sup>2</sup> over 46h) together with leucovorin 200mg/m<sup>2</sup>, oxaliplatin 85mg/m<sup>2</sup>, bevacizumab 5mg/kg, all IV, repeated every two weeks, with HCQ as above. After 12 cycles, oxaliplatin was omitted and patients were continued on 5FU, bevacizumab, and HCQ. Imaging was performed every 8 weeks. <br/>Result(s): Twentyfour patients (pts) have been accrued, of whom 23 are eligible: 10 female/13 Male; 19 Caucasian/3 Black/1 EastAsian. Toxicity has been generally tolerable. Grade 3 effects included neutropenia 9/23), diarrhea (1/23), and anorexia (1/23). There were two episodes of myocardial infarction, one fatal, one of atrial arrhythmia, and two of pulmonary embolism in the course of the trial. 20/23 patients were able to maintain full dose of HCQ. Patients evaluable for response include 19 (4 pts too early). There were 1 complete response (5%), 9 partial responses (47%), and 7 stable disease (37%). Four patients went off study for resection of metastatic disease after 325 months. Median Progression-free and overall survival have not been reached. Autophagy biomarkers in peripheral mononuclear cells show autophagy inhibition in the majority of patients. Six of thirteen patients with genomic testing available had a TP53 mutation. Four of these six patients had a major response (1CR, 3 PR). <br/>Conclusion(s): The combination of FOLFOX/bevacizumab with HCQ is an active regimen in unselected patients with colorectal cancer. A randomized Phase II trial of the combination is in development.

1. **Cardiac conduction disorders in patients with rheumatic disease receiving hydroxychloroquine**  
   Prasanna P.V. Indian Journal of Rheumatology 2014;9(5):No page numbers.

Introduction: Prolonged use of chloroquine has been implicated in development of conduction disorders. Limited data is available with hydroxychloroquine (HCQ). <br/>Objective(s): To evaluate cardiac conduction disorders over one year in patients receiving HCQ as a part of their treatment. <br/>Method(s): This is longitudinal observational study between 2013-14. All patients with rheumatic diseases initiated on HCQ (200e400mg/day) were included. Patients with established cardiac diseases, electrolyte abnormalities, on drugs causing conduction disorders, those refusing consent, were excluded. Each patient had ECG at baseline, six and twelve months. Electrolytes at baseline Echocardiography when necessary was done and when any cardiac abnormality was detected. ECG's were cross checked by cardiologist. <br/>Result(s): 276 patients were screened and six excluded. 166 patients completed six months and 92 one year follow-up. First degree AV block at 6 months in one patient, ventricular premature beats in one patient after 15 days on HCQ observed. One had exfoliative, blistering skin rash temporally correlated with HCQ. One patient of RA died at home of unknown cause. <br/>Conclusion(s): Periodic cardiac evaluation of patients receiving long term antimalarial drug is necessary. Conduction disorders observed were similar to that expected in general population thus adding further evidence on safety of hydroxychloroquine.

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1. **Ciprofloxacin-induced syndrome of inappropriate Antidiuretic hormone; Anaphylactic Shock due to Thrombolytic administration; Hydroxychloroquine- induced qt-interval prolongation; Complex regional pain syndrome after tetanus Toxoid injection**  
   Mancano M. Hospital Pharmacy 2014;49(4):329-333.

The purpose of this feature is to heighten awareness of specifi c adverse drug reactions (ADRs), discuss methods of prevention, and promote reporting of ADRs to the US Food and Drug Administration's (FDA's) MedWatch program (800-FDA-1088). If you have reported an interesting, preventable ADR to MedWatch, please consider sharing the account with our readers. Write to Dr. Mancano at ISMP, 200 Lakeside Drive, Suite 200, Horsham, PA 19044 (phone: 215-707-4936; e-mail: mmancano@temple.edu). Your report will be published anonymously unless otherwise requested. This feature is provided by the Institute for Safe Medication Practices (ISMP) in cooperation with the FDA's MedWatch program and Temple University School of Pharmacy. ISMP is an FDA MedWatch partner.&#xa9; 2014 Thomas Land Publishers, Inc.

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1. **DMARD use after an initial acute mi is associated with reduced risk of a recurrent event and mortality**  
   Zhang J. Arthritis and Rheumatology 2014;66:No page numbers.

Background/Purpose: Previous studies have suggested that disease modifying anti-rheumatic drugs (DMARDs) may reduce cardiovascular risk among patients with rheumatoid arthritis (RA). This analysis examined whether DMARDuse after an initial acute myocardial infarction (MI) was associated with reduced risk of having a recurrent MI and mortality among older RA patients. <br/>Method(s):We identified RA patients who were enrolled in Medicare (which covers more than 90% of all individuals 65 or older in the U.S.) and had an acute MI from 2006 to 2011. Eligibility criteria included the following: 1) had &gt;=2 rheumatologist visits with a diagnosis code for RA during a baseline period of at least 365 days prior to follow-up start; 2) had an acute MI defined as having an inpatient hospital claim with a discharge ICD-9 diagnosis code 410.X (excluding 410.x2) in any position and at least one overnight inpatient stay, unless the patient died. Follow-up started at time of discharge from the hospital after the initial MI. We used multivariable proportional hazard regression to examine the association between DMARD use after the initial MI and risk of having a recurrent MI and mortality, adjusting for factors ascertained during baseline (socio-demographics and CHD risk factors [diabetes, hypertension, chronic kidney disease, abdominal aortic aneurism, peripheral arterial disease, atrial fibrillation, hyperlipidemia, tobacco use, overweight/obese, heart failure, chronic obstructive pulmonary disease]), and after MI (medications for hypertension, hyperlipidemia, and RA). Exposure to DMARDs after MI was categorized into the following exclusive hierarchical groups: 1) any anti-TNF biologic DMARD use; 2) any non-anti-TNF biologic DMARD use; 3) any methotrexate (MTX) use; 4) any non-MTX non-biologic DMARDs use (reference group, mostly hydroxychloroquine, sulfasalazine, and leflunomide use); and 5) no DMARD use. <br/>Result(s):We identified 13,985 eligible RA patients with mean age 74 (SD 11) years, 74% of whom were women. Compared to the reference group of any non-biologic and non-MTX DMARD use, non-TNF biologic DMARD use was associated with reduced mortality (hazard ratio [HR] 0.30 and ; 95% confidence interval [CI] 0.14-0.68]) and recurrent MI (HR: 0.22, 95% CI: 0.07-0.69). Compared to the same reference group, any MTX use was associated with reduced mortality (HR: 0.71, 95% CI: 0.62-0.81) but not with recurrent MI. Oral glucocorticoid use (compared to no use) was significantly associated with increased mortality at low (&lt;= 7.5mg/d [HR: 1.26, 95% CI: 1.18-1.34]) and high doses (&gt; 7.5mg/d [HR: 1.73, 95% CI: 1.60-1.87]) and with recurrent MI at doses &gt; 7.5 mg/d (HR: 1.29, 95% CI: 1.12-1.48). <br/>Conclusion(s):Our findings suggest that among older RA patients, non-TNF biologic use and MTX use after an acute MI were associated with reduced risk of having a recurrent MI and mortality compared to non-biologic and non-MTX DMARD use, where glucocorticoid use was associated with increased risk of both outcomes. These results should be interpreted with caution given the possibility of residual confounding in observational studies.

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1. **Evolution of systemic sclerosis overlap syndrome**  
   Desinova O. Clinical and Experimental Rheumatology 2014;32(2):No page numbers.

