EXPERIENTIA

Vol. XXI – Fasc. 3 Pag. 113–176 15. III. 1965

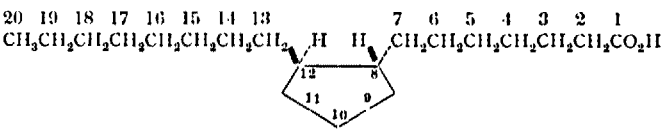
Biological Activities of Pure Prostaglandins

By E. W. HORTON

Department of Physiology, Medical College of St. Bartholomew's Hospital, London (England)

Prostaglandin was the name given by EULER in 1935 to a substance in extracts of human semen which contracts isolated smooth muscle and lowers arterial blood pressure, and which differs from all other known naturally-occurring substances[1–4]. Using prostaglandin-containing extracts of various degrees of purity, EULER and others investigated its biological actions. These results were the subject of a comprehensive review by ELIASSON in 1959[5]. About that time BERGSTRÖM et al. announced the isolation of prostaglandin[6,7], and soon these workers were able to elucidate its chemical structure[8]. It became apparent that prostaglandin was not a single substance but a family of closely-related compounds. Six of these have now been isolated from natural sources, including semen[9–11], vesicular glands[7,12,13], menstrual fluid[14], lung[13,15], brain[16], thymus[17] and iris[18] (Table I). Chemically, the prostaglandins are hydroxy unsaturated C_{20} fatty acids, five of the carbon atoms forming a cyclopentane ring (Figure). Prostaglandin E's have oxo and hydroxy substituents in the ring whereas the prostaglandin F's have two hydroxy substituents. The three E's (and three F's) differ from each other only in their degree of unsaturation (Figure).

The object of the present paper is to review the work which has been done using prostaglandins known to be



Prostanoic acid[19]

Prostaglandin E_1	11α,15-dihydroxy-9-oxo-prost-13-enoic acid[8].
Prostaglandin E_2	11α,15-dihydroxy-9-oxo-prost-5,13-dienoic acid[12].
Prostaglandin E_3	11α,15-dihydroxy-9-oxo-prost-5,13,17-trienoic acid[19].
Prostaglandin $F_{1\alpha}$	9α,11α,15-trihydroxy-prost-13-enoic acid[8].
Prostaglandin $F_{2\alpha}$	9α,11α,15-trihydroxy-prost-5,13-dienoic acid[15].
Prostaglandin $F_{3\alpha}$	9α,11α,15-trihydroxy-prost-5,13,17-trienoic acid[19].

The formulae of six prostaglandins and of the parent acid, prostanoic acid, which has not been isolated from natural sources.

Table I. Distribution of prostaglandins. Prostaglandins have been isolated in pure form from the sources indicated below. The figures refer to concentrations in μg/g (μg/ml in the case of semen). + indicates that the compound has been isolated from that source, but the amount present is unknown; – indicates that the evidence suggests that the prostaglandin is not present

Tissue	Prostaglandin						Reference
	E_1	E_2	E_3	$F_{1\alpha}$	$F_{2\alpha}$	$F_{3\alpha}$	
Semen (human)	20	20	22	3	5		9, 10
Semen (sheep)	+						11
Vesicular gland (sheep)	+	+	+	(+)	–	–	7, 12, 13
Menstrual fluid (human)		+			+		14
Lung (human)					+		13
Lung (monkey)					+		13
Lung (ox)					+	+	13
Lung (pig)					+		15
Lung (sheep)	–	+	–	(+)	0.5	(+)	13, 15
Lung (guinea-pig)					+		13
Brain (ox)					0.3		16
Thymus (calf)	0.8	–	–	–	–	–	13, 17
Iris (sheep)					+		18

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chemically pure. No attempt has been made to include results obtained with impure preparations.

