



The Laughter - Immune Connection

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The research below was presented by Drs. Berk and Tan at the American Association of Therapeutic Humor in Nov. 1996. It is unedited below so that you may use it in your own way with medical staff.

Physical and psychological stress produce neural and endocrine changes that translate into behavioral and psychological expressions. Negative stress, or distress, increases the secretion of stress hormones - corticotrophin and cortisol, catecholamines, beta-endorphin, growth hormone, and prolactin. Conversely, our research has shown that good stress or "eustress" such as mirthful laughter induced by humor can produce quantifiable changes in "stress" hormones.

Research in psychoneuroimmunology (PNI) has verified the presence of interrelated pathways connecting the brain and immune system (neural innervation of lymphoid tissues and hypothalamic-pituitary-adrenal neuroendocrine links). The understanding of these pathways leads to the hypothesis that mirthful laughter, a eustress effect, may produce beneficial health effects as the result of physiological and immunological changes.

In previously reported research, we have demonstrated that the positive effects of mirthful laughter not only decrease stress and certain neuroendocrine hormones, but spontaneously increases the activity of natural killer cells that are vital to fighting and preventing disease (see *Humor & Health* November/December, 1994 issue, Volume III, Number 6). Mirthful laughter serves to modulate specific immune system components somewhat like the conductor of an orchestra. The conductor has the option to increase tempo and volume, rendering the music more harsh, rapid and less harmonious. Incorporating the metaphor of mirthful laughter, however, the conductor can calm the tempo, enhance sonic integration, and ensure a melodious performance.

In our most recent research study presented at the Psycho Neuro-Immunology Research Society Meetings on April 18, 1996 in Santa Monica, California, Dr. Stanley Tan and I, investigated the effects of eustress, related to mirthful laughter, on interferon-gamma (IFN), an immunoregulator. IFN is a lymphokine, a soluble product produced by some lymphocytes that exert numerous biological functions including a variety of specific and nonspecific effects on other cells. IFN is produced by activated T cells and natural killer cells. It is active in fighting viruses and regulating cellular growth. Its capacity, however, to regulate or modulate immune properties is believed to be its most important quality. Gamma interferon serves to ensure cooperation between certain cells in the adaptive immune response. It interacts with other cytokines in either a synergistic or antagonistic manner.

The precise role of IFN in human diseases and therapy is not clearly understood. However, we know that it is clearly involved in

the defense against parasites, viruses (intracellular pathogens), and possibly tumor cells. It is interesting to note that new gene therapy approaches in cancer show promise in immunomodulation for the induction of anti-tumor effects. Chiron Viagene, an immunology technology company, has developed two retroviral vectors for gene therapy of cancer, one of which is IFN Retrovector. Direct injection of IFN Retrovector results in significant tumor regression in several syngeneic mouse tumor models. Additionally, treatment with IFN Retrovector enhances anti-tumor cellular lytic activity in mice, yielding complete tumor regression. This finding clearly demonstrates its potential effectiveness. A separate but related point is that a deficiency in the production of gamma interferon has also been related to persistent viral (EBV) infections.

Our study's experimental group consisted of ten healthy, fasting male adult volunteers. They viewed a preselected 60-minute mirthful/humor video. Blood samples for gamma interferon were obtained through an IV catheter. We measured IFN before the subjects viewed the humor video (baseline), during (intervention), after (recovery) and also the following day. With exquisite attention to detail, we utilized state-of-the-art methods to quantify measurements and sophisticated statistical multivariate analysis of variance (MANOVA) to interpret the results. Baseline data were gathered 10 minutes prior to viewing the video; intervention measures were taken 30 minutes into the video; and recovery measures were collected 30 minutes after the video ended. The following day (twelve hours after viewing the video) samples were again taken.

Examining baseline data and contrasting it with intervention measurements (while viewing the humor video) demonstrated significant increases in IFN ($p < 0.001$). Comparisons with "recovery" ($p < 0.001$) and "next day" samples ($p < 0.001$) also revealed significant increases. Within group effects over time by repeated measures (MANOVA) showed a significant increase for IFN ($p = 0.02$) in experimental subjects. Plasma volume, hematocrit and total serum protein showed no significant change over the time points studied.

As medical scientists, we must express considerable caution relative to drawing conclusions. However, when combining the results of this research with our previous studies, an interesting pattern appears to emerge. As mentioned earlier, our initial investigations have shown that mirthful laughter is a positive stress or "eustress" phenomena. It is associated with activation of T cells, B cells and increases in immunoglobulins and natural killer cell activity. It is well known that IFN plays important roles in the growth and differentiation of cytotoxic T cells, activation of NK cells and functions as a B cell maturation factor (B cells are responsible for making immunoglobulins). Based upon this understanding, it is reasonable to propose that there indeed may be a correlative relationship (at a molecular level) between the presence of IFN and other components of the immune system. Further research, however, is necessary to elucidate these effects on the composite immune response.

Therefore, these data suggest that the eustress paradigm of the mirthful laughter metaphor may be capable of modifying components of the immune response by increasing production of IFN and subsequent immunomodulation.

The results of this study support and validate the existence of our eustress paradigm that links brain, behavior and immune function in a positive manner. As medical scientists, it is gratifying and fulfilling to continue to discover objective scientific data to support beliefs that many have held intuitively for centuries. "A Merry Heart Doeth Good like a Medicine." Proverbs 17:22.