Objective. To study evolution and outcome of SSc-RA and SSc-PM/DM. Material and methods. There were 100 pts SSc overlap syndrome: 68 SSc-PM/DM and 32 SSc-RA (17 male, 83 females; mean age 45+/-14,4; disease duration 7 [2-10] years; follow-up 10 years). Results. 71% pts has had SSc-PM/DM and SSc-RA within the first three years of disease and in 40% of them during the 1st year after onset. The first symptoms of pts were Rainaud's syndrome, edema hands, arthralgia and rare isolated joint and musculskeletal involvement (7% and 2%). All pts were treated corticosteroids and 74% of them received cytotoxic (methotrexate 48%; cyclophosphamide 10%; azathioprine 5%), hydroxychloroquine 11%, D-penicillamine 7%. Identified two variants of evolution: I- favorable 79%; II unfavorable 21% (includ deaths (10%)). The favorable evolution was observed in pts with onset before 40 years, the relative stabilization of the process - from the onset of the disease before the age of 25 years, an unfavorable outcome - in pts with age of onset of the disease for more than 40 years, where pts SSc-PM/DM prevailed. The peripheral symptoms SSc-RA has not progressed for 10 years and has decreased: skin induration (lSSc/dSSc 97%/3% and 100%/0%), hyperpigmentation (34% and 9%), flexion contractures (81% and 72%), arthritis (100% and 78%), rheumatoid nodules disappeared. Rainaud's syndrome was less expressed. Howere clinical features SSc increased: telangiectasias (37,5% and 47%), calcinosis (31% and 47%), osteolysis (25% and 28%), conduction blocks(53% and 56%) and arrhythmia (9% and 19%), interstitial lung disease (9% and 19%), esophageal involvement (66% and 69%). Decrease of ESR was observed in 1/3 of pts. The SSc-PM/DM pts has decreased skin induration (lSSc/dSSc 68%/32% and 100%/0%), hyperpigmentation (27% and 18%), skin symptoms of DM (44% and 7%), joint involvement (56% and 15%) for 10 years. PM was in remission in all patients. Rainaud's syndrome progressed with the development mainly scars (18% and 37%), increased telangiectasias (50% and 59%), calcinosis (32% and 56%), osteolysis (23,5% and 26%), conduction blocks(53% and 57%) and arrhythmia (15% and 18%), interstitial lung disease (12% and 15%), esophageal involvement (78% and 88%). Decrease of ESR was observed in 2/3 of pts. Conclusion. Adverse prognostic factors of SSc overlap syndrome: age of onset after 40 years, rapidly progressive acute with generalization of the process and features of the PM in the first year of the disease, late diagnosis of the disease and inadequate therapy.

1. **Immunosuppressive therapy and upgrade of conventional pacemaker to CRT-D for dilated cardiomyopathy due to cardiac sarcoidosis, with discordance of disease activity between PET-CT and CMR**  
   Arnold A.D. European Heart Journal 2014;35:1205.

Cardiac sarcoidosis can result in arrhythmia and heart failure. Diagnosis is aided by multiple imaging techniques whilst immunosuppression and device therapy are therapeutic options. PS, 49-year-old man, was referred to our tertiary cardiac and respiratory centre for management of heart failure. Three years previously, he presented to his local hospital with third degree AV block and an MRI-compatible dual chamber pacemaker was implanted. A high-resolution CT thorax revealed mediastinal lymphadenopathy and beading of the septae in keeping with pulmonary sarcoidosis. Transthoracic Echocardiography (TTE) and Cardiac Magnetic Resonance (CMR) were suggestive of cardiac involvement. Recently, he developed dyspnoea and fatigue. On cardiopulmonary exercise testing his peak VO2 was 18.7ml/kg/min (57% of his predicted value) and further imaging was undertaken. TTE revealed a moderately dilated LV with severely impaired function (EF 26%, significant hypokinesis or akinesis in all segments except for a preserved basal to mid inferolateral wall) with a severely dilated and impaired RV. CMR confirmed severe biventricular dysfunction and dilatation. There was extensive sub-epicardial late gadolinium enhancement, sparing the endocardium, but becoming transmural in the anterior, septal and inferior LV walls and RV anterior wall. On STIR sequences, no active myocardial inflammation or oedema was seen. Resting Myocardial Perfusion Studies (MPS) and cardiac Positron Emission Tomography (PET) CT imaging demonstrated perfusion-metabolism mismatch with active inflammatory uptake in the inter-ventricular (SUVmax 7.0) and inter-atrial (SUVmax 8.1) septum with patchy LV and RV uptake and active inflammation in lymph nodes. These findings were felt to be in keeping with a diagnosis of dilated cardiomyopathy and complete heart block secondary to cardiac sarcoidosis with coexistent pulmonary sarcoidosis. Pulsed intravenous methylprednisolone was initiated along with methotrexate and hydroxychloroquine. ACE inhibitors were started and spironolactone will be introduced (beta blockade was not tolerated). As his underlying rhythm was complete AV block, he was RV pacing over 95% of the time. In view of this and the risk of ventricular arrhythmia, we will upgrade his pacemaker to a cardiac resynchronisation therapy defibrillator (CRT-D). This case is unusual as there was evidence of active inflammation on PET-CT but not CMR, highlighting the challenge of integrating imaging modalities to guide management. There is also the question of applying evidence established in ischaemic and dilated cardiomyopathy (CRT-D) to a sarcoid population.

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1. **Prevention and treatment in utero of autoimmune-associated congenital heart block.**  
   Saxena Amit Cardiology in review 2014;22(6):263-267.

Transplacental transfer of maternal anti-Ro and/or anti-La autoantibodies can result in fetal cardiac disease, including congenital heart block and cardiomyopathy, called cardiac neonatal lupus (NL). Thousands of women are faced with the risk of cardiac NL in their offspring, which is associated with significant morbidity and mortality. There are no known therapies to permanently reverse third-degree heart block in NL, although several treatments have shown some effectiveness in incomplete heart block and disease beyond the atrioventricular node. Fluorinated steroids taken during pregnancy have shown benefit in these situations, although adverse effects may be concerning. Published data are discordant on the efficacy of fluorinated steroids in the prevention of mortality in cardiac NL. β-agonists have been used to increase fetal heart rates in utero. The endurance of β-agonist effect and its impact on mortality are in question, but when used in combination with other therapies, they may provide benefit. No controlled experiments regarding the use of plasmapheresis in cardiac NL have been performed, despite its theoretical benefits. Intravenous immunoglobulin was not shown to prevent cardiac NL at a dose of 400 mg/kg, although it has shown effectiveness in the treatment of associated cardiomyopathy both in utero and after birth. Retrospective studies have shown that hydroxychloroquine may prevent the recurrence of cardiac NL in families with a previously affected child, and a prospective open-label trial is currently recruiting patients in order to fully evaluate this relationship.

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1. **Prolongation of heart rate-corrected QT interval is a predictor of cardiac autonomic dysfunction in patients with systemic lupus erythematosus.**  
   Nomura Atsushi Rheumatology international 2014;34(5):643-647.

Heart rate-corrected QT interval duration (QTc) has been shown to be related to cardiac autonomic dysfunction in patients with diabetes mellitus, although this association has not been previously described in patients with systemic lupus erythematosus (SLE). We retrospectively reviewed the medical records of 91 SLE patients and 144 non-SLE connective tissue disease patients visiting our clinic from November 2010 to April 2011. We compared ambulatory heart rate identified by pulse measured by automated machine in an outpatient waiting area versus resting heart rate identified on prior screening electrocardiogram. Heart rate differences were analyzed in relation to QTc interval and other characteristics. Ambulatory and resting heart rate differences were larger among SLE patients with QTc prolongation (QTc > 430 ms) than those without QTc prolongation (mean difference, 15.9 vs. 9.6, p = 0.001). In multivariate analysis, differences in heart rate were associated with QTc prolongation (OR 1.10, 95 % CI 1.01-1.21; p = 0.038), independent of age, duration of disease, immunosuppressant use, hydroxychloroquine use, diabetes mellitus, cardiac abnormality, anti-Ro/SS-A antibody positivity, or resting heart rate. Cardiac autonomic dysfunction is a common manifestation of SLE and may be related to QTc prolongation.

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1. **Warfarin related nephropathy in the absence of supra-therapeutic INR**  
   Iqbal H.I. American Journal of Kidney Diseases 2014;63(5):No page numbers.

Warfarin therapy can result in acute kidney injury (AKI) or an accelerated progression of chronic kidney disease (CKD) by glomerular hemorrhage, renal tubular obstruction by red blood cells (RBCs) casts or interstitial nephritis (IN). To date the combination of glomerular hemorrhage with hypersensitivity to warfarin resulting in leucocytoclastic vasculitis (LCV) in the absence of supra-therapeutic INR (International normalized ratio) has not been reported. We are presenting a 73 year old male with history of atrial fibrillation (on warfarin), hypertension and CKD stage-2 (baseline creatinine 1.3), presented with sudden onset of dark colored urine, increasing creatinine associated with a diffuse palpable erythematous non-pruritic rash in extremities for 5 weeks. He was started on prednisone and Plaquenil after a skin biopsy showed LCV. With one week of the above therapy and holding warfarin transiently around skin biopsy, the rash completely resolved but he continued to have intermittent hematuria with worsening renal parameters when warfarin was restarted. On review of records he did not have any INR value of greater than 2.5 in the last 2 months prior to presentation. Urine microscopy was consistent with dysmorphic RBC's, raised concern about vasculitis glomerulopathy in the presence of the skin biopsy findings. Renal workup for AKI revealed unremarkable C3, C4, hep B Ab, hep C Ab, SPEP, serum immunofixation, ANA, anti-GBM Ab and PR3 Ab. MPO Ab was borderline positive at 1.0 Units. Urine spot collection showed 542mg of proteinuria and the renal ultrasound was unremarkable. The renal biopsy revealed RBC's in the tubular lumen and in the bowman space, highly suspicious for WRN. There were no signs to suggest IN or vasculitis. Warfarin was withdrawn and subsequently the patient's renal parameters started to improve. Literature has shown cases of acute interstitial nephritis with LCV from warfarin as well as cases of WRN but no case has been reported thus far in the absence of supratherapeutic INR (i.e. INR &lt;3). Hence raising concerns for what the mechanism of AKI is in WRN as well as awareness for nephrologists to look out for WRN even when the INR is &lt;3.

