

Joy of the heart. Positive emotions and cardiovascular health

The relationship between stress and cardiovascular disease is firmly established in scientific literature and has cultural acceptance. There is a wide variety of stress definitions and in this case it covers a collection of negative emotions, conditions or adverse experiences, as well as the inadequate or conflictive capacity of responding to different problems. (1)

In recent years there has been a growing interest in the study of positive emotional dimensions under different conceptual frames, such as the concept of "happiness" or "well-being" and its relationship with cardiovascular health and disease. In a general sense, the question is whether the capacity to enjoy life, to experience well-being or to have an optimistic point of view is related to a general lower morbimortality and cardiovascular risk and, if this phenomenon exists, whether it is independent of negative emotions or merely its mirror image.^a

The purpose of this letter is to review the information on positive emotions and cardiovascular disease, and to analyze the possibility of applying this information to our medical (and personal) practice.

HOW HAS THE RELATIONSHIP BETWEEN POSITIVE EMOTIONS AND CARDIOVASCULAR HEALTH BEEN STUDIED

We have information of numerous cohort studies. After a thorough classification different populations have been surveyed in these trials for long periods of time. In each case, the evaluation included demographic conditions, plasmatic and biological parameters, ordinary risk factors and different tools to assess dimensions of the emotional environment.

At the emotional level, the definitions of well-being or positive affections have stemmed from different criteria. In a meta-analysis revision of observational studies, the authors proposed the definition of "positive affect" as a condition and/or pleasant interaction with the environment that generates feelings such as happiness, joy, excitement and contentment.

Techniques for the evaluation of positive affect

There was a wide diversity in the evaluated domains, as will be seen in the following examples.

Structured interview and association style

The Canadian Nova Scotia Health Survey (2) used a 12 minute structured interview, called Expanded Structured Interview, based on study designs to define Type A personality. The interviews were performed by trained nurses following a strict procedure and were completely videotaped. The videotapes were then classified by a group of coders, establishing scores of 1 when no positive affects were expressed to 5 when "extreme" positive affects were evidenced. The expression of positive affects during the interview was obtained from the words used, and from the smiles or warmth in the relationship with others, among other criteria. In parallel, a series of attitudes in everyday problems were examined.

Questions drawn from psychological questionnaires. Emotional vitality and optimism

The Whitehall II study of English civil servants is one of the best well known studies for its contribution in understanding the relationship between socio-economical status and cardiovascular health. For the purposes of positive emotion analysis, two dimensions were retrospectively considered, emotional vitality and optimism, with questions drawn from different initially applied questionnaires. (3)

Emotional vitality defined as an "active association with the world, with an effective emotional regulation and an overall sense of well-being" was measured with five items.

- 1 "I have a sense of direction and purpose in my life"
- 2 "How often do you feel emotionally or mentally exhausted at the end of the day?"
"How long during the past 4 weeks did you feel"
- 3 "Full of life,"
- 4 "Having a lot of energy,"
- 5 "A happy person?"

Optimism was assessed with a single item.

- 1 "Over the next 5-10 years, I expect to have a lot more positive than negative experiences,"

Participants answered on a 5 point Likert-scale ranging from "strongly disagree" to "strongly agree" to each statement.

^aIn his book *The Ethics according to the geometrical order*, philosopher Baruj Spinoza named negative emotions as *Tristitia* and positive emotions as *Laetitia*, declaring that *Tristitia* decreases the being's power whereas *Laetitia* increases it. Denying the authority of an intervening God or of religious authorities as their interpreters, he perceived that what should be considered good or bad should derive from that which produced positive or negative emotions, respectively, and hence it was written in the corporal-spiritual experience of the relationship with the world. For example, he classified repentance promoted by the religious cult as a double error: to pretend one could have acted otherwise, which he deemed impossible, and in turn generate a negative emotion, which diminished the power of the being. In this sense a system of government that was not inclined to the population's well-being could not be good. The system had to respect each individual's rights to well-being as an equal and contribute to his happiness. His thoughts agreed with those of other revolutionaries of his time and contributed to the triumph of modernity and secular democracy.

