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# PHYSIOLOGY OF LACTATION

**Report of a WHO Scientific Group**

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## CONTENTS

	Page
1. Introduction . . . . .	5
2. Growth of the mammary gland . . . . .	7
2.1 Foetal growth . . . . .	7
2.2 Postnatal growth . . . . .	8
2.3 Problems requiring investigation . . . . .	10
3. Milk secretion . . . . .	11
3.1 Hormonal control . . . . .	11
3.2 Control of pituitary function in milk secretion . . . . .	12
3.3 Role of the central nervous system in milk secretion . . . . .	14
3.4 Cytological changes in the secreting mammary gland . . . . .	14
3.5 Problems requiring investigation . . . . .	15
4. Biochemical activities of the mammary gland . . . . .	15
4.1 Biosynthesis of milk proteins . . . . .	15
4.2 Biosynthesis of lactose . . . . .	15
4.3 Biosynthesis of milk fats . . . . .	16
4.4 Problems requiring investigation . . . . .	17
5. Physiology of suckling . . . . .	17
5.1 Problems requiring investigation . . . . .	19
6. Aspects of human lactation and breast-feeding . . . . .	19
6.1 Lactation . . . . .	19
6.2 Breast-feeding . . . . .	19
6.3 Particular problems of developing countries . . . . .	20
6.4 Problems requiring investigation . . . . .	21
7. Recommendations . . . . .	22



# PHYSIOLOGY OF LACTATION

## Report of a WHO Scientific Group

### 1. INTRODUCTION

Lactation is the final phase of the complete reproductive cycle of mammals. In almost all species the newborn are dependent on maternal milk during the neonatal period; in most the young are dependent for a considerable time. Adequate lactation is therefore essential for reproduction and the survival of the species and, biologically, failure to lactate can be just as much a cause of failure to reproduce as is failure to mate or to ovulate. In view of this necessity for lactation, it is not surprising that the lactating mother will, if necessary, produce milk at the expense of her own body tissues and that suckling young, like foetuses, can metabolically cannibalize the maternal organism. Correspondingly, the reproductive cycle is usually in abeyance during at least the early stages of lactation.

This applies with equal force to man except where adequate substitutes for human milk are available; in large areas of the world, therefore, the newborn infant is dependent on its mother's milk and the undernourished mother will convert her tissues into milk for her offspring. In such areas, the death of the mother or the failure of lactation presents a problem which can be solved only by foster-mothering or death of the baby. Anthropological literature abounds in accounts of extraordinary rites and concoctions used to prepare foster-mothers by the induction of lactation in virgins or grandmothers.

The problem presented is threefold: the provision of adequate nutrients for the nursing mother, the provision of adequate substitutes for human milk when necessary, and the prevention of failure of lactation. In more developed communities, the first two of these problems are naturally less obtrusive but the third remains important. From the biological point of view, it is interesting to speculate whether deprivation of breast-feeding has the same effects as deprivation of maternal care and whether the removal of the species-survival value of capacity for lactation will in time lead to the retention of the human breast only as a sex symbol.

This report is essentially concerned with man, but human lactation cannot be considered in isolation, partly because the evolutionary and comparative aspects are illuminating as well as fascinating and partly

because the neural and endocrinological background has necessarily been analysed mainly by experiments on laboratory and farm animals.

In the egg-laying but mammalian monotremes, modified skin glands secrete a nutrient fluid which runs down the bristly hairs of the belly and is licked off by the newly-hatched young. There are no nipples. In the marsupials, organized glands are formed within the pouch and it is reported that the young of very different ages may obtain milk of appropriately different composition from different nipples within the same pouch. In the higher mammals, the milk may be very dilute or highly concentrated and may be produced in small or large quantities. The female seal produces milk containing at least 50 % fat and does so for a six-week nursing period during which she does not eat and her pup gains about 45 kg in weight at the expense of her tissues. A litter of mice puts on about 50 g in body weight while suckling for three weeks from a mother weighing 25 g, who eats 40 % of her own body weight in dry food per day. A cow has produced 20 500 litres (4 500 UK gal) of milk, about 45 times her own body weight, in a year and rats have lactated continuously for a year after one pregnancy when supplied with relays of suckling young.