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1. **An unusual case of chest pain: Pericarditis secondary to hydralazine-induced lupus**  
   Wrenn K. Journal of General Internal Medicine 2013;28:No page numbers.

LEARNING OBJECTIVE 1: Recognize clinical manifestations of druginduced lupus LEARNING OBJECTIVE 2: Diagnose drug-induced lupus CASE: A 60-year-old male with hypertension, hyperlipidemia, diabetes, and coronary disease presented to the emergency department reporting a two-day history of intermittent chest pain with exertion, followed by an episode of chest pain at rest. He denied associated symptoms. His electrocardiogram was unchanged, and cardiac enzymes were negative. He was admitted for a stress test, which was negative for ischemia. During the admission, he developed fevers, leukopenia, transaminitis, arthritis, and new onset atrial fibrillation. His exam was notable for a pericardial friction rub and pulsus paradoxus of 12. Echocardiogram revealed a moderate pericardial effusion with evidence of elevated intra-pericardial pressure, and he underwent pericardiocentesis. Diagnostic work-up revealed a positive antinuclear antibody (ANA) with a 1:160 titer. Anti-dsDNA antibody was negative, but anti-histone antibody was positive. He had been on hydralazine for 1.5 years, and was diagnosed with hydralazine-induced lupus. Hydralazine was discontinued, he was started on prednisone and hydroxychloroquine, and he has since fully recovered. DISCUSSION: More than 80 medications have been identified as causes of drug-induced lupus (DIL). Procainamide, hydralazine, and quinidine are most commonly implicated; other medications include minocycline and anti-TNF alpha therapy. Unlike idiopathic systemic lupus erythematosus (SLE), which usually affects females ages 20-40, DIL affects men and women equally, with the average age of onset around 50. Clinical manifestations vary based on the inciting agent, and range from limited cutaneous involvement to systemic symptoms including fever, myalgias, arthralgias, arthritis, hepatosplenomegaly, and serositis. Hematologic abnormalities, renal disease, and neurologic disease are less common. Symptoms are generally milder than with SLE, but some cases are life threatening. Typical symptoms of hydralazine-induced lupus include fever, rash, arthralgias, myalgias, pleuritis, and leukopenia (1). Pericarditis is less common, occurring in &lt;5 % of cases (2). Approximately 95 % of patients with DIL have a positive ANA, and &gt;90 % have anti-histone antibodies. Anti-dsDNA antibodies are rare. When a patient taking one of the implicated medications presents with the above symptoms, DIL should be suspected. However, confirming the diagnosis can be difficult, as there are no formal diagnostic criteria for DIL. A proposed set of criteria includes sufficient and continuing exposure to a specific medication, at least one symptom compatible with SLE, no previous history of SLE, and resolution of symptoms within weeks to months after discontinuation of the medication (2). The presence of anti-histone antibodies in the absence of anti-dsDNA antibodies strongly suggests DIL, but is not an official criterion for diagnosis (2). ANA positivity is also not a requirement for diagnosis. In general, DIL is a reversible condition with a favorable prognosis, but it is critical to diagnose early. Treatment involves cessation of the medication and supportive care. NSAIDs and anti-malarial agents may be used for musculoskeletal symptoms, and severe cases may benefit from treatment with corticosteroids. If symptoms do not resolve after stopping the medication, other diagnoses should be considered.

1. **Case report: A complex case of heart failure**  
   Novati P. Italian Journal of Medicine 2013;7:88.

It is reported a case of multifactorial heart failure. 69 years old woman, smoker, hypertensive, multinodular goiter, rheumatoid arthritis and previous pericarditis. Her treatment was discountinous and she did not perform checks for years. Admitted to hospital for severe dyspnea, peripheral edema, weight loss and hiporexia, she presented the framework of congestive heart failure, atrial fibrillation (AF) and signs of left ventricular disfunction. Alcohol dependance was later discovered. She was treated with high-dose diuretics, beta-blocker, digital plus verapamil, thiamazole and steroids plus hydroxychloroquine; warfarin was also started. Her conditions improved but AF and moderate pleural effusion persisted. At home she returned to fever, unresponsive to antibiotic therapy. At readmission it should be noted massive pleural effusion on the right, restoring of sinus rythm; modest peripheral edema, fever up to 38degree. After microbial cultures we removed three times transudate pleural fluid and then she started again high dose steroidal and antibiotic therapy with resolution of fever. Echocardiography showed moderate to severe pulmonary hypertension and normal systolic function of ventricles. After optimising medical therapy, she remained in good control and sinus rhythm; well-controlled the thyroidal function and autoimmune disease. The case is interesting for the multifactorial genesis: thyrotoxicosis, autoimmune disease, damage from alcohol, hypertensive heart disease, pulmonary hypertension, etc. that stimulated discussion for complex diagnosis and therapy.

1. **Long QT and hydroxychloroquine; a poorly recognised problem in rheumatology patients**  
   Negoescu A. Arthritis and Rheumatism 2013;65:No page numbers.

Background/Purpose: Hydoxychloroquine (HCQ) is widely used for the treatment of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) with a side-effect profile including myopathy and cardiotoxicity. Acute HCQ poisoning has been reported to cause a prolonged QT interval, hypokalaemia and a prolonged QRS complex. RA itself is an independent risk factor for cardiovascular (CV) disease and a recent study has shown that patients are 40% more likely to develop atrial fibrillation. Our objective was to determine if alterations in cardiac conductivity with HCQ is appreciated and whether patients should undergo monitoring ECGs. <br/>Method(s): A retrospective analysis of our electronic medical records was undertaken to determine whether patients had had an ECG prior to, and at least 6 months after, starting HCQ and whether there had been a resultant change in the QT interval. Only resting standard 12-lead ECGs with both QT and QTc interval values measured were used. A past history of cardiac disease, arrhythmias or other medications know to prolong the QT interval were documented. The threshold for diagnosis of long QT syndrome was a QTc interval of 450 ms. <br/>Result(s): 1537 patients currently taking HCQ were identified. 102 patients were found to have had ECGs before, and at least 6 months after, starting HCQ therapy. Of these only 19 patients had suitable ECGs for analysis. This comprised 16 females and 3 males, with a mean age of 62.5 years (range 19-87). CV risk factors included hypertension (n=7), obesity (n=5), ischaemic heart disease (n=4), deep vein thromboses (n=3) and cerebral vascular accidents (n=3). Known diagnoses of arrhythmias included atrial fibrillation (n=2), supraventricular tachycardia (n=1) and an unspecified arrhythmia (n=1). The patients had been on HCQ therapy for a mean of 3.6 years (range 1.3-9.2) and were receiving either 200 mg (n=4) or 400 mg (n=15) per day. The initial ECGs had a mean QTc interval of 424 ms (range 377-584). The post HCQ ECGs had a mean QTc interval of 449 ms (range 387-620). The mean change in QTc was 25 ms (range 66-143). Overall 4 patients had a long QTc prior and 8 patients after initiation of HCQ therapy (table 1). 8 patients were also taking &gt;=1 medication known to prolong the QT interval. <br/>Conclusion(s): The appreciation of potential drug-induced arrhythmias in Rheumatology patients to date has not been well described. Our analysis showed a trend in prolongation of the QTc following treatment with HCQ. As we examined only a surrogate outcome, namely a change in QTc interval, we were unable to determine whether this was clinically relevant. It is difficult to distinguish whether the ECG changes observed were due to HCQ or due to other factors. Nevertheless as only a small number of patients had ECGs we have highlighted the under-recognition of this particular problem. In order to truly determine HCQ as a culprit, a prospective study is required in this area. (Table Presented).

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1. **Maternal autoantibody levels in congenital heart block and potential prophylaxis with antiinflammatory agents.**  
   Tunks Robert D. American journal of obstetrics and gynecology 2013;208(1):64.