Optimism questionnaire for the elderly: SSWO

The University of Groningen in Holland (4) developed the SSWO scale to assess well-being in the elderly, considering 30 questions which included five conceptual items: health, self-respect, morale, optimism (7 questions) and personal contacts.

The seven questions used for optimism were:

- "I frequently feel life is full of promises."
- "I still expect much from life"
- "My life has many happy moments."
- "I do not make any plans for the future." (Negative).
- "I frequently laugh with joy."
- "I still have goals to accomplish."
- "Most of the time I am in a good mood."

The participants had to answer according to a Likert scale as the one listed above.

Other methods

In a meta-analysis in 2008, (5) the authors specified a long list of technical tools to assess positive affects, well-being and optimism. Conceptually, they differentiated the positive concept of hedonism, as for example, the capacity to enjoy and have a good time and the concept of eudaimonia that summarizes the satisfaction of having achieved life goals and the motivation for current achievements.

Positive affects were assessed by association traits in structured interviews, self-assessment questionnaires inquiring about different dimensions such as optimism, emotional vitality and capacity to deal with problems, recent moods assessed by reminiscences or in prospective estimations of the usual emotional condition (mood recording throughout a week with multiple, daily self assessments) among many others. As expected, each of these dimensions may have different implications.

RELATIONSHIP BETWEEN POSITIVE AFFECTS, CARDIOVASCULAR DISEASE AND MORTALITY

Healthy population studies

Meta-analysis of 2008

The publication (5) systematically reviewed the relationship between positive psychological well-being and mortality in observational studies. It included 26 studies in initially healthy populations. The aims were to summarize all the existing up-to-date knowledge, to analyze whether the positive affects added independent and complementary information to the assessment of negative affects and to know what type of positive affects had a better correlation with the prognosis. For this last aim a difference was established between "positive affects" studies and those which explored "predisposition and type of relationship".

A total of 36598 subjects were included and followed-up for more than 5 years in 81% of the studies.

The result was very impressive: the hazard ratio (HR: equivalent to the relative risk in follow-up

studies with actuarial adjustment) for mortality was 0.82 (95% CI 0.78 – 0.89), which is a very significant association. In other words, subjects with a higher qualification in positive affects had 18% less mortality during the follow-up. Methodologically, this meta-analysis has many limitations: the authors verified the presence of heterogeneity and inconsistency, publication bias and poor quality in some of the studies. However, when the analysis was limited to the better qualified studies, the association became even stronger, HR 0.74 (95% CI 0.63-0.88), namely, 26% less mortality. It is worth mentioning that most of the information comes from subjects over 60 years, and in this age group the beneficial tendency was also strong, HR 0.74 (95% CI 0.64-0.85). In studies reporting by cause of mortality, the overall mortality reduction was 19% and 29% of cardiovascular cause.

Studies reporting positive affects in general or in strict periods as well as those that analyzed positive mood predisposition had the same beneficial correlation with the prognosis. After this meta-analysis, several better qualified series with larger numbers of participants, have been published, confirming the same tendency.

I will summarize The Canadian Nova Scotia Health Survey, the Women's Health Initiative and the Whitehall II findings owing to their magnitude and relevance.

The Canadian Nova Scotia Health Survey

In 2010, the authors published in "Don't worry, be happy", the results of a 10-year thorough follow-up study in 1739 young healthy adults with an average age of 46 years, to evaluate the incidence of coronary disease. The number of participants was not large enough to evaluate mortality. During the 10 years, 145 subjects (8.3%) developed cardiovascular disease, 136 of which were nonfatal and 9 were fatal.

As we have previously mentioned, in addition to a series of depressive, anxiety and hostility scales questionnaires, the authors performed a videotaped structured interview which was afterwards assessed for positive affects in a 1 to 5 scale.