Here, then, is a physiological event which merits close investigation on both practical and scientific grounds. Unfortunately, the endocrine background has been analysed fully only in some species of animals from which all the main endocrine organs—gonads, adrenals, pituitaries, and thyroids—can be removed and endocrinologically synthetic animals built up. This type of analysis has been extended partially to other species but, as might be expected, only in modified form to man. Evidently, full analysis of the endocrine requirements for mammary growth and secretion is likely to be restricted for many years to experimental animals and information obtained from them will have to be extrapolated to man. Nevertheless, information about the endocrinological background of human lactation has been obtained directly by observation and minor experimentation. Unusual happenings have also contributed to this knowledge of human lactation. Thus the fundamental fact of its endocrine control was observed in 1910 from the well-known case of the Bohemian identical twins joined at the pelvis and having a common vagina. One became pregnant and both lactated. Again, the occasional appearance of "witch's milk" in newborn babies is a good example of the *crise génitale* caused by the sudden withdrawal of maternal hormones and is homologous with the regression of the hyperplastic prostate of the newborn baby boy. More practical interest attaches to the occurrence of gynaecomastia, especially where it is thought to arise from the failure to destroy endogenous oestrogens in cases of liver damage.

Analysis of the involvement of the central nervous system in lactation again relates mainly to experimental animals, but a good deal of

information about the nature of the suckling stimulus, milk ejection, and the results of emotional stress is available for man. Conditioned reflexes and sensory stimuli are obviously involved.

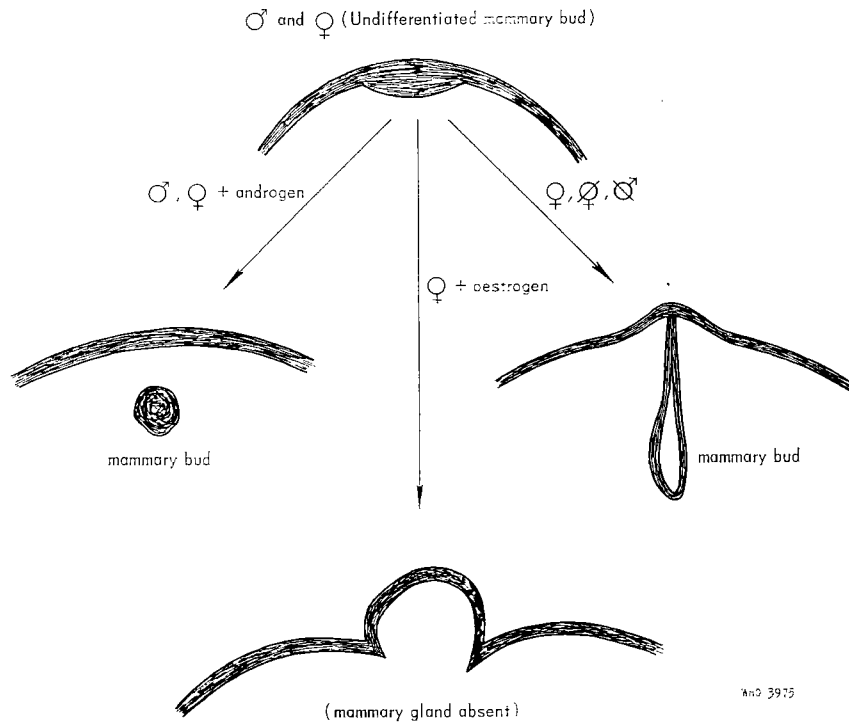
## 2. GROWTH OF THE MAMMARY GLAND

### 2.1 Foetal growth

The various stages in the embryonic and foetal growth of the mammary gland have been described in some detail in a number of species, including man, but only in the rat and mouse is there any substantial information about the mechanisms which control this growth process.

In the rat and mouse the early stages of mammary growth in the embryo apparently occur independently of any hormonal influence of the embryonic gonads, and growth may indeed take place without hormones. In the rat and mouse, sex differentiation appears in the rudimen-

FIG. 1. SEX DIFFERENTIATION IN THE RUDIMENTARY MAMMARY GLAND



tary mammary gland from the fourteenth or fifteenth day of intra-uterine life (Fig. 1). In these animals, the formation of the male breast is due to a modification of the normal female type by a hormone (or hormones) from the foetal testis. This type of differentiation, the diversion of the neutral (female) pattern to the male pattern under the influence of foetal androgen, is characteristic also of the early differentiation of the reproductive tract and of the sexual differentiation of the central nervous system.