OBJECTIVEThe importance of maternal autoantibody levels in congenital heart block and elucidation of maternal factors that may reduce disease burden require further clarification.STUDY DESIGNPregnancies complicated by maternal anti-Ro antibodies from 2007 through 2011 were retrospectively reviewed.RESULTSIn all, 33 women were followed up throughout pregnancy. Semiquantitative maternal anti-La levels were significantly higher in pregnancies complicated by fetal heart block of any degree (median difference, 227.5; P = .04), but there was no difference in maternal anti-Ro levels. In all, 94% of fetuses maintained normal conduction when the mother was treated with hydroxychloroquine or daily prednisone therapy throughout pregnancy, compared to 59% in the untreated group (odds ratio, 0.1; P = .04).CONCLUSIONPregnancies complicated by fetal heart block did not have higher levels of maternal anti-Ro antibodies. Maternal anti-La level may be a useful predictor of fetal heart block. Maternal treatment with either hydroxychloroquine or daily low-dose prednisone throughout pregnancy may provide a protective effect.

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1. **Preventing congenital neonatal heart block in offspring of mothers with anti-SSA/RO and anti-SSB/LA antibodies: Review of literature and registered trials**  
   Elkayam U. Fertility and Sterility 2013;100(3):No page numbers.

OBJECTIVE: Since offspring of women with anti-SSA/Ro - SSB/La antibodies are believed at risk for congenital heart block (CHB), and since it is unknown whether this risk can be reduced, to review current knowledge of what constitutes standard of care treatment. DESIGN: Review of literature. MATERIALS AND METHODS: Under appropriate key words and phrases we searched Medline/PubMed and Google Scholar for years 2000-2013. Reference lists were further reviewed, and relevant manuscripts were pulled. We also reviewed www.clinicaltrials.gov for registered studies. In absence of randomized prospective clinical trials, a meta-analysis was not feasible. We, therefore, reviewed lower evidence level studies individually. <br/>RESULT(S): Risk of CHB actually appears more closely associated with general autoimmunity than, specifically, with SSA/Ro - SSB/La antibodies. This and other observations raise questions whether CHB is caused by passively transferred maternal autoimmunity, as is currently widely believed. Observational studies suggest possible effectiveness of intravenous gamma globulin (IV-Ig) and hydroxychloroquine (Plaquenil) in reducing CHB risk. Evidence for both is, however, inconclusive, and studies are biased in favor of hydroxychloroquine and against IV-Ig. <br/>CONCLUSION(S): Current evidence of effectiveness for any treatment has to be judged as insufficient. Amongst available treatment options, some considerations favor IV-Ig over hydroxychloroquine or, alternatively, suggest treatment with IV-Ig periconceptionally and into early gestation, with hydroxychloroquine added or replacing IV-Ig at approximately 10 weeks gestational age. Benefits for the utilization of steroid drugs are unclear. Since no treatment can be considered as established, prevention of CHB in offspring should be considered experimental, and performed under appropriate study conditions.

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1. **Preventing congenital neonatal heart block in offspring of mothers with anti-SSA/Ro and SSB/La antibodies: a review of published literature and registered clinical trials.**  
   Gleicher Norbert Autoimmunity reviews 2013;12(11):1039-1045.

Offspring of women with anti-SSA/Ro-SSB/La antibodies are believed to be at risk for congenital heart block (CHB). Whether this risk can be reduced, and what constitutes standard of care treatment is, however, unclear. The objective of this review therefore was to determine whether currently proposed standard of care treatments to avoid CHB in offspring of mothers at risk are evidence-based. To do so, we conducted a review of the literature under appropriate keywords and phrases in Medline/PubMed and Google Scholar for the years 2000-2013. Reference lists were further reviewed, and relevant manuscripts were pulled. We also reviewed www.clinicaltrials.gov for registered studies. In the absence of randomized prospective clinical trials, a meta-analysis was not feasible. We, therefore, reviewed lower evidence level studies individually. Risk of CHB actually appears more closely associated with general autoimmunity than, specifically, with SSA/Ro-SSB/La antibodies. This and other observations raise questions whether CHB is caused by passively transferred maternal autoimmunity, as is currently widely believed. Observational studies suggest the possible effectiveness of intravenous gamma globulin (IV-Ig) and hydroxychloroquine (Plaquenil) in reducing CHB-risk. Evidence for both is, however, inconclusive, and studies are biased in favor of hydroxychloroquine and against IV-Ig. Based on the review of the literature, current evidence of effectiveness for any treatment has to be judged as insufficient. Among the available treatment options, some considerations favor IV-Ig over hydroxychloroquine or, alternatively, suggest treatment with IV-Ig periconceptionally and into early gestation, with hydroxychloroquine added or replacing IV-Ig at approximately 10weeks gestational age. Benefits for the utilization of steroid drugs are unclear. Since no treatment can be considered as established, prevention of CHB in offspring should be considered experimental, and performed under appropriate study conditions.

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1. **Suspected hydroxychloroquine-associated QT-interval prolongation in a patient with systemic lupus erythematosus.**  
   Morgan Nadia D. Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases 2013;19(5):286-288.

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1. **The development of scleroderma in a young child following resolution of hypereosinophilic syndrome (HES)**  
   Jones I. Journal of Allergy and Clinical Immunology 2013;131(2):No page numbers.

RATIONALE: HES is a myeloproliferative disorder characterized by persistent eosinophilia leading to end-organ damage. Scleroderma has been reported following eosinophilic fasciitis(EF). We present a patient with no history of EF developing scleroderma with cardiac fibrosis leading to arrhythmia requiring implantable cardioverter-defibrillator(ICD) years after HES remission. <br/>METHOD(S): Biopsies: liver, bone marrow(BM), lymph node(LN), GI, skin, endomyocardium. <br/>RESULT(S): Ten-month old infant presented with fevers, hepatomegaly, pericardial and pleural effusions. Severe peripheral eosinophilia: initially 14,259cells/mL increasing to 26,316cells/mL. Liver biopsy: marked eosinophilia without fibrosis/cirrhosis. BM biopsy: 15% eosinophils, no malignancy. LN biopsy: no malignancy. Negative infectious work-up. Prednisone resulted in downtrend of eosinophilia, but she developed vomiting/diarrhea episodes with small-bowel obstruction. GI biopsy: esophageal and colonic fibrosis with eosinophilic infiltration. GI symptoms required treatment with azathioprine, methotrexate and total parenteral nutrition. At age 3, she developed scalp scarring, thigh dimpling, and chest lesions concerning for scleroderma versus EF. Skin biopsy: morphea scleroderma without eosinophils. Intestinal biopsy: consistent with scle-roderma. Hydroxychloroquine and D-penicillamine resulted in skin improvement. At age 6, apneic episode led to cardiac evaluation: right bundle-branch block, intermittent ventricular tachycardia(VT). Echocardiogram: pericarditis with effusion. Endomyocardial biopsy: myocarditis-]lymphocytic infiltrate and endocardial fibrosis. At age 9, she presented with VT prompting ICD placement. Ten years following ICD she did reasonably well with occasional gastrointestinal symptoms, and currently not on medications. <br/>CONCLUSION(S): HES presentation during infancy is rare and later development of scleroderma in absence of eosinophilic fasciitis is rarer. Patient's clinical course may be instructional for better understanding of natural history of these disease entities.

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1. **[Possibilities myocardial biopsy in the diagnosis of myocarditis verification in patients with idiopathic arrhythmias].**  
   Blagova O. V Kardiologiia 2013;53(11):21-30.