In the follow-up they reported a hazard ratio corrected by age, gender and risk factors of 0.78 (95% CI 0.63-0.96) for each scale point. Starting, for example, from 10% risk in the group with the worst score, a subject in the group with the lowest score would have 3.7% risk, that is, a difference in risk above 60%. In the negative emotions questionnaires, both the depressive and hostility symptoms were associated with the development of coronary disease. Surprisingly, positive affect kept an independent value from the depression, hostility and anxiety scales and its HR adjusted by these negative emotions was even stronger: 0.73 (95% CI 0.59-0.90).

Women's Health Initiative Study

The study (6) included 97253 women with no

cardiovascular or neoplastic pathology, with an 8-year follow-up as part of different feeding (low-fat diet) or pharmacological (post menopausal estrogen therapy) interventions. The optimistic vision (positive expectations) was assessed with the Life Orientation Test questionnaire, and the negative affects, hostility and cynicism with the Cook Medley questionnaire. The most optimistic quartile compared with the most pessimistic quartile reported 9% reduction in coronary disease, 30% decrease in cardiomyopathy mortality and 14% decline in overall mortality. The opposite was observed in the scores for cynicism and hostility. The positive and negative dimensions had an independent prognostic value.

Whitehall II Study

Similar findings were observed in 7942 participants in the Whitehall II study. (3)

Both studied dimensions, optimism and emotional vitality, were associated with a lower incidence of coronary disease. Compared with groups with the worst score, those with the highest score in positive emotions had at least 26% lower incidence of coronary disease in a 5-year follow-up. In this same population, (7) researchers analyzed satisfaction in seven life environments. Once more, the highest satisfaction score was associated with a reduced incidence of coronary disease, corrected for several risk factors. The four most relevant situations were work, family, sexual life and self-esteem.

Patient studies

(2008) meta-analysis

In this meta-analysis, the authors included 28 cohort studies with different pathologies. The total number of patients was 15711 and the result was similar, although with a much smaller magnitude than in subjects without pathology. The mortality hazard ratio was 0.98 (95% CI 0.95-1) and the detection of heterogeneity and publication bias was repeated. When the best quality studies possessing an adequate evaluation of the initial health condition and treatment level were selected, the HR was 0.91 (95% CI 0.84-0.97), that is, a 9% reduction in mortality risk associated with positive affects. This result was evident in renal pathology and HIV patients but was not confirmed in patients with cancer or cardiovascular disease.

Recovery expectations and long-term prognosis

A recent publication from Duke University provided highly relevant data on the association between recovery expectations and prognosis in patients with known coronary disease. (8) The study included 2818 patients after angiographic coronary disease confirmation. At that moment, in the years 1992-1996, prior to the decision on the type of therapy (physician,

angioplasty or surgery), different psychological tests were applied. For this purpose, the ECS (Expectations for Coping Scales) questionnaire inquired through 18 questions how patients evaluated the possibility of preserving future life quality and return to work. The questionnaire used the Likert scale scheme to establish the agreement levels to an affirmative statement such as:

“I can still hope for a long and healthy life”

My heart condition will have little or no effect on my working capacity”

Corrections in the results were performed according to the social support, the depressive symptoms and a variety of demographic, coronary disease extension and ventricular function factors.

The result was very impressive: dividing the population into four equal groups according to the expectation score, risk decreased by 16% for each ascending category, [HR 0.84 (95% CI 0.77-0.91)]. This is shown in Figure 1. Although a relationship was found between the depression score and less positive expectations, the latter kept an independent prognostic value.

PHYSIOPATHOLOGY OF POSITIVE AFFECTS AND CARDIOVASCULAR DISEASE

The explanations to understand these observations are originally directed in two very different senses but which may result complementary:

1 Positive affects are associated with biological answers that may result in a lower development of atherosclerosis and diseases in general.

2 Positive affects are associated with other beneficial conducts: a tendency to health care, healthy diet and exercise, adherence to prevention measures and treatments and, in case of eventual health problems in general, implementation of the adequate decisions.

