STRESS: THE TRIGGERING FACTOR OF CARDIOVASCULAR DISEASE

The Myogenic Theory of Myocardial Infarction

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Kingdom of Saudi Arabia

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http://infarctcombat.org

- *"The cardiac patient does not die from coronary disease, he dies from myocardial disease.“**

- *Burch GE and col., Ischemic cardiomyopathy, Am Heart J. 1972 Mar;83(3):340-50

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- It is important to note the coronary thrombosis theory, introduced by James Bryan Herrick, in 1912, remains suffering serious doubt on its cause and effect relationship.
- This has led Friedberg and Horn to suggest in 1939 that the term coronary thrombosis should be abandoned in favor of the more generic one of acute myocardial infarction. In their paper they say that "the clinical and electrocardiographic features of coronary thrombosis may be observed in patients in whom a coronary artery thrombus is subsequently not found at necropsy as has been noted by Libman, Obendorfer, Buchner, Hamburger and Saphir, Dietrich, Levy and Bruenn and others."
- After that time many other investigators came to the same conclusion as we will see following...

- * Friedberg CK and Horn H. Acute myocardial infarction not due to coronary artery occlusion. J. Am Med Assoc 1939;112(17):1675-1679

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (1941) Hermann and colleagues found the thrombotic occlusion could occur without infarction when the collateral circulation appeared adequate and if an infarct has happened, it could be attributed to an occlusive thrombus at a critical location in the coronary tree.

- (Angina Pectoris, coronary failure and acute myocardial infarction: The role of coronary occlusions and collateral circulation, JAMA 1941;116(2):91-97; Multiple fresh coronary occlusions in patients with antecedent shock, Arch Intern Med 1941;68(2):181-198; Experimental studies on the effect of temporary occlusion of coronary arteries; The production of myocardial infarction, American Heart Journal 1941 V22;I3 -374-389)

- (1951) Miller and colleagues pointed out that subendocardial infarcts were rarely associated with coronary thrombi.

- (Myocardial infarction with and without acute coronary occlusion: A pathologic study. AMA Arch Intern Med 1951;88(5):597-604)

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (1960) Spain and Bradess found complete coronary obstruction of atherosclerotic nature, representing around of 75% of the cases and recent coronary thrombosis in just 25% of the autopsied cases. Also, they have observed crescent incidence of coronary thrombosis with the crescent duration of survival after the myocardial infarction. Less than a hour with 16% of thrombosis, between 1 and 24 hours with 37% and in more than 24 hours with 52% of coronary thrombosis*.

- (Spain, DM and Bradess VA. The relationship of coronary thrombosis to coronary atherosclerosis and ischemic heart disease – a necropsy study covering a period of 25 years, Am J Med Sci, 240:7-1, 1960; Spain DM and Bradess VA. Frequency of coronary thrombosis related to duration of survival from onset of acute fatal episodes of myocardial ischemia. Circulation, 22:816, 1960)

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (1970) Hellstrom demonstrated experimentally the coronary thrombosis secondary to acute myocardial infarction caused by ligature of the coronary artery.

- (Hellstrom, HR. Myocardial infarction as a cause of coronary thrombosis. Circulation, 42, Suppl. III); 165, 1970)

- (1972) William Roberts suggested that the coronary arterial thrombi are consequences rather than causes of acute myocardial infarction. In his study involving 107 patients who were submitted to necropsy he found that only 54% of those with a transmural infarction, and only 10% of those with subendocardial necrosis, had a thrombus in the infarct related artery.

- (Frequency of coronary thrombosis related to duration of survival from onset of acute fatal episodes of myocardial ischemia, Circulation, 22:816, 1960; Roberts, W.C.:; Coronary arteries in fatal acute myocardial infarction, Circulation,42:215, 1972, Roberts W. C.)

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (1980) DeWood and colleagues demonstrated the prevalence of total coronary occlusion during the early hours of transmural infarction by means of coronary arteriography. Their results were accepted by the cardiology community as the definitive clinical evidence about the causal role of thrombosis in acute myocardial infarction.

- (DeWood MA, Spores J, Notske R et al. Prevalence of total coronary oclusion during the early hours of transmural myocardial infarction. N Engl J Med 1980;303:897-902)

- (1996) Quintiliano H. de Mesquita pointed out that the interpretation given by DeWood about the angiographic image, suggestive of intracoronary thrombus, do not correspond to the absolute reality whether it represents a true thrombus or just aggregated platelets that are precocious, unstable or reversible commonly registered in the first hours of unstable angina and in the course of the acute myocardial infarction.