UNLABELLEDAim of the study was to elucidate nosological nature of "idiopathic" arrhythmias by means of right ventricular endomyocardial biopsy (EMB) and to assess effect of etiotropic and pathogenetic treatment.MATERIAL AND METHODSWe included into this study 19 patients (mean age 42.6 +/-11.3 years, 9 women) with atrial fibrillation (AF, n = 16), supraventricular (n = 10) and ventricular (n = 4) extrasystoles (SVE and VE), supraventricular (n = 2) and ventricular (n = 1) tachycardia (SVT and VT), left bundle branch block (LBBB, n = 2), atrioventricular block (n = 2) without structural changes of the heart. In addition to standard examination we performed the following tests: determination of IgG to herpes and Coxsackie B virus, polymerase chain reaction (PCR) for DNA detection of human herpesviruses 1, 2, and 6, Epstein-Barr virus, Varicellae-zoster virus (human herpesvirus 3) and cytomegalovirus in blood; determination of anticardiac antibodies; EMB with subsequent PCR-diagnostics including that of parvovirus B19 and pathomorphological study. DNA diagnostics (n = 4), coronary angiography (n = 6), skin biopsy (n = 1) and some other studies were also performed when indicated.RESULTS AND CONCLUSIONSHistological picture was abnormal in all cases. Nosological diagnosis was established in all patients: infectious-immune myocarditis (n = 11), parvovirus positive endomyocarditis (n = 1); systemic vasculitis (n = 2); myocardial vasculitis (n = 1), Fabri disease (n = 1), arrhythmogenic right ventricular dysplasia (ARVD, n = 1), undetermined genetic cardiomyopathy (n = 2). Level of various anticardiac antibodies including antinuclear factor with bovine heart antigen was most valuable for diagnosis of myocarditis (sensitivity 78.6%, prognostic value of positive result 91.7%). The following therapy was used in patients with myocarditis/vasculitis: intravenous or oral acyclovir (n = 10), gabreglobine (n = 2), meloxicam (n = 12), hydroxychloroquine (n = 15 for 15 [7.0; 24.] months), glucocorticosteroids (n = 14 for 18 [4.0; 25.5] months), azathioprine (n = 2). Mean duration of follow up was 4 years (48 [31; 62] months). At baseline 62.5% of patients with AF were resistant to all antiarrhythmic drugs. Treatment of myocarditis resulted in significant reduction of mean frequency of attacks of AF from 8 to 3 points, more than in 40% of patients AF emerged less than once a month and 1 patient had no attacks at all. Disappearance of tachycardia dependent LBBB was also noted. Cardioverter defibrillator and cardiac pacemaker were implanted to patients with ARVD and Fabri disease, respectively. EMB helped to establish immunoinflammatory and genetic diseases as causes of idiopathic arrhythmias (in 78.9 and 21.1% of patients, respectively). Antiviral immunosuppressive therapy of myocarditis allowed to increase efficacy of antiarrhythmic therapy in resistant patients and when necessary to optimize their preparedness to interventional treatment.

1. **A case of pulse steroid induced bradyarrhythmia in a patient with SLE**  
   Tuliani T.A. Journal of General Internal Medicine 2012;27:No page numbers.

LEARNING OBJECTIVE 1: Recognizing a rare side effect of pulse steroids in a patient with SLE. CASE: A 20 year old woman with Systemic Lupus Erythematosus diagnosed at 14 and stage 3 lupus nephritis (FSGS) was admitted for fever and symptoms of upper respiratory tract infection. Her medications included: hydrochloroquine, acetaminophen, hydrocodone, mesna, trimethorpim- sulfamethoxazole, sildenafil, pantoprazole, ondansetron, mycophenolate mofetil, methylprednison, leuprolide, folic acid, diphenhydramine, cyclophosphamide, and calcium carbonate. Vital signs revealed a temperature of 39.1 C, blood pressure 114/77, heart rate 89, respiratory rate 18. On examination the patient had a dry discoid rash present over her face, arms and posterior neck. The remainder of her exam was normal without signs of infection. Initial WBC was 3.7 (neutrophils of 2.5 and lymphocytes of 0.7). Serum electrolytes were normal. Estimated GFR was 36 mL/min/1.73 m2. Urinalysis showed 3+ blood, 2+ protein with 2-5 granular casts per low power field. The initial differential diagnosis was infection versus a lupus flare. Treatment was initiated for health care associated pneumonia in the Emergency Depratment. The patient was started on pulsed methylprednisone at 500 mg IVPB BID for a total of three days for lupus flare. The patient developed asymptomatic bradycardia while she was on steroids. EKG revealed sinus bradycardia 37/ min with normal intervals (PR 0.154 s, QRS 0.096 s, QTc 0.412 s). Previous EKGs showed normal sinus rhythm. Troponins were normal. Thyroid function was normal. Bradycardia could not be attributed to her medications as the patient had not been on anti hypertensive agents for more than a week. The patient's heart rate ranged from 55-38/min during her course of steroid treatment. Five hours after her last dose her heart rate had risen and varied between 51-68/min. No abnormalities were noted upon cardiology follow up. DISCUSSION: The major cardiovascular adverse effects of pulse steroid therapy include myocardial infarction, asystole, supraventricular arrhythmias, atrial flutter and fibrillation, ventricular tachycardia and cardiac arrest. However high dose pulse steroid induced bradycardia has been reported in the past in the pediatric population. In our case, underlying involvement of the cardiac conduction system secondary to SLE is unlikely. The patient had normal EKGs both before and after completion of pulse steroids. The patient had no alternative cause of bradycardia. Overt hypothyroidism was ruled out by a low free T4 and normal TSH (euthyroid sick syndrome). She was not on any medications known to cause bradycardia and her anti hypertensive agents had been discontinued for more than a week. An Echocardiogram revealed pulmonary hypertension and elevated right ventricular systolic pressure of 60-65 mm of Hg but no other abnormalities. Chronotropic competence was intact during her hospital stay with her heart rate increasing to more than 60/min on walking. Practitioners should be aware of the potential for bradycardia with high-dose pulse steroids in both children and young adults.

1. **Fatal antimalarial-induced cardiomyopathy: report of 2 cases.**  
   Azimian Morteza Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases 2012;18(7):363-366.

Chloroquine and hydroxychloroquine are used to chronically treat certain rheumatologic diseases and are generally considered safe. We describe 2 patients with skeletal myopathy and fatal cardiomyopathy-uncommon and underrecognized adverse effects of these agents. Both patients developed arrhythmias and heart failure, and 1 patient had documented diaphragmatic involvement. Muscle specimens showed typical vacuolar myopathy (indicative of impaired autophagy) with myeloid bodies in both patients and curvilinear bodies in 1 patient. Antimalarial-induced cardiomyopathy should be considered in patients receiving these medications with otherwise unexplained muscle weakness or cardiac symptoms. Whether autophagy enhancers can be used to manage such myopathies merits investigation.

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1. **French cohort study of 141 cases of autoimmune congenital heart block**  
   Levesque K. Arthritis and Rheumatism 2012;64:No page numbers.

Background/Purpose: Cardiac neonatal lupus manifestations mainly include congenital heart block (CHB), endocardial fibroelastosis and dilated cardiomyopathy. We report the preliminary results of the French registry of neonatal lupus. <br/>Method(s): This French registry was established in 2000 and includes foetuses or children with neonatal lupus, born to mothers with anti-SSA or/and anti-SSB antibodies. This database has Institutional Review Board approval. Here, we report data on CHB. <br/>Result(s): 141 cases of CHB born to 124 mothers were included. When the first CHB was diagnosed, 45 mothers (36 %) had an autoimmune disease: 16 had systemic lupus erythematosus (1 with an antiphospholipid syndrome), 15 had Sjogren syndrome, and 14 had another connective tissue disease (CTD). After a median follow-up period of 5.6 years, [0.03-36.5], 85 women (60%) had a diagnosis of autoimmune disease (Sjogren syndrome in 33, systemic lupus erythematosus in 32, and other CTD in 20 ). At the time of the CHB diagnosis, 24 (17%) of the pregnant women were treated with corticosteroids, 13 (9.2%) with hydroxychloroquine, and 21 (14.9%) with acetylsalicylic acid. The median term at diagnosis of CHB was 22WG[16-37 WG]. Twenty-two foetuses (15.6%) were also diagnosed with endocardial fibroelastosis. Among the 141 fetuses with CHB, there were 9 intrauterine deaths, 10 elective terminations of pregnancy, and 122 (86.5%) children born alive at a median term of 37 WG [28-40]. After a median follow-up period of 5.6 years, [0.03-36.5], 11 children (9%) had died. Three died in the neonatal period (2 from complication of CHB and one from prematurity) and 8 later on at a median age of 10 months [2-60]. Of those 8 children, 7 deaths were attributed to a cardiomyopathy associated with CHB, and one to a nosocomial infection. Ninety five children (77.8 %) had a pacemaker, implanted at a median age of 3.7 months [0.01-14.4]. Fifteen children (12.3%) developed a cardiomyopathy requiring a medical treatment and 9 of those 15 children died from complications of this cardiomyopathy. There was no cardiac transplantation. After a first pregnancy complicated with a CHB, 57 women had a total of 84 subsequent pregnancies. The following pregnancies were complicated by a CHB in 20.2% of cases (n=17). There were 14 cases of CHB in the 52 pregnancies non-exposed to hydroxychloroquine (26.9%) versus 3 cases in the 32 pregnancies exposed to hydroxychloroquine (9.4%; p=0.052). <br/>Conclusion(s): 87% of foetuses diagnosed with CHB were alive at birth, and 9% died during a median follow up of 5.6 years. A pacemaker was inserted in 77.8% of the cases. Our data confirm that the use of hydroxychloroquine may protect against recurrence of CHB in a subsequent pregnancy.