Biology of positive affects

The last decades have supplied numerous emotion researches from a biological point of view. (9)

Briefly, from this approach we describe emotion as the entire organism's stereotyped response to external (and internal) environmental circumstances which trigger simultaneous mechanisms that represent an advantage for survival. Although we tend to think emotions simply as an activation of the autonomic system and of catecholamines, each emotional response has actually a wide specificity.(10) As an example, the facial expressions of “basic” emotions (anger, fear, surprise and annoyance) are regulated by sub-cortical areas and are established at a surprising speed without cortical participation. (11) These expressions require the conjugated action of multiple facial muscles, and they are not manifestations of higher or lower levels of catecholamines, but of a pre-

^b This is obtained by estimating 0.78*10 initially, and then 0.78 by the previous result, repeating the calculation four times. Each point has 22% less risk than the former.

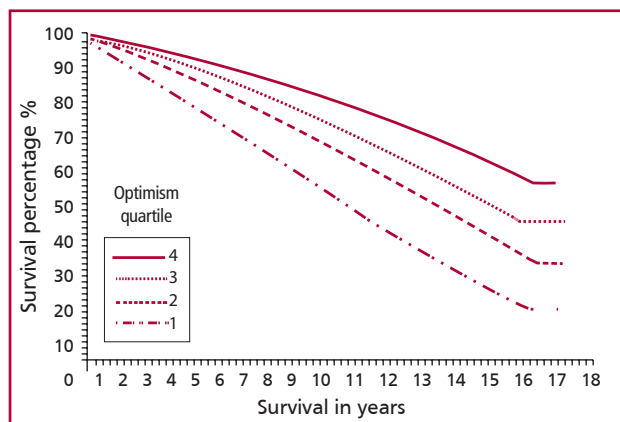


Fig. 1. Cox regression model, analyzing survival according to growing quartiles of positive expectations of recovery after angiographic diagnosis of coronary disease. Actuarial survival was corrected by age, gender, extension and severity of coronary lesions, applied therapy and smoking. (8)

established response program.

From a neuroscience point of view, “affects are the mind/body economy currency that establishes the value for the survival of objects or of pathways of action in the world”. (12)

Emotions set the body in determined valence states, which involve an array of body modifications: fear, the best studied, is accompanied by piloerection, cold hands and skin in general and increased peristaltic activity, and each one of these reactions represents an evolutionary advantage. In general, it is simple to explain the function of a negative emotion: annoyance, for example, activates mechanisms of food rejection (elevation of the upper eyelid in an attempt to close the nostrils and increase of stomach muscle movements with nausea).

What is the biological role and the substrate of positive emotions?

Biological answers observed in positive affects

In a review of the relationship between positive affects and biological processes, (13) the authors summarized numerous studies accepting that positive affects are associated with:

1. Decrease of adrenergic activation and increase in parasympathetic activity. The most recurring finding is that well-being and positive affects contribute to an earlier cardiovascular recovery after stressful situations or negative emotional conditions.
2. Decrease in plasmatic and saliva cortisol levels
3. Improvement of the immune system function, with the increase of antibody levels. In a remarkable experiment, an author evaluated during three weeks the presence and duration of positive affects in 334 healthy volunteers who afterwards underwent rhinovirus inoculation. Those classified as having “a positive emotional attitude” had a threefold lower incidence of upper

respiratory infection. (14)

4. Decrease in interleukin IL-6 and interferon gamma levels. (15)
5. Reduction in the increased levels of fibrinogen and of C reactive protein during stressful situations. These observations were confirmed in women but not in men.

A recently published study, English Longitudinal Study of Ageing, confirms the mentioned observations. (16) It included 7795 participants aged 50 or older who underwent well-being, positive affects and depressive symptoms evaluations. Affective well-being was associated with lower levels of plasmatic triglycerides and better respiratory capacity. In men, it was associated with a smaller waist circumference and higher levels of testosterone and in women with lower C reactive protein and fibrinogen concentrations and higher HDL cholesterol levels. Several of these factors were associated with reduction of vascular disease risk.