- (Book: Remédio boicotado substitui cirurgia de ponte de safena, Compset,, 1996)

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (2005) Giorgio Baroldi and colleagues, discussing the findings from DeWood, told that the first main question is how many of the 87% cineangio occlusion are pseudo-occlusion and whether the "layered" thrombus recovered at bypass surgery was a true thrombus or a coagulum which frequently show a layering of blood elements not seen in thrombus formation. Also saying that "Red" thrombus, namely a coagulum, is frequently and erroneously considered as thrombus.
- In another paper from the same year they say that the frequency of an occlusive thrombus is significantly higher in the largest infarcts supporting its secondary formation.

- (Baroldi G, Bigi R, Cortigiani L: Ultrasound imaging versus morphopathology in cardiovascular diseases: coronary collateral and myocardial ischemia. Cardiovasc Ultrasound 2005, 3:6; Giorgio Baroldi, Riccardo Bigi and Lauro Cortigiani. Ultrasound imaging versus morphopathology in cardiovascular diseases. Myocardial cell damage. Cardiovascular Ultrasound 3:32., 2005)

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (2001) In a significant number of cases angioscopic examination continues to find thrombus on the presumed culprit lesion, at 6 months after myocardial infarction.
- (Yasunori Ueda, Masanori Asakura, et al. 2001. The healing process of infarct-related plaque: Insights from 18 months of serial angioscopic follow-up. Am Coll Cardiol, 38:1916-1922.)
- (1998) Murakami and colleagues from Japan using intracoronary catheters to aspirate occlusive tissues, performed during the acute myocardial infarction, have confirmed the pathological findings that intracoronary thrombus is absent in a substantial number of patients indicating it contributes little to the pathogenesis of average acute myocardial infarction.
- (Murakami T. Intracoronary aspiration thrombectomy for acute myocardial infarction, Am. J Cardiology 1998 Oct 1;82(7):839-44)

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (2005) Rittersma and colleagues examined retrieved thrombus material aspirated using the percutaneous thrombectomy catheter in 211 patients undergoing primary percutaneous coronary intervention within six hours of symptom onset. They then established, by histological indicators, the age of the aspirated thrombi. The researchers found thrombus in 199 of the 211 patients, of whom fresh thrombus was identified in just under half. By contrast, 51% of patient samples contained thrombus that had lytic or organized changes suggesting that it had originated days or weeks before the occlusive event. They said that "Strikingly, clinical characteristics did not differ between the patients with fresh thrombus and those with 'older' thrombus, although men were more likely to have fresh thrombus than were women."

- (Rittersma SZH, van der Wal AC, Koch KT, et al. Plaque instability frequently occurs days or weeks before occlusive coronary thrombosis. A pathological thrombectomy study in primary percutaneous coronary intervention. Circulation 2005; 111:1160-1165

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- The PASSION trial, recently published, found that the use of thrombus aspiration in adjunct to primary percutaneous coronary intervention (PPCI) did not affected rates of major adverse cardiac events at 2 years follow-up, as compared with convencional PPCI. So, based in this study, it is fair to say that thrombus aspiration do not prevent the occurrence of the myocardial infarction.

- Martin A Vink, Maurits T Dirksen, et al. Lack of long-term clinical benefit of thrombus aspiration during primary percutaneous coronary intervention with paclitaxel-eluting stents or bare-metal stents: Post-hoc analysis of the PASSION trial. Catheterization and Cardiovascular Interventions, 1 May 2012;Volume 79: Issue 6, pages 870-877

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- Myocardial infarction associated with normal coronary arteries is a well known condition. The overall prevalence rate of myocardial infarction with normal coronary arteries is considered to be low, varying from 1% to 12% depending on the definition of "normal" coronary arteries.

- (Legrand V, Deliege M, Henrard L, Boland J, Kulbertus H: Patients with myocardial infarction and normal coronary arteriogram. Chest 1982, 82(6):678-685; Raymond R, Lynch J, Underwood D, Leatherman J, Razavi M: Myocardial infarction and normal coronary arteriography: a 10 year clinical and risk analysis of 74 patients. J Am Coll Cardiol 1988, 11(3):471-477.)

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- (1993) Arbustini and colleagues found in a series of 132 autopsies of hearts from patients who died of noncardiac causes, that coronary thrombi were shown to overlay the intima of a coronary vessel independently of plaque type and severity.

- Arbustini E, Grasso M, Diegoli M, et al. Coronary thrombosis in non-cardiac death. Coron Artery Dis 1993;4:751–9.

Coronary Thrombosis: Cause or Consequence of Myocardial Infarction?