Actions on reproductive smooth muscle. Smooth muscle from the female reproductive tract of all species so far investigated responds to prostaglandin. Rat and guinea-pig uteri are contracted by prostaglandins E_1, E_2, E_3, $F_{1\alpha}$ and $F_{2\alpha}$[20–24], and in addition to a direct stimulant action on guinea-pig myometrium prostaglandin E_2 potentiates subsequent responses to other oxytocic substances[24]. In vitro, the non-pregnant uterus of the rabbit shows little or no response to prostaglandin E_1, but contracts in response to prostaglandin $F_{1\alpha}$[20]; in vivo, spontaneous contractions of the rabbit uterus are inhibited by prostaglandin E_1[25]. Similar inhibitory effects of prostaglandin E_1 have been observed on contractions of the cervix in the anaesthetized rabbit, but the part of the reproductive tract in this species most sensitive to prostaglandin is the oviduct smooth muscle[25,26]. Prostaglandins E_1, E_2 and E_3 injected intravenously reduce the tone and contractions of the oviduct, but prostaglandins $F_{1\alpha}$ and $F_{2\alpha}$ usually have the opposite effect, although higher doses of these compounds are required[22,27].

The suggestion[28] that prostaglandins from semen are absorbed from the vagina into the circulation and thence act upon the reproductive tract smooth muscle receives some support from the finding that prostaglandin E_1 is absorbed from the rabbit vagina[26]. Although this is unlikely to be a physiological mechanism in the rabbit in view of the absence of prostaglandin from rabbit semen, nevertheless it is of great interest that prostaglandin can reach the circulation in this way and it would seem to justify an investigation in humans to determine whether a similar process operates after coitus. This could equally well be investigated in sheep, since ram semen, like that of humans, contains prostaglandin. HORTON, MAIN and THOMPSON, however, have shown[25] that injections and infusions of prostaglandin in anaesthetized ewes produce detectable changes in the intraluminal pressure of the oviduct only in amounts greatly in excess of those present in a single ejaculate of ram semen[29]. These observations do not exclude the possibility that seminal prostaglandin acts locally upon vaginal or cervical smooth muscle. Nor do they exclude the possibility that circulating prostaglandin has a more subtle and less easily recordable effect which is of physiological importance. If this is so, the demonstration that a prostaglandin has an effect on the muscle tone of the oviduct of a species may be irrelevant to the question of a physiological mechanism.

These points should be borne in mind when considering results obtained on tissues of the human female reproductive tract in vitro. BYGDEMAN and ELIASSON[30] showed that isolated myometrial strips from non-pregnant females are inhibited by prostaglandins E_1, E_2 and E_3. Prostaglandins $F_{1\alpha}$ and $F_{2\alpha}$ usually cause contraction but are rather inactive. PICKLES and HALL[31] obtained similar results, but their preparations were more sensitive to prostaglandin $F_{2\alpha}$ (contracting in the approximate range of 2 to 20 ng/ml), and the responses they obtained with prostaglandin E_2 were sometimes stimulant and sometimes inhibitory. Human Fallopian tubes in vitro are contracted by prostaglandin E_1 at their uterine ends but elsewhere are relaxed like the uterus itself[28].

Although SANDBERG, INGELMAN-SUNDBERG and RYDÉN[28] postulate that prostaglandin is absorbed from the posterior fornix and transported to the uterus and tubes, a simple calculation indicates that the concentrations likely to be achieved by such a process would be low. For example, assuming that 5 ml of semen containing 70 μg of prostaglandin/ml (Table I) is deposited in the vagina of a woman with a blood volume of 5 l, then the maximum concentration of prostaglandin which could be achieved in the circulation would be 70 ng/ml. In order to act upon tissues the prostaglandin would have to pass into the interstitial fluid and so further dilution would occur. This calculation assumes that all the prostaglandin would be absorbed before any had been lost by excretion or inactivation, yet we know that prostaglandin is removed from the blood during its passage through the heart and lungs, and that it is excreted in the urine (see below). The problem of whether or not prostaglandin is absorbed from the vagina in physiologically significant amounts will probably have to be solved by experiments on human subjects.