It should be noted that the administration of oestrogenic hormones can cause premature nipple development in foetuses of both sexes as well as a variety of malformations of the mammary bud ranging from complete inhibition of development (i.e., absence of the mammary gland) to lesser irregularities in the normal structure of the gland.

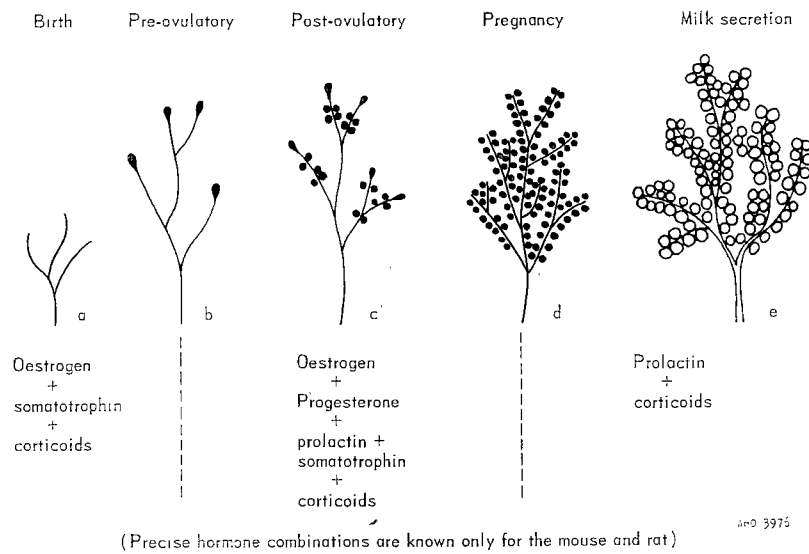
Whether these findings are applicable to other species is as yet unknown, but these malformations of the mammary gland of the mouse and rat foetus are induced by doses of oestrogen that might be given to pregnant women. Malformations of the reproductive tract may also be similarly induced. There are some indications, however, that the human foetus can protect itself against the natural sex steroids.

## 2.2 Postnatal growth

Postnatal growth of the mammary gland can follow several patterns, associated mainly with the type of sex cycle of the species in question. In most species, except in those exhibiting a long luteal phase, mammary growth is restricted to extension and proliferation (Fig. 2b) of the duct system (Fig. 2a) and limited alveolar development occurs (Fig. 2c). In women some alveolar growth of this type occurs during the menstrual cycle. When pregnancy occurs further development of the duct system and extensive development of the alveoli take place (Fig. 2d). Recent studies, using biochemical methods of assessing lobule-alveolar development (determination of deoxyribonucleic acid, DNA) have shown that, contrary to earlier beliefs, cell hyperplasia continues not only to the end of pregnancy but also into the period of early lactation (Fig. 2e).

The phases of postnatal mammary growth are hormonally controlled, but only for the rat and mouse has detailed experimental analysis of the hormones involved been carried out. In these two species growth of the gland requires oestrogen, progesterone, prolactin, pituitary growth hormone (somatotrophin, STH), and adrenal corticoids (Fig. 2). In man, rat, mouse, and sheep the placenta secretes hormonal substances which in their biological actions are similar to pituitary prolactin and somatotrophin, so that in normal pregnancy mammary growth may be controlled by hormones from the ovary, adrenal, anterior pituitary, and placenta working in synergism. Human STH can be substituted for

FIG. 2. MAMMARY GROWTH AT DIFFERENT PERIODS OF LIFE



the combination of prolactin and STH in eliciting mammary growth in rats, and is now being tested in primates for the same function.

The hypothalamus is undoubtedly important in mammary growth, since it controls the mammary growth-stimulating (mammogenic) and gonadotrophic activity of the anterior pituitary. The hypothalamus is itself subject to influences from higher centres and from the peripheral nervous system, but on these there is little information.