- A recent "State-of-the-Art" review and commentary published at the Journal of the American College of Cardiology made the following conclusion:
- "A large body of evidence conclusively suggests that coronary artery obstruction is only 1 element in a complex multifactorial pathophysiological process that leads to Ischemic Heart Disease (IHD) and that the presence of obstructive lesions in patients with IHD does not necessarily imply a causative role. A more comprehensive approach seems necessary to refocus preventive and therapeutic strategies and to decrease morbidity and mortality. To this effect, we propose a shift in approach to include the myocardial cell as well as the coronary vessel"

- Mario Marzilli, C. Noel Bairey Merz,, William E. Boden, Robert O. Bonow,
- Paola G. Capozza, William M. Chilian, Anthony N. DeMaria, Giacinta Guarini, Alda Huqi, Doralisa Morrone, Manesh R. Patel, William S. Weintraub. Obstructive coronary atherosclerosis and ischemic heart disease: An elusive link!. JACC Vol 60, No. 11, 2012; September 11: 951-6

Prof. Dr. Quintiliano H. de Mesquita, Brazilian Cardiologist and Scientist

One of the major developments of Doctor Mesquita was the Myogenic Theory of Myocardial Infarction, from 1972. The Myogenic Theory supports the use of cardiac glycosides (cardiotonics) for the prevention and clinical treatment of acute coronary syndromes. Among other developments are the Ventricular Aneurism Surgery of the Heart performed by Charles Bailey in 1954 and the first diagnosis of Right Ventricular Infarction, in vivo, by ECG, made in 1958. (He did more than 30 pioneer contributions to medical literature)

Dr. Mesquita deceased in 2000 with 82 years old

His memorial is at the following webpage:
http://www.infarctcombat.org/qhm/homepage.html

Introduction and Fundamentals of the Myogenic Theory

- The coronary atherosclerosis and slow coronary flow in the normal extramural coronaries develop myocardial ischemic process through the imbalance between demand and blood supply to the myocardial segments, dependent on the right and left coronary arteries. Basically, the large extramural coronary arteries are responsible for nutrition of the segmental myocardium and mainly by the contractile balance of each segment of the ventricular wall.
- Every time when is developed a relative coronary insufficiency through physical or psycho-emotional stress results in an immediate loss of contractility of the ischemic area and simultaneous exaltation of other unaffected contractile ventricular segments.
- The continuity of such repetitive ischemic manifestations tend to contribute to the installation of assynergic segments, by ischemia + loss of contractility and overload imposed by the remaining intact ventricular segments, during the ventricular ejection phase.
- Consequently, the coronariopathy contributes to the deterioration of the ventricular segment, constituting areas of myocardiosclerosis or segmental myocardial disease, possible future site of the myocardial infarction.

- Book “Myogenic Theory of Myocardial Infarction”, 1979.

Myogenic Theory Mechanism
The sequence of events

- **Coronary Atherosclerosis**
  - Slow Coronary Flow
  - ↓
- Stable Angina Pectoris – Silent Coronariopathy
  - 1- Relative Myocardial Ischemia
  - 2- Reciprocal Contractile Loss
  - ↓
- Physical and Psycho-Emotional Stress Factors
  - / or
- Pharmacological Factors - Negative Inotropic Agents
  - ↓
- **Segmental Myocardial Disease**

Myogenic Theory Mechanism
The sequence of events

- **Segmental Myocardial Disease**
- ↓
- Unstable Angina/ Intermediate Syndrome

- **Infarctioning Clinical Picture**

- 1- Regional Myocardial Insufficiency
- 2- Reciprocal Myocardial Ischemia
- ↓
- Primary Myocardial Necrosis
- **(Infarction)**
- ↓
- Coronary Stasis or Fragmentation and
- Displacement of Atheromatous Plaque by Edema
- ↓
- Secondary Coronary Thrombosis
- (Not Obligatory)

Appropriated terms to the myogenic theory of myocardial infarction

- The term “coronary” has become synonymous with ischemia and it is used to define an atherosclerotic occlusive lesion that is believed to be responsible for all clinical patterns.
- So, inside the sense of the myogenic theory of myocardial infarction I will take the liberty to use some new terms more adequated to it like coronary myocardial disease rather coronary heart disease, coronary artery disease or ischemic heart disease and acute myocardial syndromes rather acute coronary syndromes.

Stress and acute myocardial syndromes

- Several studies have shown a close connection between catecholamine and myocardial infarction. The hyperactivity of the sympathetic nervous system, with a deep outflow of catecholamines (adrenaline/epinephrine and noradrenaline/norepinephrine) also occur in unstable angina, alternatively called preinfarction angina or intermediate syndrome, being smaller and less long than in acute myocardial infarction. Takotsubo cardiomyopathy, also known as broken heart syndrome, a sudden temporary weakening of the myocardium, which simulates an evolving myocardial infarction clinical picture, likewise has a deep outflow of catecholamines.