Little is known about the actions of prostaglandins on smooth muscle of the male reproductive tract. Adrenaline induced contractions of the vas deferens of the rabbit both in vivo and in vitro are inhibited by prostaglandin E_1[32], but the absence of prostaglandin from the semen and male reproductive tract organs of the rabbit suggests that this effect is of no physiological significance.

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Actions on respiratory smooth muscle. MAIN[33] has shown that prostaglandins inhibit respiratory smooth muscle. In experiments on isolated tracheal chains from cats, monkeys, rabbits, guinea-pigs, ferrets, pigs and sheep, prostaglandin E_1 inhibited contractions produced by adding acetylcholine to the organ bath. On preparations which possessed inherent tone the inhibitory action of prostaglandin could be detected without the prior addition of a stimulant drug. The cat isolated tracheal chain was the most sensitive of all the preparations, sometimes responding to as little as 1 ng of prostaglandin E_1/ml. On this tissue prostaglandin E_2 is equi-active with E_1, but E_3 has $^1/_5$ and $F_{1\alpha}$ only $^1/_{500}$ of the activity of E_1. More recently, HORTON and MAIN[27] have shown that prostaglandin $F_{2\alpha}$ is also less active on the cat isolated trachea, having about $^1/_{30}$ of the activity of E_1, but even at high concentrations the response to prostaglandin $F_{2\alpha}$ is always inhibition. ÄNGGÅRD and BERGSTRÖM had previously reported very weak contractions of cat, rabbit and guinea-pig tracheal chains at rather high concentrations of prostaglandin $F_{2\alpha}$ (2.5 μg/ml); prostaglandin $F_{2\alpha}$ had no effect on isolated bronchial chains from cats in concentrations up to 2.5 μg/ml[23].

When the peripheral stump of the vagus nerve is stimulated in the neck or when histamine is injected intravenously, bronchial resistance is increased in anaesthetized rabbits and guinea-pigs as measured by the Konzett and Rössler method. This increased bronchial resistance, or perhaps more accurately 'increased resistance to inflation', is partially antagonized by prostaglandin E_1 injected intravenously in doses of 0.1 μg/kg (guinea-pig) and 1.6 μg/kg (rabbit)[33]. The inhibitory action of prostaglandin E_1 on bronchial resistance in the guinea-pig cannot be demonstrated unless bronchial tone is first increased by vagal stimulation or a bronchoconstrictor drug[21,33], but in the rabbit there is sometimes a decrease in the normal level of bronchial resistance following an injection of prostaglandin E_1. In the cat both prostaglandin E_1 (0.3 μg/kg)[33] and prostaglandin $F_{2\alpha}$ (15 μg/kg)[23] increase resistance to inflation.

Although prostaglandin E's are more potent inhibitors of smooth muscle than prostaglandin F's, $F_{2\alpha}$ is the prostaglandin which occurs most commonly in the lungs (Table I). Perhaps prostaglandin $F_{2\alpha}$ is stored as a less active precursor of prostaglandin E_2 which is the compound of more immediate physiological importance.

Actions on the cardiovascular system. Prostaglandins lower systemic arterial blood pressure when injected intravenously, the E's being more potent than the F's[20,22,23,27,34]. Part at least of this depressor action of the prostaglandins is due to vasodilatation; blood flow through skeletal muscle in the cat is increased by intra-arterial injection of prostaglandins E_1, E_2, E_3, $F_{1\alpha}$ and $F_{2\alpha}$[22,23,27]. Intravenous infusions of prostaglandin E_1 in two healthy human subjects caused some reduction in cardiac output accompanied by slight tachycardia[35], suggesting that decreased cardiac output may be contributory to the depressor action. Tachycardia was also observed in the cat following an intravenous injection of prostaglandin E_1[33], but intravenous prostaglandin $F_{2\alpha}$ in the cat produces a bradycardia which is abolished by atropine[26]. Prostaglandin E_1 has no effect on the isometric contractions of the spontaneously beating isolated guinea-pig atria, nor does it affect the positive inotropic responses of this preparation to catechol amines[32].