Progress in the understanding of the mechanism of human mammary growth has been slow. There are technical difficulties associated with the evaluation of mammary growth; the over-all size of a mammary gland may provide little indication of the amount of glandular tissue within it. There exist several accurate histometric methods for assessing the amount of glandular tissue in autopsy or biopsy material, but they are unfortunately tedious and have been little used. The recent introduction of biochemical methods, such as the determination of the DNA content of the gland, may prove to be of great value because of their quickness. Their reliability, however, has still to be established and for the moment they cannot entirely take the place of the histometric procedures. In man, several clinical methods of assessing glandular development (such as changes in over-all volume, palpation of the mammary parenchyma, and radiographic procedures) have been used, but their accuracy and reliability have still to be established.

Measurements of breast growth in human pregnancy by displacement indicate a declining response with age in primigravidae, but not in multigravidae. That displacement is indicative of mammary growth is supported by records of milk production. The areolae of the nipples follow the same pattern as growth of the breast. These differences may be genetic, and parallel studies from different ethnic groups might illuminate this question. There is a wide range of individual variation in mammary growth at all ages. The mobility of the nipple—and therefore the success with which it can be grasped by the infant—improves during pregnancy but is not affected by maternal age.

Little is known of the levels of the various mammogenic hormones in body fluids because of difficulties in their assay. Assay methods are now available for oestrogen and progesterone, and assays for blood STH and prolactin are becoming available. Until reliable clinical methods for assessing mammary-gland growth and reliable assay methods for following the levels of the mammogenic hormones in body fluids exist, research on the correlation of the level of hormone activity with the degree of mammary growth in man is likely to proceed slowly, if it proceeds at all.

It is possible that useful information on the hormonal control of the growth of the human mammary gland may be provided by studies of the causes of gynaecomastia and by the treatment of intersexuality, gonadal dysgenesis, and pituitary dwarfism. There is, however, some doubt as to whether the mammary tissues of the human male and female respond in an identical manner to mammogenic hormones. Gynaecomastia has been associated with a wide range of clinical conditions, including malnutrition, endocrinopathies, and paraplegia, and with the after-effects of chest surgery. The connecting links are obscure at present, but gynaecomastia associated with malnutrition is widespread in some parts of the world. A study of the pathogenesis of this condition may shed light on normal breast growth.

### 2.3 Problems requiring investigation

(1) Comparative studies on the mechanisms of mammary histogenesis in species other than the rat and mouse should be carried out. This should help to throw further light on the processes of human mammary growth.

(2) Studies on the possible effects of hormones and drugs administered during pregnancy on congenital malformations of the mammary gland should be made in primates and human infants. In stillbirths and neonatal deaths, where the mother has been subjected to treatment with hormones or drugs, the foetal mammary glands should be examined histologically.

(3) Techniques for measuring mammary gland growth in man should be devised. Such methods should help to distinguish between parenchymal and non-parenchymal tissue. Assay procedures for mammogenic hormones in body fluids should be developed.

(4) Studies of ethnic differences in the growth response of the breast at different ages and during pregnancy might help to elucidate genetic differences in breast-feeding performance.

(5) Studies on the etiology of gynaecomastia, and particularly its relation to malnutrition and liver disease, might help to elucidate the mechanisms regulating breast growth.

### 3. MILK SECRETION

#### 3.1 Hormonal control

The precise neuroendocrine mechanisms responsible for the initiation of milk secretion are still obscure. Studies indicate that reductions in the levels of oestrogens and progesterone in the blood at the time of parturition, associated with adequate blood levels of prolactin and adrenal corticoids, favour the onset of milk secretion (Fig. 2c). Whether the same complex of hormones is involved in the maintenance of lactation is uncertain.

The old idea that prolactin is the specific lactogenic hormone can no longer be upheld, for it is now clear that satisfactory milk secretion is dependent on a complex of hormones, of which prolactin is normally a component. Only in the rat and goat is there any precise information on hormone requirements for the maintenance of lactation. If the rat is hypophysectomized during lactation, prolactin and adrenocorticotrophin (ACTH) or adrenocorticoids will maintain a moderate level of milk secretion, while in the hypophysectomized goat full milk production can be maintained with prolactin (sheep) + somatotrophin (ox) + adrenocorticoids + thyroid hormone + insulin.