Conceptually, positive emotions place the organism in a lower “combat alert” state thus allowing an earlier antagonism of conditions activated by different negative emotions and stress. Further on we will analyze this subject from an evolutionary point of view.

In the field of positive emotions, laughter has deserved a special attention, even as a therapeutic prescription.

Biology of laughter and cardiovascular effects

A very brief history of laughter and health

Mirthful laughter as an evident positive emotional condition has been the subject of many poetic and scientific expressions. Umberto Eco dedicated the plot of his best novel *The Name of the Rose*, to a medieval mystery around the mythical lost book of Aristotle on Comedy & Laughter and the role it might play in subverting the rigid ideology of those times. (17)

Researches on this subject establish a contemporary starting point in Joubert’s *Treatise on Laughter* publication of 1597. (18) With a scientific and humorous style his intention was exhaustive. Here are some titles “Laughter arises from the heart’s pure emotion and not from the brain” “What harms may be caused by prodigal and prolonged laughter” “The benefits of laughter and whether any sick person may heal by laughing” In the last one he refers medical anecdotes of miraculous cures after bursts of laughter.

References to the relationship between laughter and health are very frequent in different cultures, and in my case I remember the phrase in Yiddish of the great writer Sholem Aleijem: “Laughing is healthy. Doctors order laughing”, very celebrated by my grandparents.

In 1976 the *New England Journal of Medicine* published Norman Cousins’ experience which had an unexpected and remarkable communitarian response. (19) This journalist while traveling with a group of

Soviet Union representatives was submitted to heavy stress and when he returned he started suffering from strong muscular pain and high erythrocytation rate. He was diagnosed with ankylosing spondylitis with a 1 in 500 recovery possibility. Cousins reasoned that if negative emotions had harmed him, perhaps a collection of positive emotions might cure him. He locked himself in a hotel for several months, devoted to resting and watching funny movies, specially those of the Marx Brothers, as well as to reading books of humor. As he was suffering from intense pain, he learnt that by watching these films he enjoyed some hours of predictable relief. After some time his pains subsided and he then lived 18 years working as a journalist and publishing books on positive emotions and health that became best sellers. Surprisingly, his original article received 3000 letters from doctors who shared his same opinion and trusted in positive affects to improve and cure diseases. In that sense the Patch Adams movement (20) generated to give love and a warm care to patients is well known and represented in Argentina by the clown-doctors and other groups. In recent years intentional laughing exercises in group sessions have been proposed, and there is a discipline called Laughing Yoga which also has promoters in our country.

Biological effects and evolutionary function of laughter

Recent studies where brachial flow was assessed following ischemic occlusion before and after the projection of comic or terror films have revealed a clear response of endothelial function: a flow increase after the comedies and a flow decrease after the terror films (21) The hypothesis is that laughter releases β -endorphins which would act on $\mu(3)$ receptors for endorphins at the endothelial level increasing the release of nitric oxide. (22) Some authors have hypothesized that the greater release of nitric oxide might have a chronic anti-inflammatory effect, inhibiting leucocyte adherence and decreasing platelet aggregation through the cGMP pathway.

The hypothesis of endorphin release has been supported by findings reporting that after episodes of merry laughter, the threshold of pain awareness changes towards higher tolerance, in agreement with Cousins' self-observations. (23) In a series of researches with laboratory rats, Panksepp et al. (24) managed to evoke a response which is surprisingly similar to human laughter. Laboratory rats, especially young animals, emit a 50 kHz sound in playful situations. This sound is evoked by tickling performed by the researchers. The animals establish a tickling dependence and constantly seek them at the sight

of the investigator. By observing the behavior of laboratory rats and establishing a correlation with the spontaneous laughter during children's games, researchers propose that laughter transmits positive social harmony, promoting cooperative relationships. Thus, it connects the perception of belonging and a positive bonding, with the absence of alarms or dangers. Furthermore, it can be seen that the greatest source of laughter in children (preserved in adulthood in the form of sophisticated jokes) are falls or sudden events. Quoting the author, "...the intrinsic ability of the nervous system to laugh and experience social joy is a pre-condition for the emergence of the types of mental sophistication that allow to find joy and laughter both in life slapstick incongruence as in the game of unpredictable cognitive events". "This system is evolutionary prepared to facilitate social interaction and to guide it in positive pathways that promote cooperative activities and bonding." This idea of the role of laughter is coherent with the finding establishing that positive behaviors are strongly linked with the disposition for a social interaction network. In recent years it has been proposed that oxytocin might be the mediator in positive belonging and bonding perception. (25) This hormone is released during loving skin contact and also in tickling, producing well-being and modifications similar to those described after laughing episodes.