During the period following injection of prostaglandin E_1 intravenously or intra-arterially, the pressor and vasoconstrictor responses to angiotensin, vasopressin, adrenaline and noradrenaline are reduced[32]. This is not due to a simple algebraic summation of opposite effects but appears to represent a decreased responsiveness of the vascular smooth muscle to vasoconstrictor substances for some time after exposure to prostaglandin.

Unlike several naturally-occurring vasodilator substances (for example bradykinin, histamine and acetylcholine), prostaglandin E_1 does not release adrenaline from the adrenal medulla when injected close-arterially[21]. Prostaglandin E_1 also has only a weak action in increasing capillary permeability[21].

The effects of prostaglandins on blood vessels are of doubtful physiological significance. It is improbable that prostaglandins would be released as local metabolites in functional hyperaemia, other more potent vasodilators being readily available in larger amounts. The vasodilator potency of the most active prostaglandins, namely E_1 and E_2, is certainly less than that of bradykinin for example[21]. If prostaglandins ever circulate in the blood under physiological conditions, it seems likely that they would do so at concentrations considerably lower than those necessary to produce a depressor effect (compare the concentrations of vasopressin necessary to produce antidiuresis and vasoconstriction).

Actions on intestinal smooth muscle. Isolated segments of intestinal smooth muscle of most species investigated contract in response to low concentrations of the prostaglandins, the rabbit isolated duodenum and jejunum respond to 0.25 ng prostaglandin $F_{2\alpha}$/ml for example[23,27]. This type of preparation has therefore been widely used for the estimation of prostaglandin. Other sensitive tissues include the guinea-pig ileum, hamster colon, chicken jejunum, chicken rectal caecum and rat jejunum[5,20-23,27,34]. In contrast to tissues on

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which prostaglandins exert an inhibitory effect where prostaglandin E's are more potent than the F series, these intestinal preparations are often more sensitive to the prostaglandin F's. Whether prostaglandins have any local role in the control of intestinal movements which are independent of innervation is a problem which awaits further study.

Actions on the nervous system. Injections of prostaglandins E_1, E_2 and E_3 in doses of 10 to 60 μg into the cerebral ventricles of unanaesthetized cats are followed after a latent period of 20 min or more by signs of sedation and catatonic stupor[36]. The stupor lasts for several hours and the cat shows diminished spontaneous activity for up to 48 h after the injection. On the other hand, the righting reflex is always present and when the cat is disturbed its movements are brisk and show no evidence of ataxia. In marked contrast, prostaglandin $F_{2\alpha}$, the only prostaglandin so far found in tissues of the central nervous system[16], produces no detectable changes in cats following injections into the ventricles in doses equal to or higher than those of prostaglandin E_1 necessary to produce pronounced catatonia[37]. The catatonia and stupor are therefore not due to some non-specific physico-chemical effect of long-chain fatty acids since a simple reduction of the oxo group in the prostaglandin E molecule abolishes (or lessens) its activity.

Using an iontophoretic technique for applying substances to single cells, KRNJEVIĆ (personal communication) detected no significant effect of prostaglandin E_1 on 18 cortical neurones in two cats. There was no excitation of quiescent cells, no excitation or depression of spontaneously active cells, no effect on glutamate firing, no change in response of cholinoceptive cells to firing by acetylcholine and no change in the effectiveness of γ-aminobutyrate as a depressant of glutamate firing.

Some rather transient sedation is the only effect seen following intravenous injection of prostaglandin E_1 (20 μg/kg) in cats. A decrease in spontaneous activity of mice lasting for about 1 h is observed following intravenous or subcutaneous injections (unpublished observations). In the young chick, which is believed to lack a blood brain barrier, prostaglandins are particularly active on the central nervous system. Prostaglandins E_1, E_2 and E_3 in doses as low as 1 μg injected intravenously cause sedation with cessation of spontaneous movements, closure of the eyes and, in higher doses, loss of righting reflexes[36]. In contrast, prostaglandin $F_{2\alpha}$ produces not sedation but a postural defect. The limbs extend or abduct often to extreme degrees, but the legs appear not to be paralysed[37]. All these effects are temporary; the chicks recover completely after 10 min to 2 h depending upon the dose.

