

EDITORIAL

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PROSTAGLANDINS IN DERMATOLOGY

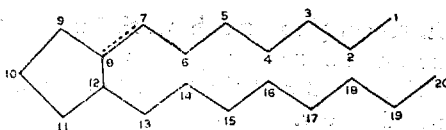
The striking upsurge of interest in the prostaglandins in the last few years has been accompanied by an almost explosive development of prostaglandin research. Primarily the rapid expansion of research has been fostered by the development of methods of biosynthesis, and later total chemical synthesis making pure prostaglandins available for biological testing and clinical investigation.

The discovery of prostaglandins will always be associated with the name of the Swedish physiologist Von Euler. Indeed it was Von Euler who presuming that the biologically active substance found in semen was a product of the prostate gland, coined the term "Prostaglandin". The earliest reference to the biological activity of prostatic extracts and semen was that of Kurzrok and Lieb (1930) who reported that human semen either inhibited or contracted the uterus in vitro.

A few years later Von Euler and Goldblatt working independently demonstrated the base depressor and marked uterine and other smooth muscle stimulating properties of human seminal fluid. For many years little more was heard of the prostaglandins and it was only after the commencement of Bergstrom's outstanding work on the identification of the prostaglandins that interest was rekindled. Working at the Karolinska Institute in Stockholm, Bergstrom (1949) first showed that prostaglandin was not a single substance but rather a mixture of chemically related lipid soluble

hydroxy-fatty acids. Today we know that all prostaglandins are long chain fatty acids. At least 14 naturally occurring prostaglandins have so far been recognised and their molecular structure determined. All are 20 carbon hydroxy-fatty acids and two adjacent carbon side chains—one bearing a carboxylic group in the terminal position. Prostanic acid is the parent substance for all prostaglandins.

Prostanic Acid



Prostanic acid can be derived from arachidonic acid. Prostaglandins are formed in a variety of tissues. They are classified into 4 groups. 10 compounds are arranged in the 4 groups as shown below :

<b>E-series</b>	<b>A-series</b>
PGE <sub>1</sub>	PGA <sub>1</sub>
PGE <sub>2</sub>	PGA <sub>2</sub>
PGE <sub>3</sub>	
<b>F-series</b>	<b>B-series</b>
PGF <sub>∞1</sub>	PGB <sub>1</sub>
PGF <sub>∞2</sub>	PGB <sub>2</sub>
PGF <sub>∞3</sub>	

The prostaglandins have different actions on different organs. Consequently they are put to very many uses in medicine.

1. They are used to induce labour.
2. They can be used as abortifacients.
3. They can be used as "once-a-month" contraceptives.
4. Some preparations decrease the blood pressure. Hence they can be used in the management of hypertension. However some preparations increase the blood pressure.
5. They can be used to diminish gastric acidity and thus find place in the treatment of peptic ulcer.
6. They find place in the treatment of bronchial asthma.
7. They can be used in the treatment of hay fever, and allergic rhinitis.

In recent years much work has been done on the role of prostaglandins in the skin. Some of the findings are summarised below.

1. Prostaglandins appear to have the ability both to depress and to stimulate cyclical AMP levels depending on the tissue and system. In the hair bulb, there are two cells; the melanocyte and the keratinocyte. The result of prostaglandin stimulation showed more rapid complexing and transfer of melanosomes in the melanocytes and their increased degradation in the keratinocytes.

2. In the epidermis of several species including frog, mouse and man, the prostaglandin synthesising activity has been demonstrated. In the control of epidermal cell duplication, a possible role for prostaglandin ( $PGE^1$ ) has been suggested. An increase in DNA<sup>1</sup>, synthesis was confirmed in epidermal cell cultures.  $PGE^1$  also increases total protein synthesis in epidermal cell cul-

tures. Skin is rich in prostaglandin synthetase and the existing knowledge shows that prostaglandins may play an important part in the regulation of epidermal growth.

3. The relation between ultra-violet light induced inflammation and uv induced changes in DNA synthesis is not properly understood. Eaglstein and Weinstein injected  $PGE_2$  into normal human skin and evaluated its effects on DNA synthesis by autoradiography. All  $PGE_2$  injections produced redness within 2-6 minutes. A dosage of 1 kg. produced redness lasting for about 5 hours. An erythema producing intradermal injection of  $PGE_2$  into normal skin is associated with an increase in epidermal DNA synthesizing cells, 48 hours after injection. The findings suggest that  $PGE_2$  may be a mediator of the increase in S-phase cells that follow uv irradiation. The demonstration that defined chemical molecules can stimulate proliferative cell activity in the skin may be significant for future biochemical and cytokinetic studies.

4. A relationship of the prostaglandin to the cyclical AMP system has recently been suggested. Adachi et al<sup>2</sup> report basic data on how prostaglandins affect the adeny cyclase system in the epidermis. Epidermal slices from pigs and human beings were preincubated in Hanks' medium before being exposed to various concentrations of prostaglandins and to 2 mm theophylline. The cyclical AMP content of the skin slices was measured by a protein binding method. Stimulation by  $PGE_1$  and  $PGE_2$  was marked and about equal.  $PGA_1$ ,  $PGA_2$ , and  $PGF_{\infty}$ , stimulated adeny cyclase only slightly. The effects of  $PGE_2$  and epinephrine appeared to be either additive or slightly synergistic suggesting independent sites of action on the adeny cyclase system. Propranolol did not inhibit  $PGE_2$  stimulation in either psoriatic or uninvolved human epidermis

or in pig epidermis. The degree of response of adenylyl cyclase to prostaglandins appeared to be more sluggish in involved psoriatic skin than in the uninvolved skin of patients with psoriasis.

**5. Inhibitors of prostaglandin synthesis in psoriatic plaque.**

Penneys et al<sup>3</sup> report the detection of inhibitor(s) of prostaglandin synthesis in psoriatic plaque that is not present in extracts of uninvolved skin obtained

from psoriatic patients or normal volunteers.

Prostaglandins interfere with lipolysis by suppressing the action of cellular lipases. Wheal and flare reactions have been produced by intradermal injection of prostaglandins. It also induces histamine release. It is thought that because of their probable relationship to adenylyl cyclase and certain biologic properties, prostaglandins have a role in immediate hypersensitivity and the pathophysiology of asthma.

**REFERENCES**

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