- (Increased cardiac sympathetic nervous activity in patients with unstable coronary heart disease, McCance AJ, Thompson PA, Forfar JC. Eur Heart J 1993 Jun;14(6):751-7 ; Sympathetic neural hyperactivity and its normalization following unstable angina and acute myocardial infarction, Graham LN, Smith PA et al. Clin Sci (Lond) 2004 Jun;106(6):605-11)

Acute Stress: The main risk factor for Acute Myocardial Syndromes

- Beyond intense physical activity, particularly in sports competition, or unusual efforts, surpassing the limits of his/her heart conditions, or else the heavy use of stimulant drugs, there are many risk factors for acute myocardial syndromes, based on recent severe stress situations or sudden emotional stress, like:
- Marital separation or divorce, loss of work or retirement, loss of revenue or business failure, important family conflicts, important personal injury or illness, death or illness of a close family member, shock of a surprise party, armed robbery or other kind of violence, heated discussion, threats or acts of war, earthquakes, to track the team of preference in matches live football, etc…

Cardiotonic: The compatible drug with the Myogenic Theory

- The recent discovery of endogenous cardiotonic hormones (digitalis, strophanthin, proscillaridine, etc..), isolated from human tissues and body fluids, may represent a strong new argument for the myogenic theory of myocardial infarction.
- An elevated concentration of endogenous cardiotonics have been found under different conditions such as sodium imbalance, hypertension, cardiac arrhythmias, chronic renal failure, congestive heart failure and acute myocardial infarction. Vigorous physical exercises as well physiological stress situations may also elevate the concentration of endogenous cardiotonics in the body.
- We think the cardiotonics found in nature may complement a deficient production of endogenous cardiotonic hormones produced by the human body and thus support cardiac metabolism and protect the heart from the infarction, as proposed in Myogenic Theory.

- *Two quotes related to these findings:*

- ***"The diseased heart is avid for cardiotonics"***
  - *Quintiliano H. de Mesquita, 1997*

- ***"Cardiotonics are the insulin for cardiovascular disease"***
  - *Carlos Monteiro, 2005*

The use of cardiotonics for coronary heart disease during the 20th century

- (1912) James Herrick: Proclaimed the myocardial infarction (MI) as consequence of coronary thrombosis and cardiotonics (digitalis and strophanthin) as the best therapy. He declared: "The timely use of this remedy may occasionally save live".
- (1926) Louis Hamman: Shared in same concepts and enthusiasm of Herrick regarding the use of cardiotonics to treat the MI. He said: "The patient should be promptly and fully digitalized... not only is the digitalized heart better prepared to withstand the added burden of certain arrhythmias should they come on, but it is also stimulated to put forth its better efforts. How desirable the best efforts may be when a large area of heart muscle is infarcted, needs no further comment"

- (JAMA,59: 2015, 1912 ; Bull Johns Hopkins Hosp.; 38: 273, 1926)

The use of cardiotonics for coronary heart disease during the 20th century

- (1934) Ernst Edens: After 3 years using strophanthin by intravenous way in angina pectoris and MI in more than 100 patients he declared: " Subsequently to the recognition of the strophanthin as the best and safest medicine for the myocardial infarction we don't have the right to use it in a patient only for scientific reasons and tests, giving preference to other remedies losing precious time for the cure". He also told that will come the moment in which the omission of the use of strophanthin would be seen as a professional malpractice.

- (Munchener Medizinischen Wochenschrift; 37, 1934)

The use of cardiotonics for coronary heart disease during the 20th century

- (1950) Ferdinand R. Schemm: Preconized the use free from restraint of digitalis for MI treatment. He used digitalis in 265 patients recording a mortality of 10%. In practice he noticed that instead of any myocardial damages, the cardiotonic presented compatibility with the acute myocardial infarction, reason of salutary effects and lower mortality.

- (1951) John Martin Askey: Applied digitalis in 50 consecutive patients with acute MI. Citing the results achieved by Schemm with digitalis refers that the medical profession was unable to take full advantage of this valuable drug, offering the Henry Thoreau thought: "It is never too late to give up our prejudices. No way of thinking however ancient, can be trusted without proof". This affirmation from Askey was stated during the presentation about his results and to appreciate the clinical and experimental proceedings realized at that time. Likewise he demonstrated a healthy apprehension in front of the accommodation and disinterest regarding so exciting theme.

