electrophoresis, using gelatin as substrate, detected 5-7 different apparent molecular weight bands of protease activity (70, 83, 94, 128, 196 kD) while control membranes only had 1-3 weak activities (52, 65, 83 kD). Quantitative studies using fluorescent substrate cleavage assays demonstrated 10-40 fold increases in protease activity in pPROM membranes compared to control membranes (pPROM membranes mean activity 137 units/gm protein vs. 10.4 units/gm for control membranes. p<0.01). Protease inhibition studies with EDTA demonstrate that all forms appear to be metalloproteases. It is not clear if multiple zymogram forms represent denovo synthesis of different proteases or complexed forms of the same enzyme. In pPROM membranes there was a large increase in observed activity of the 83 kD protease. Western blot characterization of endogenous protease inhibitors using commercial antisera demonstrates that there is consumption and degradation of protective inhibitors including alpha-1 antitrypsin, alpha-2 macroglobulin and PAI-2 in pPROM tissues not found in control membranes. Thus, in the fetal membranes from preterm deliveries there appears to be an increase in proteolytic activity not present in normal deliveries. And within this biochemical difference there also appears to be the concomitant decrease in the availability of protease inhibitors. This effect does not appear to be due to gestational age or route of delivery. These observations provide insight into the mechanisms of pPROM and suggest that imbalances of proteases and inhibitors may contribute to the pathogenesis of pPROM and preterm birth.

THE TRANSITION OF LATENT TO ACTIVE FORM OF 92 kDa TYPE-IV COLLAGENASE IN HUMAN AMNIOCHORION IS LINKED WITH LABOR


*Departments of Obstetrics and Gynecology and Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA and **Laboratory of Pathology, National Cancer Institute, Bethesda, MD. * Visiting scholar : Instituto Nacional de Perinatología, México, D. F.  ** Visiting Scholar : Instituto Nacional de Enfermedades Respiratorias, México, D. F.

The presence of 92 kDa type IV collagenase (MMP-9) was documented in human amniochorion collected from women with active labor or during caesarean sections of term pregnancies. MMP-9 immunoreactive protein and mRNA were detected mainly in amnion epithelium and decidual cells, but also some of the trophoblast cells of the spongy layer depicted positivity. Gelatin substrate gels from amniochorion extracts of samples collected after delivery, showed the presence of at least 5 different gelatinases ranging from 150 to 68 kDa. The main activity appeared in a 92 kDa band. No activity was detected in fetal membranes collected before onset of labor, however, Western blot analyses confirmed the presence of MMP-9 in these samples. The latent (92 kDa) and active (83 kDa) forms were detected in extracts of amniochorion collected after delivery. Activation of the latent MMP-9 enzyme with stromelysin (MMP-3) was observed in both groups using gelatin gels. We conclude that the existence of a labor-related potentially physiological mediator of chorioamniotic membranes rupture can be confirmed in this study. The presence of 92 kDa type IV collagenase in amnion epithelium, chorion decidual and trophoblast cells from term fetal membranes suggests their role in extracellular matrix components degradation as a mechanism of chorio-amnios weakening during both physiological and pathological conditions. Our results suggest that this process is linked to the activation of previously existent latent MMP-9, possibly by stromelysin.