Although similar studies have not yet been made in other species, studies on the hormonal stimulation of galactopoiesis throw some light on the hormonal regulation of milk secretion, since the two phenomena must be closely related. So far no reliable evidence exists that anterior pituitary hormones of animal origin have any galactopoietic action in lactating women; indeed, this would now hardly be expected in view of the recently discovered biological species specificities of prolactin and STH. Moreover, these hormones could even be dangerous because of immunity reactions. STH preparations from human and monkey pituitaries differ chemically from those of cow, sheep, and pig, and unlike the latter exert growth-promoting and anabolic effects in man and monkey. Purified preparations

of human and monkey STH made by different methods exhibit in rats and other animals (they have not yet been tried in man) biological properties characteristic of ox and sheep prolactin that are not exhibited by STH preparations from other species. Attempts to separate off this prolactin-like activity from human STH have so far failed. Human, or possibly monkey, lactogenic hormone (STH?) may well prove a valuable agent in the treatment of hypogalactia in women when enough becomes available through purification of pituitary or placental extracts or by chemical synthesis.

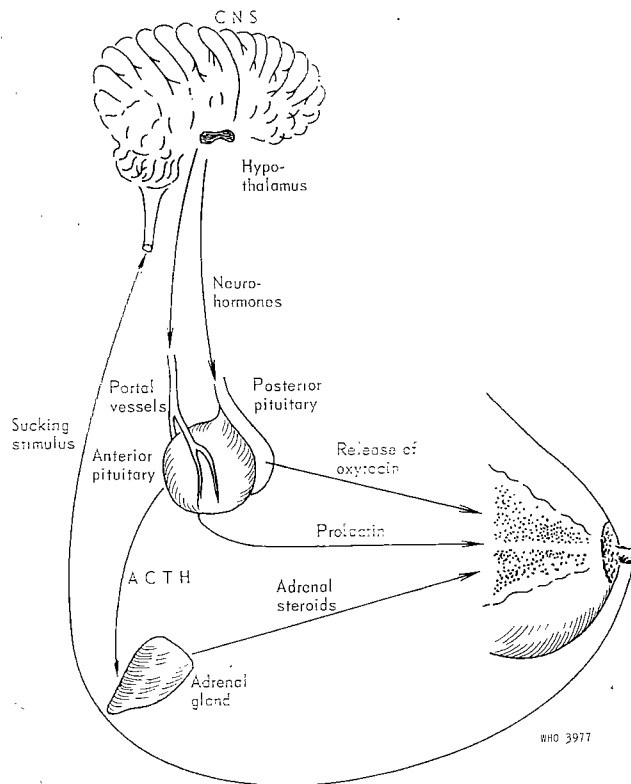
### 3.2 Control of pituitary function in milk secretion

The anterior pituitary hormones—prolactin, STH, ACTH, and thyrotrophin (TSH)—are all concerned in the regulation of milk secretion. The next question that arises is how their release from the pituitary is controlled. There is now much evidence to suggest that pituitary function is controlled from the hypothalamus by substances—neurohumoral transmitters—released there and transported to the anterior pituitary via a specialized vascular system in the pituitary stalk—the hypophysial portal system. Much research is at present being devoted to the isolation and identification of these factors. Experiments involving transection of the pituitary stalk or transplantation of the pituitary have shown that the control of prolactin release differs from that of the other hormones. Thus, when the pituitary is removed from hypothalamic control the production of ACTH, STH, and TSH is greatly reduced, whereas prolactin secretion continues at a rate that may be higher than that occurring in the normal oestrous cycle. There is now evidence from many species, including man, that the release of prolactin from the pituitary is chronically inhibited by the hypothalamus, and to effect prolactin release it is thus necessary to depress this inhibition. Evidence for the presence in the hypothalamus of a prolactin-inhibiting factor has recently been reported. The activity of this factor in the hypothalamus is greatly depressed by the suckling stimulus, by oestrogens, and by certain drugs (e.g., reserpine)—all of which are known to increase prolactin release from the anterior pituitary. This action of reserpine may well explain a number of reports of the occurrence of milk secretion in patients under prolonged tranquillizer therapy.

In addition to the control of the anterior pituitary from the hypothalamus, certain hormones (e.g., oestrogen and thyroxine) may act directly on it to cause prolactin release.

