INTRODUCTION

Bovine mastitis is an infectious disease causing inflammatory changes in the udder. Infection, inflammation and tissue injury are usually associated with lipid peroxidation and the formation of free radicals. We have studied the possible roles of some local tissue factors in mastitis. Among these, prostaglandins (PGs) are typical mediators of inflammation. The metabolism of glutathione (GSH) is in many ways involved in tissue protection particularly in limitation of excessive lipid peroxidation. GSH and GSH-enzymes like GSH-peroxidase (GSH-Px) are also closely involved in the metabolism of arachidonic acid to prostaglandins and other biologically active lipids.

CHANGES IN PROSTAGLANDIN LEVELS DURING MASTITIS

Prostaglandins (PGs) constitute a whole family of peroxidized lipids formed in most animal cells. Almost any kind of stimuli be it mechanical, chemical, physiological or traumatic, may initiate the formation of different kinds of PGs. Thus the particular importance of the local PG-impact is usually very difficult to evaluate. Some PGs, like PGEs and PGI$_2$ (prostacyclin) are potent vasodilators and they might participate in the generation of inflammatory symptoms. The main roles for PGEs and PGI$_2$ in inflammation may in fact be in generation of hyperalgesia, sensitization of the tissue to the irritant and pain producing activity of the amine and peptide type of mediators of inflammation. On the other hand these PGs have marked tissue protective functions, e.g. in preventing vasoconstriction and platelet aggregation. Other prostanoids (PG-like substances) like PGD$_2$, PGF$_2\alpha$ and thromboxane A$_2$ (TXA$_2$) are mostly vasoconstrictors. Their formation may be associated with allergic and other reactions of hypersensitivity, and TXA$_2$ is a very potent aggregator of platelets.

The presence of PGs in the normal milk of different animal species is well established. Giri and coworkers' have demonstrated that milk levels of PGF$_2\alpha$ and TXB$_2$ (the metabolite of TXA$_2$) may increase markedly the in experimental bovine mastitis triggered by an infusion of bacterial endotoxin. Our studies in spontaneous bovine mastitis revealed that both the milk and blood levels of PGs were elevated, as in any typical
inflammatory reaction\textsuperscript{3,4}. The concentration of PGE\textsubscript{2}, PGF\textsubscript{2\alpha} and TXB\textsubscript{2} in healthy milk samples were 44, 118, and 244 picograms/ml, and in mastitic samples 61, 135, and 357 pc/ml, correspondingly.

The sources of prostaglandins are not known very well and are a matter of speculation. Several possibilities are to be considered. First of all, bacterial toxins might have contributed to the PG-release. This was clearly demonstrated by Giri and coworkers\textsuperscript{5}, in experimental bovine mastitis, and similar mechanisms might operate in the spontaneous disease as well. Secondly, the production of PGs is greatly increased by polymorphonuclear leukocytes. Neutrophil invasion is a typical feature in mastitis, and in our results the PGs correlated fairly well with the somatic cell counts ($r$ values were between 0.63-0.68, $P < 0.01$). This was the best parameter predicting the PG-level. Thirdly, changes in tissue protein and electrolyte contents are factors that have marked effects on PG-production. Albumin is a typical factor increasing the formation of PGs, particularly PGF\textsubscript{2\alpha}. In our material the blood samples from mastitic animals plasma PG\textsubscript{2} was in a positive correlation with serum albumin ($r = 0.43, P < 0.05$), and finally, other factors that may have contributed are inflammatory mediators (e.g., monoamines and peptide hormones) and even mechanical stimulation of the sensitized udder during milking is a possible factor favouring PG-production.

Role of GSH-enzymes in mastitis

The tissue content of glutathione (GSH) is normally very high, in some tissues up to 5 millimolar level. The functions of GSH are often tissue protective, and there are numerous enzymes in which GSH plays a central role as a cofactor. Typical GSH-enzymes include GSH-peroxidase (GSH-Px), located in the circulation almost exclusively in the red cells, various GSH-transferases which possess peroxidase-like activity and bind chemicals and $\gamma$-glutamyl transferase which reflects the function of the liver and is involved in the transport of amino acids across the cell membrane. GSH is also consumed by some cytochromes, most notably cytochrome P-450. Recently we have demonstrated the presence of cytochrome P-450 in severely inflamed udder tissues\textsuperscript{6}. Together with GSH-Px cytochrome P-450 might participate in the proper handling of oxygen-free radicals in host defence (Fig 1).

![Fig.1 Possible roles of GSH and GSH enzymes, derived from erythrocytes or white cells, free radical related processes associated with microbial killing, and bacterial toxins in "induction" of cytochrome P-450 in inflamed udder tissue.](image-url)