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1. **Severe primary hypothyroidism presenting with torsades de pointes.**  
   Kandan Sri Raveen BMJ case reports 2012;2012:No page numbers.

An 85-year-old lady presented to our institution following multiple episodes of transient loss of consciousness. Her admission ECG revealed a junctional bradycardia with significant QT prolongation. Telemetry captured a torsades de pointes arrhythmia. Possible offending drugs (digoxin and hydroxychloroquine) were stopped and she was given intravenous magnesium and potassium. Despite this, she continued to have runs of torsades. An isoprenaline infusion was commenced to increase her resting heart rate. Her QT interval shortened and she had no further arrhythmia. Investigation into the cause of her bradycardia and prolonged QT revealed profound hypothyroidism. Levothyroxine was commenced but the patient remained bradycardia and required a permanent pacemaker. She had no further arrhythmia and was discharged home safely. This is a very rare case of severe primary hypothyroidism presenting with torsades de pointes.

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1. **The role of anti-RO/SSA antibody level in congenital heart block and possible benefit of maternal therapy with ANTI-inflammatory agents**  
   Tunks R. Journal of the American College of Cardiology 2012;59(13):No page numbers.

Background: Despite an improved understanding regarding the role of anti-Ro antibodies in the development of congenital heart block, clinical management of mothers with rheumatologic disease and their fetuses remains challenging. The association between heart block and semi- quantitative anti-Ro antibody level, presence of maternal factors that may reduce disease burden and appropriate frequency of fetal echocardiographic screening are areas that require further clarification. <br/>Method(s): We conducted a retrospective review examining the pregnancies of mothers who were positive for anti-Ro antibodies followed at Duke Hospital from 2007-2011. All outpatient clinic notes, fetal echocardiograms, and semi-quantitative levels of maternal anti-Ro antibodies were reviewed. Infant outcomes were also assessed. Association between fetal heart block and maternal anti-Ro level was assessed by the Wilcoxon Rank Sum test. Odds ratios for maternal treatment with low-dose anti-inflammatory agents were computed in the standard fashion. <br/>Result(s): 33 women were managed throughout pregnancy. 18% of fetuses (n=6) developed atrioventricular block of any degree with all degrees of fetal heart block represented. Two additional patients were referred to our institution with preexisting complete fetal heart block. There was no significant difference in semi-quantitative maternal anti-Ro antibody level in pregnancies complicated by fetal heart block versus those that maintained normal conduction. 94% of the infants maintained normal conduction when the mother was treated with hydroxychloroquine or daily prednisone therapy throughout the pregnancy, compared to 56% in the untreated group (odds ratio: 0.09; 95% CI: 0.002, 0.84; p-value: 0.02). <br/>Conclusion(s): In this cohort, pregnancies complicated by fetal heart block did not have a significantly higher level of maternal anti-Ro antibodies. Maternal treatment with either hydroxychloroquine or daily, low-dose prednisone throughout pregnancy may provide a protective effect.

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1. **Acute and severe Libman-Sacks endocarditis-report of three cases**  
   Calvo-Iglesias F. Lupus 2011;20(4):385.

Libman-Sacks (LS) endocarditis are seen as a cardiac manifestation of both, Systemic Lupus Erythematosus (SLE) and, more recently, of Antiphospholipid Syndrome (APS). Although typically mild and asymptomatic, LS endocarditis can lead to serious complications such as stroke, transient ischemic attacks, and severe valve regurgita-tion and/or stenosis requiring urgent surgery. The literature on medical strategy or valve surgery for regurgitation or stenosis caused by LS endocarditis is sparse. In this study we report three cases of acute severe LS endocarditis. Patient 1: A 27 year-old Caucasian woman with newly SLE diagnostic underwent mitral valve replacement for acute severe mitral regurgitation caused by LS endocarditis. A St-Jude mechanical prosthesis was placed. The patient's recovery from surgery was uneventful. The patient was treated with hydroxychloro-quine, dicumarin and steroid low dose. Patient 2: A 29 year-old Caucasian woman underwent aortic valve replacement for acute heart failure secondary to aortic stenosis. Previous to surgery the patient was diagnosed with primary APS. A St-Jude mechanical valve was placed. Permanent anticoagulation with dicumarin was started. Hydroxychloroquine was added. Patient 3: A 25 year-old Caucasian woman, was referred to our hospital after repeated ischemic cerebral attacks. Routine trans-thoracic and trans-esophagic echocar-diography revealed a ''tumor'' on the atrial side of the posterior mitral valve leaflet. Papillary Fibroelastoma was the initial working diagnosis. She had a complex obstetric history. Clinical and laboratory findings meet all criteria for primary APS. Medical treatment with dicumarin, hydroxychloroquine and intravenous immunoglobulins was started. Medical improvement was achieved. LS endocarditis should be strongly suspected when significant valve dysfunction develops during the course of SLE and/or APS. Differentiation from infective endocarditis and intracardiac tumors can be difficult, but is important and has different therapeutic implications. SBP max: 167mmHg, average SBP: 129mmHg; average DBP min: 58mmHg, average DBP max: 110mmHg, average DBP: 81mmHg; Hypertension presented in 7 (28%); non-dipper in 6 (24%), reverse-dipper in 1 patient (4%). <br/>Conclusion(s): Our study shows that abnormal Holter ECG and Holter RR frequently occur in patients with SLE. Early detection of cardiac arrhythmias and elevated blood pressure can institute proper treatment and improve patient's quality of life.

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1. **Efficacy of implantable cardiac defibrillators for the prevention of sudden cardiac death in patients with cardiac sarcoidosis**  
   Kron J. Circulation 2011;124(21):No page numbers.

Introduction Patients with cardiac sarcoidosis (CS) are at increased risk for sudden death from ventricular arrhythmias. There is little evidence regarding the efficacy and safety of implantable cardiac defibrillators (ICDs) in this population. Hypothesis Data on demographic, clinical, and ICD intervention history was retrospectively collected on 138 CS patients with ICDs from 11 academic centers throughout the U.S., Canada, and India. We hypothesized that patients with CS would have a high incidence of appropriate ICD therapies. Results Sixty-two of 138 CS patients (44.92%) had an appropriate ICD therapy (ATP or shock) with 39 patients (28.3%) receiving 5 or more therapies (Figure). Forty-eight of 131 patients (36.64%) received an appropriate shock. Thirty-seven of 136 patients (27.21%) had an inappropriate shock. The incidence of appropriate therapy (ATP or shock) was 10.4%/year and the incidence of appropriate shock was 8.5%/year. Twenty-two patients (15.9%) experienced an adverse event, the most common being lead dislodgement in 11 patients (8%). Appropriate therapies (ATP or shock) were more common in patients with syncope 24/37 (65%) versus patients who did not have syncope 38/101 (38%) (p = 0.0065). Appropriate therapies were more common in patients who had ventricular pacing on baseline EKG, 9/10 (90%), compared with those who did not, 53/128 (41%) (p=0.0053). The mean age of patients who received an appropriate therapy (n=59) was 51.7 +/- 11.6 compared with 56.9 +/- 10.2 for those who did not receive appropriate therapy (n=74) (p = 0.0066). Immunosuppressive medications including steroids, methotrexate, azathioprine, and hydroxychloroquine were not associated with reduced number of appropriate therapies. Conclusions Patients with CS have high rates of appropriate ICD therapies. This population also has high rates of inappropriate shocks and adverse events. Syncope, ventricular pacing, and younger age may identify the highest risk CS patients.

1. **Subacute cutaneous lupus erythematosus induced by terbinafine**  
   Budihardja D. Mycoses 2011;54(5):394.