Positive affects and self-care

As already mentioned, positive affects are linked to different biological parameters that might confer protection against vascular disease and produce in general a lower predisposition to disease. Their connection to favorable conducts and habits has also been confirmed.

A meta-analysis of 50 studies involving 11629 participants confirmed the relationship between an optimistic predisposition and a better approach to handle strategies to face complex situations or negative emotions. (26)

Several of the cohort studies we reported confirmed this association. Patients with positive emotions had a higher treatment adherence, participated in rehabilitation programs and adopted better self-care habits in general.

WHAT CAN A MEDICAL PRACTITIONER DO WITH THIS INFORMATION.

BY WAY OF CONCLUSION

The reviewed information has undoubtedly established the relationship between well-being, positive affects and optimism with a reduction in the possibility of

^c "I was afraid of Aristotle's second book, because it might, perhaps, teach us to distort the face of truth, so that we would not become slaves of our ghosts. Perhaps the task of the one who loves men consists in making them laugh of the truth, make the truth laugh, because the only truth is to learn to get rid of the unwise passion for truth. Flee Adso from the prophets and from those willing to die for the truth, because they generally cause the death of many others, often before their own, and sometimes instead of their own." Words from Bakersfield in *The Name of the Rose*, by Umberto Eco.

getting ill and a better possibility of recovery when suffering from a cardiovascular disease. Naturally, well-being and optimism cannot come from nothing; they are the result of a combination between the subject's real life status and the personality and character conditioned by genetic factors and life experience. Many public-health professionals, especially in European socialized medicine, as well as sociologists, have suggested categorizing a society not only by its economic growth and material prosperity but also by its equity level and by other well-being indices obtained from household censuses and surveys. (27)

The possibilities of social intervention are very complex and are related with the socio-economic structure, participating styles and other conditioning factors of great magnitude.

However, it is possible to work in different levels in which our action can make a small difference.

Living environments and interpersonal relationships

A remarkable finding from the Framingham study was published in the British Medical Journal in 2008 called "Dynamic spread of happiness in a large social network" (28). In this research, in which 4739 subjects were followed-up for 20 years, from 1983 to 2003, subjects with personal happiness influenced people up to a third degree relationship. Thus, people surrounded by other happy persons increased their probability of being happy in the future. The effect had a quantitative relationship with the living distance of dear friends. The closer they were, the greater the effect. The conclusion of the study is that happiness and health must be considered as a collective phenomenon. This leaves an open task: in each environment in which we act, it is necessary to generate spaces for enriching interpersonal relationships, allegiance ceremonies (seminars, graduations, and collective projects) and good treatment of others. By achieving a well-being mini-community, its effects will become contagious.

Communication styles in the doctor-patient relationship

Man- Good afternoon Mister Inodoro,
how are you today?
Inodoro- Awful, but accustomed.

Character Inodoro Pereyra
by Roberto Fontanarrosa

How are you feeling?

A first practical consequence of reading this information is that in the interviews with our patients we should ask "how are you feeling", an informal way of obtaining a well-being or happiness self-assessment, which we have seen has an important prognostic value. The mere fact of this inquiring

shows the physician's interest and the affect condition acquires a greater significance. The detection of emotional problems in the doctor's office, in this example expressed as the incapacity to have positive affects, may help us to decide referring the patient to psychotherapy or at least not to disregard this aspect in future appointments.