Little work has been reported on the actions of prostaglandins on the peripheral nervous system. Prostaglandin E_1 in concentrations from 0.1 to 100 μg/ml when applied to exposed blister bases on the human forearm did not give rise to any sensation of pain or itch[21]. Bradykinin (0.1 μg/ml) and 5-hydroxytryptamine (0.01 μg/ml) were effective in producing a sensation of pain on these preparations.

Part of the stimulant action of prostaglandin E_1 on the guinea-pig isolated ileum appears to be mediated by a nervous pathway since the response is partially antagonized by atropine (0.01 μg/ml) (unpublished observations). Contractions of the cat nictitating membrane produced by pre-ganglionic cervical sympathetic nerve stimulation were unaffected by prostaglandin E_1 injected either intravenously or into the common carotid artery, although relaxations of the membrane after cessation of stimulation were more rapid in the period immediately following prostaglandin administration[32]. There was no evidence in these experiments to suggest that ganglionic transmission is affected by circulating prostaglandin but experiments using more refined techniques are needed in order to be certain of this.

Actions on adipose tissue. Rat epididymal fat pads incubated *in vitro* release glycerol and fatty acids into the medium in response to catechol amines, corticotrophin, glucagon and thyroid stimulating hormone. The presence of prostaglandin E_1 in concentrations of 20 ng/ml or more inhibits the lipolysis induced by these agents[38]. Although prostaglandin E_1 suppresses adrenaline-induced activation of lipase, it does not affect adrenaline-induced activation of phosphorylase, an enzyme also present in adipose tissue. BERGSTRÖM, CARLSON and ORÖ[39] in experiments on anaesthetized dogs have shown that prostaglandins E_1, E_2 and E_3 are very potent also *in vivo* in inhibiting catechol amine-induced lipolysis, although prostaglandin $F_{1\alpha}$ is inactive, at least in doses similar to those of the E's. Doses which were effective in lowering plasma free fatty acid levels also produced a slight fall in blood pressure but the effect on the fatty acids was more prolonged. Increases in blood glucose due to injections of adrenaline were only moderately inhibited by prostaglandin E_1. In contrast to these results in dogs, prostaglandin E_1 infusion in human subjects increases the arterial level of free fatty acids and does not counteract the rise in free fatty acids produced by noradrenaline[13].

Actions on micro-organisms. Long-chain fatty acids inhibit the growth of certain bacteria and yeasts, and the presence of such substances accounts for the antibacterial activity of human sebaceous secretions[40].

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HOLMES[41] has recently shown that prostaglandin E_1, although a long-chain fatty acid, does not have an inhibitory action on the growth of micro-organisms in vitro in concentrations up to 1 mg/ml, whereas undecenoic, lauric and ricinoleic acids were inhibitory against some or all of the organisms tested. These observations would seem to exclude the possibility that prostaglandins provide some form of chemical defense mechanism in the tissues in which they occur.

Metabolism of prostaglandin E_1. Intra-aortic infusions of prostaglandin E_1 inhibit noradrenaline-induced fat mobilization in dogs more effectively than intravenous infusions, suggesting that prostaglandins are either taken up or inactivated by the lungs (and/or heart)[39]. Similar differences have been observed in ewes[25]. SAMUELSSON[42] has reported that when tritium-labelled prostaglandin E_1 is injected subcutaneously in rats, most of the radioactivity appears in the urine and about a one fifth in the faeces.

Miscellaneous observations (unpublished). In the water-loaded ethanol-anaesthetized rat[43], prostaglandin E_1 injected intravenously decreased urine flow but only in doses which lowered arterial blood pressure. The rats responded to 0.01 milliunits of vasopressin, but these antidiuretic responses were unaffected by previous administration of prostaglandin E_1 in doses which produce a slight depressor response. This contrasts with the observation[24] that prostaglandin E_2 potentiates oxytocic responses to vasopressin in vitro, and with the observation that pressor responses to vasopressin are temporarily abolished after prostaglandin E_1[32].