- (Postgrad Med.; 385, 1950; JAMA; 146: 1008, 1951)

The use of cardiotonics for coronary heart disease during the 20th century

- (1955) Norman H. Boyer: Mentioned that after an unexpected but fortunate experience using digitalis by intravenously way ceased his fear about the use of digitalis applying it starting from this moment in a sequence of 50 patients with MI.

- (1970) Berthold Kern: Wrote that he used sublingual strophanthin in more than 15.000 cardiac patients during the period of 1947 till 1968 resulting in a very low mortality rate and few myocardial infarctions.

- (New England J. Med; 252: 536, 1955; Der Myokard-Infarkt. Haug Verlag. Heidelberg, 1970)

The use of cardiotonics for coronary heart disease during the 20th century

- (1972) Quintiliano H. de Mesquita: Advocated that treatment with cardiotonics should be started the earliest possible in order to correct the regional myocardial collapse in progress. He also stated that cardiotonic administration protects the myocardial fibers in collapse, ischemic, but viable to be kept from the necrosis which would certainly occur in case of non-use of this remedy. Surpassing the acute period, the cardiotonic should be used, according him, as a maintenance treatment, which blends with the MI prophylaxis, in order to defend the ischemic myocardium in its functional side. During 7 years applied cardiotonics by intravenously way (digitalis and strophanthin) in 1183 patients with acute MI, recording a survival of almost 90%. Professor Mesquita was awarded in 1975 with the Ernst Edens Traditionspreis by the International Society Against Myocardial Infarct located in Stuttgart- Germany.

- (Mesquita, QH De: Angina de esforço e síndrome de enfarte miocárdico iminente: aspectos sintomáticos dependentes de insuficiência miocárdica regional. Nota prévia. Trabalho apresentado ao XXVIII Congresso Brasileiro de Cardiologia, Curitiba (PR), Julho de 1972)

The use of cardiotonics for coronary heart disease during the 20th century

- (1980) Peter Schmidsberger, medical journalist: Report the results obtained by Professor Mesquita in Brazil informing that Rolf Dorhman from the Berliner Waldkrankenhauses in Berlin - Germany, achieved during 5 years similar results of the Brazilian professor applying the same treatment with strophanthin during the acute myocardial infarction.

- (1993) Qiao DR told that from the hemodynamic studies the beneficial effect of cedilanid is greater than its adverse effect, concluding that digitalis can be safely and effectively used in the treatment of AMI.

- (In This Manner a Brazilian Fights Against The Infarction "- BUNTE magazine, Offenburg – Germany; R.E.Dohrmann; H.D.Janisch & M.Kessel: Klinisch-poliklinische Studie über die Wirksamkeit von g-Strophanthin bei Angina pectoris und Myokardinfarkt,; Cardiol Bull (Cardiologisches Bulletin) 14/15: 183-187, 1977; Qiao DR. A study on the hemodynamic effect of cedilanid in the treatment of acute myocardial infarction, Zhonghua Xin Xue Guan Bing Za Zhi. 1993 Apr;21(2):83-4)

The use of cardiotonics for coronary heart disease during the 20th century

- (1995) Leor J and colleagues found in patients recovering from myocardial infarction that one year mortality was significantly higher among patients treated with a full dose [19 of 112 (17%)] than patients treated with a low dose of digoxin [1 of 41 (2%)]

- (Leor J, Goldbourt U et al. Digoxin and increased mortality among patients recovering from acute myocardial infarction: importance of digoxin dose, Cardiovasc Drugs Ther 1995 Oct;9(5):723-9)

Old citations about the use of digitalis in heart disease

- *"I wish it was as easy to write upon the Digitalis – I despair of pleasing myself or instructing others in a subject so difficult. It is much easier to write upon a disease than upon a remedy. The former is in the hands of nature and a faithful observer with an eye to tolerable judgment can not fail to delineate a likeness; the latter will ever be subject to the whims, the inaccuracies and the blunders of mankind". William Withering, Letter, Sep 29, 1778*

- *"Digitalis: A God-given remedy" by Friedrich Ludwig Kreysig – Berlin, 1814*

- *"Digitalis: The opium of the heart" by Jean Baptiste Bouillaud – Paris, 1841*

Dissociation between the severity of stenosis and the risk of infarction

- The risk of a heart attack or other acute myocardial events is not proportional to the severity of coronary stenosis. Several studies in which more than one angiography was performed in patients who developed acute syndromes showed that most of these syndromes appear to be developed from lesions that on the first angiography caused not significant stenosis. These less severe stenotic lesions lead to myocardial infarction because they have not developed a sufficient collateral circulation around that would prevent or limit the extent of myocardial necrosis. This means that a 30% reduction in arterial caliber may have an increased risk for a myocardial infarction than an obstruction 90%.

