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Discussion

Dr. Erle E. Peacock, Jr., (New Orleans, Louisiana): I would like to raise four questions about what I consider to be the quantum leap between the data and the conclusions.

My questions are biased because my own work in this field has led me to an opposite conclusion, namely, that development of groin hernia in elderly men is a local phenomenon, involving a specific, difficult-to-measure, enzyme. In spite of such a bias, I would like to raise four questions.

The first question concerns the clinical or biologic significance of the data. The data appear mathematically significant, but, in my experience, removing transversalis fascia in amounts sufficient to allow penetration of intestine requires four or five times greater enzyme levels than reported. So I acknowledge the mathematic significance of the data, but question their biologic significance.

Second, I raise the question of whether any of the substances measured have the ability to digest dense connective tissue. In my experience, only highly specific tissue collagenase or bacterial collagenase will digest collagen at neutral pH.

The third question relates to difficulty in following Dr. Read's general thesis. Through the years Dr. Read has almost convinced us that human groin hernia was caused by a generalized condition featuring reduced net collagen synthesis and deposition. If I understand the present paper, however, increased collagen destruction is the major cause of groin hernia.

Last, simultaneous development of groin hernia and Dupuytren's contracture, common conditions in elderly men, is difficult to explain by a generalized metabolic abnormality. In many ways the two conditins are metabolically opposite. Groin hernia is characterized by replacement of dense connective tissue with fat; Dupuytren's contracture is characterized by replacement of subcutaneous fat by dense connective tissue.

Dr. Ronald W. Busuttil (Los Angeles, California): At UCLA we, too, have been intrigued with the role of elastolytic activity in the development of certain connective tissue disorders. Our studies, which have recently been published, suggested that these enzymes may, indeed, play a role in a more lethal degenerative disease process, namely, abdominal aneurysm formation.

We have now studied 37 patients with abdominal aortic aneurysms or atherosclerotic occlusive disease and have found that there is a marked difference in aortic wall proteolytic enzyme activity between those patients with aneurysmal disease and those with occlusive disease.

(slide) In a group of patients who had abdominal aortic aneurysms, we found a significant level of aortic wall collagenese activity, approximately 33 units per gram of tissue. In contradistinction, patients who had occlusive atherosclerotic aortas had no detectable collagenese activity in the aortic specimens. Similarly, samples of rectus fascia from patients who also had aneurysms did not contain collagenolytic activity.

(slide) Additionally, we have found that collagenase activity was approximately three times greater in patients who had thoracoabdominal, expanding, or ruptured aneurysms, compared with patients who have had elective, stable abdominal aortic aneurysms.

(slide) We have performed regression analysis on these data to determine if a correlation existed between aneurysm size and aortic collagenase activity. A significant relationship was found between these two variables with $P < 0.005$.

I would like to conclude by asking Dr. Read two questions. First, have you measured collagen synthesis in these patients, and have you seen the replacement of Type 3 collagen with Type 1 collagen, as we have seen in patients with aortic aneurysm? Second, did you actually measure the collagen content in the rectus fascia, and have you found any correlation between hernia recurrence and increased collagenase activity, which I think would be important for the support of your thesis?

DR. LLOYD M. NYHUS (Chicago, Illinois): Far be it from me to get into the middle of this one, but we would be remiss if we did not remind the membership that the Harrison shown on an early slide was the father of our own Timothy S. Harrison, of Hershey, Pennsylvania.

Paul W. Harrison worked for more than 40 years as a missionary doctor to the people of the Persian Gulf and Saudi Arabia. He wrote beautifully on the subject of hernia.

DR. RAYMOND C. READ (Closing discussion): I would have been disappointed if Dr. Peacock had not discussed this in his inimitable fashion. Dr. Peacock and I have been involved in some of these problems at least ten years. He asks, "How can these enzymes in this concentration cause hernia?" Well, we have to realize that it takes 20 or 30 years for a hernia to develop, just the same as it takes 20 to 30 years for lung cancer to develop. It does not happen overnight, and not everybody gets it. Further, elastase is not only increased in the blood of these patients, but the antiproteolytic capacity is simultaneously compromised. We do not know all the mechanisms, but we have made these observations which we intend to investigate further. We also know that these enzymes have been well-documented to destroy lung tissue, and if they can destroy the lung, they can weaken a fascial area, which is a known *locus minoris resistentiae*.

Dr. Peacock says I have said for some time that the synthetic rate of this collagen is decreased, and now I am suddenly saying that the collagenolytic rate is increased.

Well, I believe both can occur. In other words, when a tissue is under attack by proteolytic enzymes, it may not respond in the vigorous, normal way of youth. Dr. Peacock has stressed for some years that collagenolysis is important in this hernia problem. I believe he has also stressed that it is a local phenomenon, in which I believe he is wrong. I believe it is a systemic change. Then he keeps talking about these senile patients. They are not aged. It is not in patients in their eighties and nineties that we see the great incidence. As Dr. Harrison said, it is persons in their fifties and sixties who are having this particular problem in its maximal intensity.

Just because Dr. Peacock has one patient who has Dupuytren's contracture—he could have a patient with a blind left eye—I am not sure that it is definitely related to the problem. In cirrhosis of the liver with antiprotease deficiency, one also sees increased fibrosis.

Dr. Busuttil's study in which he measured for the first time collagenase activity in the walls of abdominal aortic aneurysms is important. He did not find that this enzyme was present in Leriche's syndrome. Interestingly, we have now measured the elastolytic activity, as an index of proteolytic and collagenolytic activity, in the blood of patients with aneurysms, and we find that the blood level is increased in aneurysm of the abdominal aorta, as compared with Leriche's syndrome, where it does not change.

This indicates that some persons respond to smoking with increased blood levels of enzymes and some do not, which may be important as to why only a certain percentage of smokers get accelerated atherosclerosis.

Dr. Busuttil asks have we observed changes in the Type 3 and Type 1 collagen? We have not studied this. Collagen content in the fascia does go down, as we demonstrated some years ago. We have not studied whether recurrence of hernia is related to elastolytic activity, but we intend to do that. All of these patients had primary herniation.

As to Dr. Nyhus's comment, he has this wonderful book that I have the pleasure of being included in, and I did not realize Dr. Harrison was the father of one of our members here. I am glad to hear that.