The presence of high concentrations of prostaglandin in human semen (Table I) does not appear to be essential for sperm motility. Two equal portions of a freshly collected sample of human semen were centrifuged and the deposited sperms were re-suspended in artificial seminal plasma. One plasma contained prostaglandin E_1 (100 μg/ml), the other contained no prostaglandin. The total number of motile sperms in the two aliquots was not significantly different even after three such washings when the % motility was still 75% of the initial figure.

The beating of cilia of the epithelium lining the rabbit trachea was not affected by the presence of prostaglandin E_1 (10 μg/ml) as measured by observing the rate of movement of foreign particles under the microscope. The movement of the particles could be blocked by atropine and the rate increased by eserine.

Discussion. The concept that the significance of prostaglandin is confined to the reproductive tract is no longer tenable. Prostaglandins are widely distributed throughout the body and they have an equally wide range of biological activities; indeed all organs from which prostaglandins have been isolated contain some cells (in addition to vascular smooth muscle) which respond to their presence. The thymus may be an exception to this generalization.

The idea that prostaglandins are hormones which circulate and act upon a variety of tissues is also difficult to accept on the present evidence. Prostaglandin E_1, for example, inhibits the tone of vascular, respiratory and reproductive smooth muscle, inhibits the mobilization of fats and, if the dose is adequate, depresses central nervous activities. Under what circumstances would such a combination of diverse effects be likely to occur? It is conceivable, of course, that prostaglandins circulate in concentrations lower than those required to produce the effects described above and that the truly physiological responses to these low concentrations remain to be elucidated.

Another possibility is that prostaglandins act locally, perhaps intracellularly as coenzymes. For example, the prostaglandin E's and F's may function in pairs, the conversion of an F to an E providing two hydrogen atoms for a hydrogenase system and vice versa. Some observations are difficult to explain on this hypothesis. If a prostaglandin E acting as a hydrogen acceptor relaxes smooth muscle then the corresponding F acting as a hydrogen donor might be expected to have the opposite action to E or possibly no action, but not to have the same effect as occurs with respiratory and vascular smooth muscle.

The position may be analogous to that of the adrenal corticosteroids. Many biologically-active steroids have been isolated from the adrenal cortex but only a few are actually secreted, the remainder being precursors in the biosynthetic pathway. If the prostaglandins are similar in this respect, then the F's must be considered as less active precursors of compounds of greater physiological significance (the corresponding E's). It is the F's which are predominantly stored in many tissues. According to this hypothesis $F_{2\alpha}$ in lung is functionally important only as a precursor of E_2, which possibly has some role in the control of respiratory smooth muscle tone. In the brain prostaglandin E_2, having been formed in small amounts from $F_{2\alpha}$, may act upon a similar biochemical pathway in nervous tissue. The dramatic effects seen on intracerebroventricular injection of the E's could be interpreted as due to the presence of a great excess of a compound which is normally present in only minute quantities. On the other hand $F_{2\alpha}$, although it is the compound normally present in larger amounts, is less active and therefore has no effect on intraventricular injection. Furthermore, the rate of conversion of $F_{2\alpha}$ to E_2 is probably too slow for any detectable effects

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due to increased E_2 to be observed following an injection of F_{2x}.

The idea that F is a less active precursor of E is, to some extent, supported by the findings in semen. If the E's are the physiologically important compounds, then it is to be expected that E's and not F's would be secreted by the seminal vesicles. In this instance the semen is not a storehouse for prostaglandin (like lung and brain) but a secretion which must contain its prostaglandins in an already active state. Both human and sheep semen contain predominantly prostaglandin E's (Table I).