- (Ambrose J A, Tannenbaum M A et al, Angiographic progression of coronary artery disease and the development of myocardial infarction, J Am Coll Cardiol 1988; 12:56-62; Little W C et al, Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild to moderate coronary artery disease?, Circulation 1988; 78:1157-66; John A Ambrose, Valentin Fuster, The risk of coronary occlusion is not proportional to the prior severity of coronary stenoses, Editorial, Heart 1998; 79:3-4)

Collateral circulation and infarction

- Dr. Quintiliano de Mesquita, said in his book "Myogenic Theory of Myocardial Infarction, 1979:
- *"The collateral coronary circulation is absolutely prevalent in cases of total obstruction of the coronary artery (74%). He also told: "The net of coronary collateral circulation is not always able to prevent myocardial infarction, because it develops depending on the anatomical features of the obstructive process, and is not always sufficient to face the demands of the physical activity of the coronary patient. The role of the cardiotonic is to complete the effects of collateral circulation and ensure functional preservation of the ischemic myocardium, thus avoiding the infarction."*
- A recent meta-analysis confirmed that heart disease patients with a well-developed collateral coronary circulation have an improved survival compared with patients with less developed collaterals*.

- *Meier P, Hemingway H, Lansky AJ, et al. The impact of the coronary collateral circulation on mortality: a meta-analysis. Eur Heart J 2011; DOI: 10.1093/eurheartj/ehr308*

Cardiotonic Effects and Stress

In my view cardiotonics may also have possible benefic effects for cardiovascular disease, including in halting acute myocardial syndromes, through the reduction of heightened catecholamine levels in blood and in reduction of the resulting elevated lactic acid production by the cardiac muscle.

(Schobel HP et al. 1991. Contrasting effects of digitalis and dobutamine on baroreflex sympathetic control in normal humans, Circulation V84, 1118-1129; M Gheorgiade and D Ferguson, 1991. Digoxin: A neurohormonal modulator in heart failure? 84: 2181-2186; Gutman Y, Boonyaviroj P. Naunyn Schmiedebergs. 1977. Mechanism of inhibition of catecholamine release from adrenal medulla by diphenylhydantoin and by low concentration of ouabain (10 (-10) M). Arch Pharmacol Feb;296(3):293-6)

The cardiotonic use in stable coronary disease

- The myogenic theory recommends the use of the cardiotonic + coronary dilator in stable coronary myocardiopathy, with or w/out previous infarction in the long run, complementing the beneficial and protective effects of collateral coronary circulation in front of severe coronary obstructions.

- In short, according the myogenic theory, cardiotonics are the anti-infarction drugs.

- Excerpts from the paper from Mesquita QHde et al "Efeitos do Cardiotônico + Dilatador Coronário na Coronario-Miocardiopatia Crônica Estável, Com e Sem Enfarte Prévio, A Longo Prazo", Ars Cvrandi 2002 (setembro);35:7. Text available at following webpage: http://www.infarctcombat.org/qhm/cme.pdf

The cardiotonic use in stable coronary disease

Dr. Mesquita and colleagues say that the following effects should be highlighted from the uninterrupted use of cardiotonic + coronary dilator in chronic stable coronary-myocardiopathy, with or w/out previous myocardial infarction:

- To counteract the negative inotropic effects of ischemia;
- To preserve the ventricular function, leveling over the ischemic segments - contractile deficient - with non-ischemic segments, annulling the deleterious segmental confrontation;
- To prevent Unstable Angina, Myocardial Infarction, Heart Failure and Sudden Death - symptomatic and myocardial instability, ensuring permanent state of stability;
- To Increase and to provide peaceful survival, comfortable and long, predominantly asymptomatic, in front of the common efforts and according to the achieved parameters.

Again, they have said that "the coronary collateral circulation has its role in the fate of coronary artery disease and represents the compensatory reinforcement of the "Nature", complemented by the cardiotonic, in the preservation of myocardial contractility."

The cardiotonic use in stable coronary disease

- In a paper published in 2002, Quintiliano Mesquita and his assistant, Cláudio Baptista, have prospectively analyzed data from a period of 28 years (1972 - 2000) using cardiac glycosides at low concentration (low dose) in patients with stable coronary artery disease with or without previous infarction *. Their results have showed very low rates in mortality and morbidity. The patients were divided in two groups...