I think everything will be fine

Together with a publication from Duke University observing better outcome after a pathological coronariography in patients with an optimistic point of view, an editorial titled "Optimism in the face of a serious disease" (29) was published. As already established, an optimistic point of view may help to improve the outcome through behavioral aspects related to disease management, and also through anti-atherogenic biological mechanisms. The question that obviously arises is how doctors can contribute to a more optimistic vision and the author also wonders if we have the right to lie to generate this vision.

Several studies have assessed, for example, different styles of information at medical discharge following a coronary event and their future implications.

In a New Zealand experiment (30) three 30 minutes sessions were devoted to patients and relatives with information on the disease, expectations, effort possibilities, and other aspects. This revealed an earlier return to work, less telephone consultations, anxiety reduction and a greater compliance of medical indications and attendance to rehabilitation programs. (31)

Similarly, another intervention in patients with a first myocardial infarction was focused in modifying the perception of the seriousness of the pathology. Patients also reduced their anxiety degree, returned to work earlier and had a better outcome with fewer consultations for chest pain.

These are only two examples of the influence that intra-hospital communication may exert on the subsequent outcome even in patients with severe pathologies and prescribed with multiple medications.

The matter entails high complexity in personal communication, it is related to medical language, (32) and we have at least to study the speech and prudently choose the communicative style.

Optimism towards diseases as those of cardiovascular origin does not essentially emerge from a rational and dispassionate analysis of objective data presented by the physician, but from a combination of previous beliefs, personal or family experiences, individual personality and what the doctor transmits convincingly. Hope must not contradict the information of a complex or dangerous reality. It does no sound easy but it is not impossible, it requires formal training and institutional time to choose the best pathways adjusted to the population's sociocultural level.

FINAL OBSERVATION

In my opinion, it is very clear that there is a small portion of this issue in which we can exert an influence as human beings, clinic physicians and members of scientific societies, in at least three fields of action:

Generating messages to the community that take into account life's well-being when we discuss primary and secondary prevention strategies,

Creating working places in our areas of influence that promote creative well-being, and

Promoting a communication style to know our patients' affective condition, to collaborate whenever possible in this sense, individually or with the help of psychotherapists, to keep a warm bond and an optimistic vision to face what concerns us with the greatest commitment.