Table II shows the relative activities of prostaglandin E's and F's on seventeen biological preparations. On those which are inhibited by prostaglandins, E's are always more potent than F's, but on tissues which are stimulated the ratios of activity are more variable, the two prostaglandins tending often to be equiactive. It is of interest in this connection to compare these effects with those of adrenaline and noradrenaline. In general, adrenaline (like prostaglandin E's) has more potent inhibitory actions but both catecholamines (and both prostaglandins) are very active on tissues which are stimulated. A further point of similarity may be that in both cases a more potent inhibitor (adrenaline and prostaglandin E) is formed in the tissues from a less potent inhibitor (noradrenaline and prostaglandin F). The inhibitory and excitatory effects of prostaglandins, like those of the catecholamines, may each have a physiological importance at different sites.

Most of these speculations are based upon insufficient and incomplete evidence. Our knowledge of the distribution, metabolism and actions of the prostaglandins is still fragmentary and certainly does not allow any but the most tentative conclusions to be drawn at the time of writing. The functional significance of the prostaglandins still eludes us.

Table II. Relative biological activities of prostaglandins E's and F's on various preparations. An asterisk indicates that the figure was calculated from results obtained from two sources

Biological preparation	Response	$E_1/F_{1\alpha}$	$E_2/F_{2\alpha}$	Reference
Cat isolated trachea	Inhibition	500	30*	33, 27
Guinea-pig isolated ileum	Contraction	45, 43		20, 22
Chicken jejunum	Contraction	40		20
Cow isolated iris	Contraction	>30		20
Rabbit B.P.	Depressor	>20, 13		20, 22
Chick	Sedation		>15*	36, 37
Rat isolated jejunum	Contraction	12		20
Cat	Stupor		>6*	36, 37
Cat skeletal muscle blood vessels	Dilatation	4.5		22
Hamster isolated colon	Contraction	4.2		22
G.P. isolated uterus	Contraction	3		20
Fat mobilization	Inhibition	>2		39
Chicken rectal caecum	Contraction	1.8		20
Rat isolated uterus	Contraction	0.5, 1.0		20, 22
Rabbit isolated jejunum	Contraction	0.6, 0.45		20, 22
Rabbit isolated uterus	Contraction	<0.5		20
Rabbit oviduct in vivo	Inhibition	(Prostaglandin F's contract)		22, 27

Résumé. Les prostaglandines sont des acides gras non saturés existant à l'état naturel et contenant un anneau de cyclopentane; elles ne diffèrent les unes des autres que par leur degré de non-saturation et la présence dans l'anneau d'un substituant oxo (prostaglandine E) ou hydroxy (prostaglandine F). Les prostaglandines ayant une ou deux liaisons doubles sont plus actives au point de vue biologique que les prostaglandines ayant trois liaisons doubles. La réduction du groupe oxo a un effet prononcé sur l'activité biologique. C'est ainsi que les prostaglandines F inhibent moins que les prostaglandines E le muscle lisse vasculaire, respiratoire et reproducteur et la mobilisation des lipides et causent une sédation et une stupeur moins fortes chez les animaux non anesthésiés. D'autre part, le muscle lisse qui est contracté par les prostaglandines, comme par exemple l'intestin du lapin, est souvent plus sensible aux F qu'aux E. Les prostaglandines F abondent dans les tissues animaux et on suggère qu'elles sont peut-être les précurseurs des E plus actives dans certains organes, par exemple le poumon et le cerveau.

On discute le rôle physiologique éventuel des prostaglandines. Il est, pense-t-on, peu probable que leur importance fonctionnelle soit limitée à la physiologie de la reproduction, bien que cette fonction puisse être importante. On postule que si les prostaglandines circulent sous forme d'hormones, elles le font dans des concentrations plus faibles que celles qui affectent la pression artérielle. Alternativement, les prostaglandines peuvent agir localement, peut-être à l'intérieur des cellules sous forme de co-enzymes. Par exemple, les prostaglandines E et F peuvent fonctionner par paires, la conversion d'une F en E fournissant deux atomes d'hydrogène par système d'hydrogénase et vice versa. L'abondance des prostaglandines et la diversité de leurs effets biologiques suggèrent certainement qu'elles jouent un rôle général de cet ordre dont l'importance est fondamentale.