- *Cardiotônico: Insuperável na Preservação da Estabilidade como Preventivo das Síndromes Coronárias e Responsável pela Prolongada Sobrevida", Quintiliano H. de Mesquita e Cláudio A S Baptista, Ars Cvrandi 2002 (maio); 35:3 . Download free of charge at the following webpage: http://www.infarctcombat.org/28anos/digitalicos.html

The cardiotonic use in stable coronary disease

- **The first group included 994 patients w/out prior infarction, presenting in 28 years the following morbidity and mortality:**
- - Myocardial infarction: 14 cases (1.4%)
- - Heart failure mortality: 32 cases (3.2%)
- - Sudden Death: 71 cases (7.2%)
- - Stroke mortality: 13 cases (1.3%)
- - Cancer mortality: 14 cases (1.4%)
- - Total Mortality: 142 cases (14.2%) - (0.5% per year!)
- - Mean Age at Death: 76 years

The cardiotonic use in the stable coronary disease

- **The second group included 156 patients with prior infarction, presenting in 28 years the following morbidity and mortality:**
- - Re-infarction: 8 cases (5.1%)
- - Heart failure mortality: 17 cases (10.8%)
- - Sudden Death: 31 cases (20.5%)
- - Stroke mortality: 7 cases (4.4%)
- - Cancer mortality: 3 cases (1.9%)
- - Total Mortality: 64 cases (41.0%) - (1.45% per year!)
- - Mean Age at Death: 72 years

The cardiotonic use in the unstable angina

- The myogenic theory recommends the use of the cardiotonic + coronary dilator in the treatment of unstable angina, for correction of regional myocardial insufficiency, presented as the determinant factor in the pathophysiological mechanism of this alarming clinical syndrome, usually characterizing the pre-infarction.

- Excerpts from the article of Mesquita QHde et al "Efeitos do Cardiotônico + Dilatador Coronário na Angina Instável" Text available at this webpage: http://www.infarctcombat.org/qhm/eai.pdf

The cardiotonic use in the unstable angina

- **Results**

- Perfect drug tolerance.
- Immediate disappearance of spontaneous anginal episodes since the first injection and in a short-term following the administration of the drug by oral route.
- Interruption of unstable angina in 199 pts;
- Only 1 case evolved to myocardial infarction in the eighth day.
- No deaths.
- ECG alterations with rapid disappearance.
- Arrhythmic benign transitional manifestations (20.5%).
- Mild enzymatic changes in the first 24 hours.

The cardiotonic use in the infarctioning clinical picture

- **Why infarctioning clinical picture?**

- Because with the use of cardiotonics the myocardial infarction can be halted as occurred in 63.5% of the cases as shown in the studies by Dr. Mesquita.

- Mesquita QHde et al "Efeitos do Cardiotônico + Dilatador Coronário no Quadro Clínico Enfartante". Text available at this webpage http://www.infarctcombat.org/qhm/eqce.pdf

The cardiotonic use in the infarctioning clinical picture

Results

- Absolute tolerance from the drug
- Reduction in administration of analgesics and narcotics
- Low incidence of cardiac arrhythmias
- Low incidence of cardiac insufficiency
- Low incidence of cardiogenic shock
- Relative lowering of enzymatic reaction peaks
- Low mortality
- Clinical picture more calm and safe

The cardiotonic use in stable coronary disease

- **Permanent Therapeutic Maintenance**

- **Cardiotonics employed:**
- Proscillaridin-A 0.75-1.50mg/day
- Acetildigoxin 0.50mg/day
- Lanatoside-C 0.50mg/day
- Digitoxin 0.1mg/day
- Digoxin 0.125-0.25mg/day
- Betamethildigoxin 0.10-0.20mg/day

- **Coronary dilators : Calcium antagonists:**
- Verapamil 120-240mg/day
- Prenilamine 120-180mg/day
- Nifedipine 20-30mg/day
- Fendiline 100-150mg/day
- Diltiazem 90-180mg/day

- Text available at http://www.infarctcombat.org/qhm/cme.pdf

The cardiotonic in the unstable angina

- **Therapeutic attack of unstable angina during 6 days**

- **Cardiotonics:**
- Strophanthin-K : 0.25-0.34 mg/day, IV
- Strophanthin-G : 0.25-0.50 mg/day, IV
- Lanatoside-C : 0.40 mg/day, IV
- Digoxin : 0.50 mg/day, IV
- Methildigoxin : 0.20-0.30 mg/day, PO
- Proscillaridin-A : 1.50-2.0 mg/day, PO

- **Coronary dilators:**
- Dipiridamol : 20 mg/day, IV
- Verapamil : 240 mg/day, PO
- Prenilamine : 180 mg/day, PO
- Nifedipine : 30 mg/day, PO

- * The strophanthin K or G (IV) was employed in 150 patients, Digitalis (IV) in 30 patients and, exceptionally, by oral route, Methildigoxin in 1 patient and Proscillaridin-A in 18 pts.