We report a case of a 77-year-old woman who developed a subacute cutaneous lupus erythematosus (SCLE) within 3 weeks of therapy with oral terbinafine. She was diagnosed with Tinea corporis in June 2010. After weeks of therapy with topical ciclopiroxolamine, no improvement was achieved; therefore she received therapy with oral terbinafine. In the first 2 weeks of therapy, the skin lesions were almost cured. One week later, however, the lesions worsened again. She complained about itching and burning of the skin, therefore we directly discontinued the therapy with terbinafine. At first examination she showed multiple annular, scaling, erythematous, and partly erosive plaques on the edge of the lesions, accentuated at the chest. The patient, with the exception of type II diabetes mellitus, arrhythmia, and arterial hypertension, which were treated with metformin, ASS, and digitoxin, had neither other medical problems nor signs of autoimmune disease. Dermatohistopathologic examination (HE-staining) showed orthokeratosis with epidermal atrophy and apoptosis of keratinocytes. Furthermore, it showed vacuolar degeneration at the junction between epidermis and dermis with lymphohistiocytic infiltrates and edema of the stratum papillare. Vacuolar interface dermatitis was diagnosed, suggesting lupus erythematosus. PAS-staining was negative. Laboratory test showed ANA-titer of 1:80 and elevation of Ro/SS-A und La/SS-B. Therapy was started with hydroxychloroquine and glucocorticosteroids, orally and topically. After 3 weeks of therapy the skin lesions were almost completely cured. SCLE induced by terbinafine was first described by Murphy and Barnes in 1998. It has been reported six times more often in females and develops normally within 5 weeks of therapy (1-12 weeks). Unfortunately, the mechanism of terbinafine-induced SCLE remains unknown. Discontinuation of terbinafine as well as the use of sunblockers is mandatory to the treatment, while systemic therapy with glucocorticosteroids or anti-malarials is not always needed. In patients with a history of light-sensitivity, arthralgias, a positive ANA-titer or former episodes of SLE or SCLE, systemic terbinafine should be prescribed only with care. Up until now there is no case of SCLE described after topical use of terbinafine<sup>1,2</sup>.

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1. **What is behind "Idiopathic arrhythmia": Endomyocardial biopsy as a clue to the precise diagnosis**  
   Blagova O.V. PACE - Pacing and Clinical Electrophysiology 2011;34(11):1450-1451.

Objective: To estimate the role of endomyocardial biopsy (EMB) of right ventricle in precise nosology diagnosis ascertainment and therapy specification in patients with &lt;&lt;idiopathic&gt;&gt; arrhythmias. <br/>Method(s): We observed seventeen patients (8 females, 42.6 11.9 y.o.) with &lt;&lt;idiopathic&gt;&gt; arrhythmias resistant to therapy (atrial fibrillation (AF) in 88%). Investigation concluded EMB with following histological examination; PCR detection of virus infections; detection of anti-heart antibodies (AB). <br/>Result(s): Perfusion defects were found in 56% of patients, moderate enlargement of the left atrium in 41%; AB against endothelium in 65%, conduction system in 76%, cardiomyocytes in 53%, and specific antinuclear AB in 65%. Virus genomes in EMB samples were detected by PCR in 4 patients: parvovirus B19 - in 2 EMB samples, herpes virus 6 type - in 1 EMB sample and in blood only - EBV in 1 patient; 11 patients had myocarditis, one of parvovirus B19 carriers had endomyocarditis; productive vasculitis was in 2 patients prevailed. Four 3 virus-negative samples had signs of immune cytolysi, and one with mytosis. Primary cardiomyopathy, ARVD, and Fabry disease were also found. The follow up is 32.7 7.3 months. Therapy of antiarrhythmic drugs, corticosteroids (n = 12, 28.8 +/- 10.9 mg/day), azatioprine 150 mg/day (n = 2), hydroxychloroquine 200 mg/day (n = 10), meloxicam 15 mg/day (n = 7), gancyclovir/acyclovir (n = 4), iv immunoglobulin (n = 2) was prescribed for 14 patients. Reduction of AF episode frequency (from several times per week up to several times per month) was noted in 69,2% of patients. None of those receiving immunosuppressive therapy had a transformation AF to the chronic form. Aggravations of arrhythmia due to an infection or a cancelling of therapy are noted at 47%; two patients required RFA. <br/>Conclusion(s): By means of EMB at 88,2% of patients it is revealed the immune-inflammatory nature of &lt;&lt;idiopathic&gt;&gt; arrhythmias (AF), the effect from specific therapy is received.

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1. **A case of chloroquine-induced cardiomyopathy that presented as sick sinus syndrome**  
   Lee J.H. Korean Circulation Journal 2010;40(11):604-608.

A 52-year-old woman with rheumatoid arthritis who had been treated with prednisone and hydroxychloroquine for &gt;12 years presented with chest discomfort and a seizure. She was diagnosed with restrictive cardiomyopathy combined with sick sinus syndrome. A myocardial muscle biopsy was performed to identify the underlying cardiomyopathy, which showed marked muscle fiber hypertrophy, fiber dropout, slightly increased interstitial fibrous connective tissue, and extensive cytoplasmic vacuolization of the myocytes under light microscopy. Electron microscopy of the myocytes demonstrated dense, myeloid, and curvilinear bodies. The diagnosis of hydroxychloroquine-induced cardiomyopathy was made based on the clinical, hemodynamic, and pathologic findings. This is the first case report describing chloroquine-induced cardiomyopathy involving the heart conduction system. Copyright &#xa9; 2010 The Korean Society of Cardiology.

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1. **Rapid progression of atrioventricular nodal blockade in a patient with systemic lupus erythematosus**  
   Makaryus J.N. American Journal of Emergency Medicine 2008;26(8):967.

Systemic lupus erythematosus (SLE) is a multisystem disorder with numerous potential adverse effects on the cardiovascular system. These complications likely develop in most patients with SLE at some time during the course of their disease, in part due to the decreased mortality associated with SLE as a result of modem medical management. Conduction disturbances have been reported in the literature to occur primarily from the progression of SLE and secondarily from pharmacotherapy used to treat SLE and may first be evident on the electrocardiogram in the emergency department (ED) setting. Electrocardiogram abnormalities such as borderline first-degree heart block may be clues to more significant cardiac disease brought upon by years of chronic inflammation, myocarditis, vasculitis, and fibrosis that are often the result of longstanding autoimmune disease. It is essential that patients with autoimmune disease be screened carefully in the ED setting for underlying myocardial disease, particularly given the increased potential for atherosclerosis, ischemia, arrhythmias, and myocardial conduction defects in these patients. Systemic lupus erythematosus (SLE), first recognized by Kaposi in 1872, has a specific relationship with heart disease that did not become evident until 1940 when Louis Grossi linked SLE to a peculiar form of nonbacterial, verrucous vegetative endocarditis described earlier by Libman and Sacks in 1924. Since then, the occurrence of heart disease in SLE has been well documented. It most likely develops in the vast majority of all patients with SLE at some point during the course of their disease likely as a result of improved survival in the modern era of medical management [1]. The most common forms of heart disease that occur in SLE are pericarditis, myocarditis, nonbacterial verrucous endocarditis, coronary artery disease, coronary arteritis, premature coronary atherosclerosis, congestive heart failure, cardiac arrhythmias, and conduction disturbances. The autoimmune response in SLE plays a role in conduction system disturbances. Correlation of autoimmune-related destruction with conduction disorders has been documented, and conduction defects may also represent sequelae of myocarditis in patients with SLE [2]. In contrast to other autoimmune diseases like rheumatoid arthritis, conduction abnormalities may regress when the underlying disease is controlled [3]. In addition to the underlying pathophysiology of SLE, treatment for this multisystem disease has been reported in the literature to contribute to conduction abnormalities. Specifically, QT interval prolongation and refractory ventricular arrhythmias have been associated with chronic hydroxychloroquine therapy for SLE [4]. There also may be a high risk of developing life-threatening ventricular arrhythmias and sudden cardiac death in these patients [5]. Different subclasses of SLE such as neonatal lupus have been associated with congenital heart block (CHB). Congenital heart block in neonatal lupus is usually permanent (despite steroid therapy) and can be isolated or associated with other structural heart diseases. Rarely, CHB can be associated with ventricular tachycardia and also has been reported to have an effect on calcium channels at the cellular level [6-9]. Although CHB associated with neonatal lupus is widely reported in the literature, rapidly progressive second-degree heart block in a young patient is a very rare occurrence. We present the case of a 34-year-old man with a history of SLE who presented to the emergency department (ED) after a syncopal event, and then developed a rapidly progressive second-degree heart block (Mobitz type I to Mobitz II), which necessitated the placement of a permanent pacemaker. A 34-year-old man with a history of SLE, lupus nephritis treated with pulse dose steroids, mycophenelate mofetil, and cyclophosphamide 9 years before, Libman-Saks endocarditis, and antiphospholipid antibody syndrome presented to the ED by ambulance after experiencing a syncopal episode. The patient was walking outside that same day with his family when he suddenly lost consciousness. The patient denied experiencing lightheadedness, nausea, vomiting, chest pain, angina, or previous syncopal episode. Medications included warfarin, enalapril, amlodipine, and simvastatin. Admission electrocardiogram revealed a sinus rhythm with first-degree atrioventricular block and was without ST or T-wave changes. Vital signs were within normal limits. Laboratory results including chemistry and complete blood count were normal. Computed tomography of the brain was without hemorrhage or midline shift. The patient was administered lopressor 25 mg intravenously and 81 mg of aspirin, and serial cardiac enzymes were drawn. The patient was admitted, and telemetry monitoring overnight revealed several episodes of Mobitz I second-degree atrioventricular block, which progressed to Mobitz II (Fig. 1). The patient remained asymptomatic during these episodes and was evaluated by the cardiac electrophysiology service. A transthoracic echocardiogram revealed a small 0.5 x 0.5-cm old echodensity (unchanged from previous echocardiography) on the posterior leaflet of the mitral valve, mild mitral regurgitation, and normal left and right ventricular size and function. Cardiac markers were normal. A permanent pacemaker was placed for heart block leading to syncope. The patient was discharged, completely asymptomatic, for outpatient follow-up with his cardiologist and electrophysiologist. Several autoimmune disorders have been shown to increase the risk for cardiovascular morbidity and mortality. Conditions such as SLE and rheumatoid arthritis, which have such wide-scale toxicity that can affect nearly every organ system, also may lead to adverse cardiovascular outcomes. Although the precise mechanisms whereby autoimmune disorders lead to cardiovascular toxicity are not fully understood, proposed mechanisms include enhanced thrombogenicity, more rapid progression of coronary atherosclerosis, myocardial inflammation, and potential fibrosis. Population data indicate a greater incidence of cardiovascular disease, including conduction defects and arrhythmias, in patients with underlying autoimmune disease, and it is essential for physicians, particularly ED physicians, to be familiar with the potential cardiovascular manifestations of the most common autoimmune disorders such as SLE [10]. Although patients with SLE are at greater risk of developing cardiac arrhythmias, the incidence of clinically significant rhythm disturbances is still relatively low. The most frequently seen arrhythmias are sinus tachycardia, ectopic atrial beats, and atrial fibrillation. Sinus tachycardia is by far the most common cardiac manifestation of SLE and is estimated to occur in approximately half of all patients with the disease [11]. Despite the increased incidence of such arrhythmias in patients with SLE, the majority of these arrhythmias resolve after treatment with steroid therapy. Further risk stratification regarding the likelihood of the development of certain arrhythmias may be made based on serology. For example, studies have shown that patients who have anti-small cytoplasmic ribonucleoprotein antibodies are at greater risk of developing QT prolongation and sinus bradycardia [5]. Although it is important to recognize the contribution of autoimmune disease to the development of cardiac arrhythmias, no specific studies analyzing the risks/benefits of using certain antiarrhythmic agents in the treatment of patients with autoimmune disease have been conducted. As a result, at least in the acute setting, current guidelines do not advocate alternative therapies for these patients, and the arrhythmias should be targeted as in any other case. Although autoimmune disorders increase the risk of cardiac arrhythmias, the effect of these disorders on the cardiac conduction system seems to be more clinically significant. The lo