Dr. Carlos D. Tajer^{MTSAC}

Director of the Argentine Journal of Cardiology

REFERENCES

- Rozanski A, Blumenthal J, Davidson K, Saab P, Kubzansky L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. *J Am Coll Cardiol* 2005;45:637-51.
- Davidson KO, Mostofsky E, Whang W. Don't worry, be happy: positive affect and reduced 10-year incident coronary heart disease: The Canadian Nova Scotia Health Survey. *Eur Heart J* 2010;31:1065-70.
- Boehm J, Peterson C, Kivimaki M, Kubzansky L. A prospective study of positive psychological well-being and coronary heart disease. *Health Psychology* 2011;30:259-67.
- Giltay EJ, Geleijnse JM, Zitman F, Hoekstra T, Schouten EG. Dispositional optimism and all-cause and cardiovascular mortality in a prospective cohort of elderly Dutch men and women. *Arch Gen Psychiatry* 2004;61:1126-35.
- Chida Y, Steptoe A. Positive psychological well-being and mortality: a quantitative review of prospective observational studies. *Psychosom Med* 2008;70:741-56.
- Tindle H, Chang Y, Kuller L, Manson J, Robinson J, Rosal M, et al. Optimism, cynical hostility, and incident coronary heart disease and mortality in the Women's Health Initiative. *Circulation* 2009;120:656-62.
- Boehm J, Peterson C, Kivimaki M, Kubzansky L. Heart health when life is satisfying: evidence from the Whitehall II cohort study. *Eur Heart J* 2011;32:2672-7.
- Barefoot J, Brummett B, Williams R, Siegler I, Helms M, Boyle S. Recovery expectations and long-term prognosis of patients with coronary heart disease. *Arch Intern Med* 2011;171:929-35.
- Panksepp J. *Affective Neuroscience. The foundation of human and animal emotions.* New York: Oxford University Press; 1998.
- Ekman P, Levenson R, Friesen W. Autonomic nervous system activity distinguishes between emotions. *Science* 1983;221:1208-10.
- Ekman P. *Emotions revealed. Recognizing faces and feelings to improve communication and emotional life.* New York Times Book; 2003.
- Panksepp J, Burgdorf J. "Laughing" rats and the evolutionary antecedents of human joy? *Physiology & Behaviour* 2002;79:533-47.
- Dockray S, Steptoe A. Positive affects and psychobiological processes. *Neurosci Biobehav Rev* 2010;35:69-75.
- Cohen S, Alper C. Positive emotional style predicts resistance to illness after experimental exposure to rhinovirus or influenza A virus. *Psychosom Med* 2006;68:809-15.
- Matsunaga M, Isowa T, Yamakawa K, Tsuboi H, Kawanishi Y, Kaneko H, et al. Association between perceived happiness levels and peripheral circulating pro-inflammatory cytokine levels in middle-aged adults in Japan. *Neuro Endocrinol Lett* 2011;32:458-63.
- Steptoe A, Demakakos P, de Oliveira C, Wardle J. Distinctive biological correlates of positive psychological well-being in older men and women. *Psychosom Med* 2012;74:501-8.
- Eco, Umberto. *El nombre de la rosa.* Buenos Aires: Editorial Lumen; 1982.
- Jobert, Laurent. *Tratado de la Risa.* Asociación Española de Neuropsiquiatría; 2002. Puede leerse en http://books.google.com.ar/books/about/Tratado_de_la_Risa.html?id=teX188XHVLmC&redir_esc=y
- Cousins N. Anatomy of an illness (as perceived by the patient). *N Engl J Med* 1976;295:1458-63.
- Adams P. Honour and love: the origination of clown therapy. *Postgrad Med J* 2002;78:447-8.
- Miller M, Mangano C, Park Y, Goel R, Plotnick G, Vogel R, et al. Impact of cinematic viewing on endothelial function. *Heart* 2006;92:261-2.
- Miller M, Fry W. The effect of mirthful laughter on the human cardiovascular system. *Med Hypothesis* 2009;73:636-42.
- Dunbar R, Baron R, Frangou A, Pearce E, van Leeuwen E, Stow J, et al. Social laughter is correlated with an elevated pain threshold. *Proc R Soc B* 2012;279:1161-7.
- Panksepp J. Neuroevolutionary sources of laughter and social joy: modeling primal human laughter in laboratory rats. *Behav Brain Res* 2007;182:231-44.
- Ishak WW, Kahloon M, Fakhry H. Oxytocin role in enhancing well-being: a literature review. *J Affect Disord* 2011;130:1-9.
- Nes LS, Segerstrom SC. Dispositional optimism and coping: a meta-analytic review. *Pers Soc Psychol Rev* 2006;10:235-51.
- Atkinson S. Moves to measure well-being must support a social model of health. *BMJ* 2011;343:d7323 *BMJ* 2011; 343 doi: 10.1136/bmj.d7323.
- Fowler JH, Christakis NA. AA first longitudinal analysis over 20 years in the Framingham Heart Study. *BMJ* 2008 Dec 4;337:a2338. doi: 10.1136/bmj.a2338.
- Gramling R, Epstein R. Optimism amid serious disease. *Clinical Panacea or Ethical Conundrum?* *Arch Intern Med* 2011;171:935-36.
- Broadbent E, Ellis CJ, Thomas J, Gamble G, Petrie KJ. Further development of an illness perception intervention for myocardial infarction patients: a randomized controlled trial. *J Psychosom Res* 2009;67:17-23.
- Petrie KJ, Cameron LD, Ellis CJ, Buick D, Weinman J. Changing illness perceptions after myocardial infarction: an early intervention randomized controlled trial. *Psychosom Med* 2002;64:580-6.
- Tajer C. Las palabras de la medicina clínica. *Rev Argent Cardiol* 2009;77:143-50.