- IV: Intravenous route PO: Oral route

The cardiotonic use in the infarctioning clinical picture

- **Therapeutic attack of the infarctioning clinical picture during 6 days**

- Cardiotonics:
- Strophanthin-K : 0.25-0.34 mg/day, IV
- Strophanthin-G : 0.25-0.50 mg/day, IV
- Lanatoside-C : 0.40 mg/day, IV
- Digoxin : 0.50 mg/day, IV

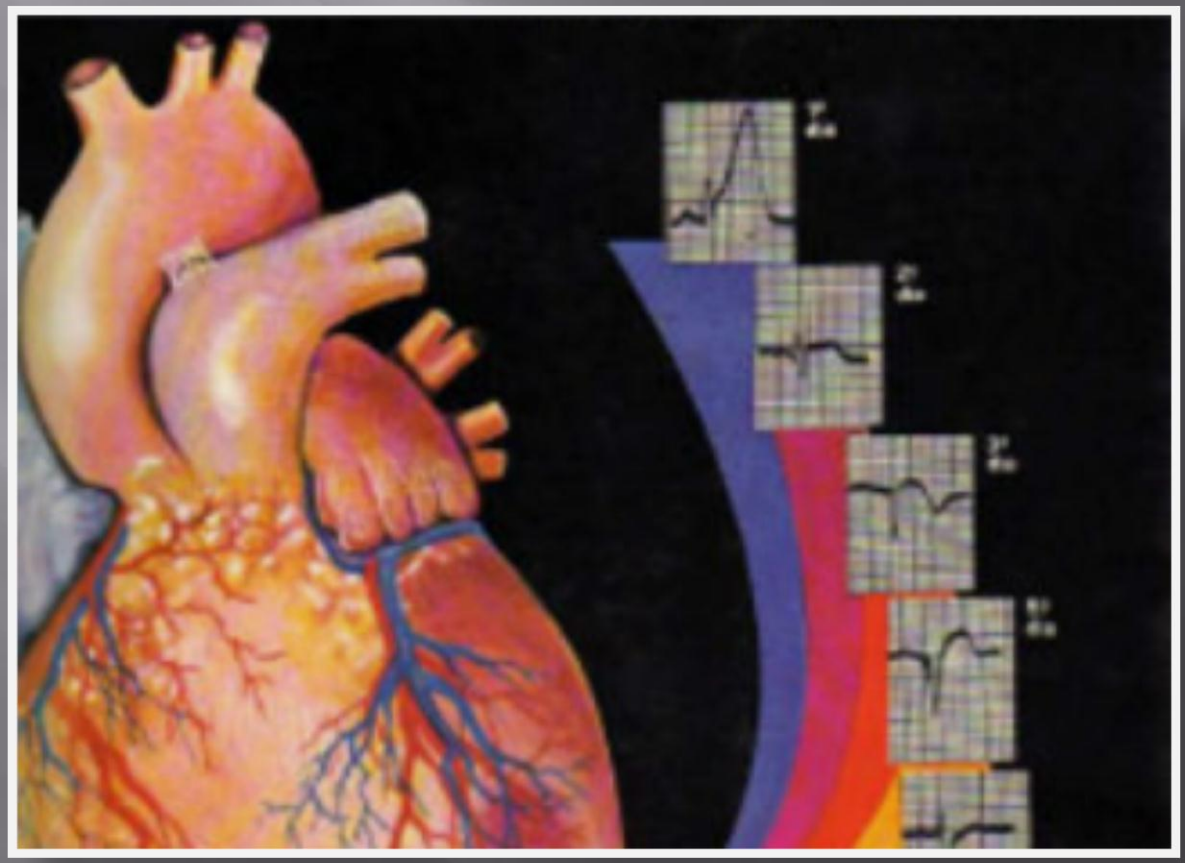
- Coronary dilators:
- Dipiridamol : 20 mg/day, IV
- Verapamil : 240 mg/day, PO
- Prenilamine : 180 mg/day, PO
- Nifedipine : 30 mg/day, PO

- * The strophanthin K or G (IV) was employed in 962 patients, and digitalis (IV) in 147 patients, during the first phase of treatment.

- IV: Intravenous route PO: Oral route

Book Myogenic Theory of Myocardial Infarction

This book in Portuguese language may be downloaded free of charge. The summary and conclusions in English are at http://www.infarctcombat.org/LivroTM/parte8.htm



Video and Powerpoint presentations on the Myogenic Theory of Myocardial Infarction

- You can find recent videos and powerpoint presentations as well articles and other information about the myogenic theory at:
- http://www.infarctcombat.org/MyogenicTheory.html