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1. **Heart conduction disorders related to antimalarials toxicity: an analysis of electrocardiograms in 85 patients treated with hydroxychloroquine for connective tissue diseases.**  
   Costedoat-Chalumeau N. Rheumatology (Oxford, England) 2007;46(5):808-810.

OBJECTIVEThe antimalarial agents chloroquine (CQ) and hydroxychloroquine (HCQ) are used in long-term treatment of connective tissue diseases (CTDs). A high incidence of heart conduction disorders, including bundle-branch block and incomplete or complete atrioventricular block, has been observed among patients treated with CQ. Since no data were available for HCQ, we studied electrocardiograms (ECGs) in 85 unselected patients with CTD treated with HCQ as the sole antimalarial.METHODSEighty-five unselected out-patients treated with HCQ for a minimum of 1 yr, and without established cardiac diseases had standard 12-lead ECGs.RESULTSTwo incomplete right bundle-branch blocks and one left bundle-branch block were observed. No atrioventricular block was observed. The mean PR interval was 137 +/- 20 ms (range 99-188). The mean QTc interval was 410 ms (range 349-464). The mean heart rate was 73 beats/min (range 53-102).CONCLUSIONPR interval, QTc interval and heart rate were not different from normal values. The rate of heart conduction disorders was similar to what is expected in the general population, and contrasted with prior results in CQ-treated patients. Our results add further evidence on the safety of HCQ compared with CQ.

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1. **Chronic hydroxychloroquine use associated with QT prolongation and refractory ventricular arrhythmia.**  
   Chen Chun-Yu Clinical toxicology (Philadelphia, Pa.) 2006;44(2):173-175.

BACKGROUNDHydroxychloroquine (HCQ) is used for treatment of lupus erythematosus. The cardiac toxicity of HCQ has focused primarily on acute intoxication. We report a case of chronic use of HCQ associated with torsade de pointes.CASE REPORTA 67-year-old female presented with acquired long QT interval syndrome with a refractory ventricular arrhythmia. She was receiving chronic therapeutic doses of HCQ for the treatment of lupus erythematosus. Torsades de pointes was diagnosed in the Emergency Department (ED). After excluding other causes of long QT syndrome, the HCQ was suspected as the cause of her ventricular tachycardia. After discontinuing the HCQ, the QT interval was shorter and the patient recovered after treatment with lidocaine and isoproterenol.CONCLUSIONThe chronic use of HCQ for rheumatic diseases, or as an anti-malarial drug, should be balanced against the risk of developing potentially lethal cardiac arrhythmias.

1. **Diazepam for treatment of massive chloroquine intoxication.**  
   Yanturali Sedat Resuscitation 2004;63(3):347-348.

1. **Electroanatomic mapping and ablation of ventricular tachycardia associated with systemic sclerosis.**  
   Lacroix Dominique Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology 2004;6(4):336-342.

Two cases of systemic sclerosis with sustained ventricular tachycardia (VT) are presented. The first patient received hydroxychloroquine for skeletal muscle disease coexisting with cardiac involvement. In both cases, 3D-electroanatomic mapping showed low-voltage areas in the right ventricle. In the first patient the tachycardia was mapped and a protected isthmus suggesting reentry was delineated and ablated. Other substrate locations were indirectly identified by pacemapping on the right and left ventricular endocardium in the second patient. VT did not reoccur during follow-up. Radiofrequency catheter ablation is safe and effective and electroanatomic mapping may be helpful in patients with systemic sclerosis.

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1. **Massive hydroxychloroquine overdose.**  
   Yanturali S. Acta anaesthesiologica Scandinavica 2004;48(3):379-381.

We report a case presenting with massive overdose of hydroxychloroquine who survived without any sequelae. A 17-year-old girl presented to the Emergency Department 45 min after the ingestion of 22 g of hydroxychloroquine in a suicide attempt. We believe this is highest dose yet reported in the medical literature. The patient developed hypotension, life-threatening ventricular arrhythmias and mild hypokalemia. She was managed with saline infusion and dopamine for hypotension, gastric lavage and activated charcoal for decontamination, lidocain, magnesium sulfate and defibrillation for pulseless ventricular tachycardia. Potassium replacement and bicarbonate administration were performed. Quick treatment of hypotension, gastric decontamination, continuous long-term cardiac monitoring, and treatment of arrhythmias are the cornerstones of hydroxychloroquine overdose management.

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1. **Development of systemic lupus erythematosus in a patient with congenital heart block [5] (multiple letters)**  
   Feist E. Arthritis and Rheumatism 2003;48(9):2697-2698.

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1. **Complete heart block in an adult with systemic lupus erythematosus and recent onset of hydroxychloroquine therapy.**  
   Comín-Colet J. Lupus 2001;10(1):59-62.

Complete heart block (CHB) is a rare complication of systemic lupus erythematosus (SLE), mainly seen during an acute flare-up of the disease or after high-dose long-term treatment with antimalarial drugs, although anti-Ro and anti-RNP antibodies have also been implied by some authors. A 40-y-old woman developed CHB in the context of an acute flare-up of SLE, first diagnosed three years ago, having recently commenced hydroxychloroquine (HCQ) treatment. Anti-Ro and anti-RNP antibodies were also positive. No features of myocarditis were found. A temporary pacemaker was required and complete resolution was achieved on steroid therapy with withdrawal of antimalarial therapy. The characteristics of previous cases are well publicised and discussion focuses on the possible aetiology and pathogenesis of the present case.

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