So far, not a great deal is known about the way in which information reaches the hypothalamus. The reflex maintenance of anterior pituitary function by the suckling stimulus appeared to supply a satisfactory explanation of the manner in which milk secretion was maintained (Fig. 3), but recent studies on the sheep and goat necessitate some reappraisal of

FIG 3. NEUROENDOCRINE FACTORS IN THE MAINTENANCE OF LACTATION



its importance. There is now evidence, virtually conclusive, that full milk secretion can be maintained in the goat and sheep after complete severing of all nerve connexions between the mammary gland and the brain. This does not necessarily imply that the suckling stimulus is not the usual factor concerned in the maintenance of milk secretion, but it does indicate that some alternative mechanism exists, at least in some species. So far there is no concrete evidence about the nature of this second mechanism, but it has been suggested that the mammary gland utilizes or inactivates the pituitary hormones present in the blood and that the fall in the blood levels of these hormones stimulates the release of further quantities; it is also possible that certain visual, olfactory, or auditory stimuli may be capable of effecting the release of the complex of galactopoietic hormones.

### 3.3 Role of the central nervous system in milk secretion

Although milk secretion can continue in the denervated mammary gland, there is some evidence that efferent nerves may play some part in the secretory activity of the alveolar cells. The central nervous system can undoubtedly influence milk secretion by affecting the activities of the hypothalamus. These influences may be complex and affect not only milk secretion but also milk ejection, or both. Nervous factors undoubtedly affect milk secretion in animals, but their role in human lactation is probably of greater importance.

Of interest are the little-known studies carried out in the USSR on the association between the temperament of animals and their capacity for lactation. The type of higher nervous activities of the animals is assessed by a series of behavioural tests based on those first developed by Pavlov. In these tests three "operational parameters" are used by which observable characters of behaviour can be ranked or measured; the parameters are usually termed "strength", "balance", and "versatility". The notion of "strength" may be related to the range of intensity over which an organism can develop a reasonable response and "balance" to the equilibrium between cortical inhibition and excitation. Classified on this basis animals fall into four main groups: (1) strong, balanced, and versatile; (2) strong, unbalanced, and versatile; (3) strong, balanced, and non-versatile; and (4) weak, unbalanced, and non-versatile. (Pavlov drew a vague analogy between these types and the four Hippocratic types: (1) sanguine; (2) choleric; (3) phlegmatic; and (4) melancholic.) When cows are tested and allocated to these types, it is found that high milk production is correlated with the "strong, balanced, and versatile" cows, and low yields with the "weak, unbalanced" cows. This typing of higher nervous activity is still a somewhat lengthy procedure extending over several months, but it may prove of value in the selection of animals with a high milk yield potential.

### 3.4 Cytological changes in the secreting mammary gland

Before the introduction of the electron microscope, microscope studies had led to no firm conclusions as to how the secretory products of the alveolar cells are passed or excreted into the alveoli. Further information may yet be gained from *in vivo* studies with the light microscope. Recent studies using electron microscope techniques, however, have considerably advanced our understanding of the processes concerned with the excretion of milk fat and protein, but the effects of hormones on the excretory processes of the alveolar cells remain to be determined.

### 3.5 Problems requiring investigation

(1) There is a very urgent need to investigate human pituitary hormones. In particular, attempts should be made to see whether human prolactin and STH are two separate hormones. To this end, the projected collection of human pituitaries should be vigorously pushed forward.

(2) The prolactin-inhibiting factor from the hypothalamus may prove to be of importance in the treatment of galactorrhoea and breast cancer. For this reason, the collection of hypothalamic tissue from various animal species should be vigorously promoted, for the extraction, identification, and biological testing of the active principle. Since the substance appears to be a small molecule, its eventual synthesis should be possible.

(3) Further research is needed on the effect of the intensity, frequency, and duration of the suckling stimulus on the level of the pituitary lactogenic hormone complex and on the secretion of milk in animals.

(4) Abnormalities of breast function, such as galactorrhoea, should be studied, since an understanding of their etiology may elucidate the mechanisms controlling normal milk secretion.

## 4. BIOCHEMICAL ACTIVITIES OF THE MAMMARY GLAND

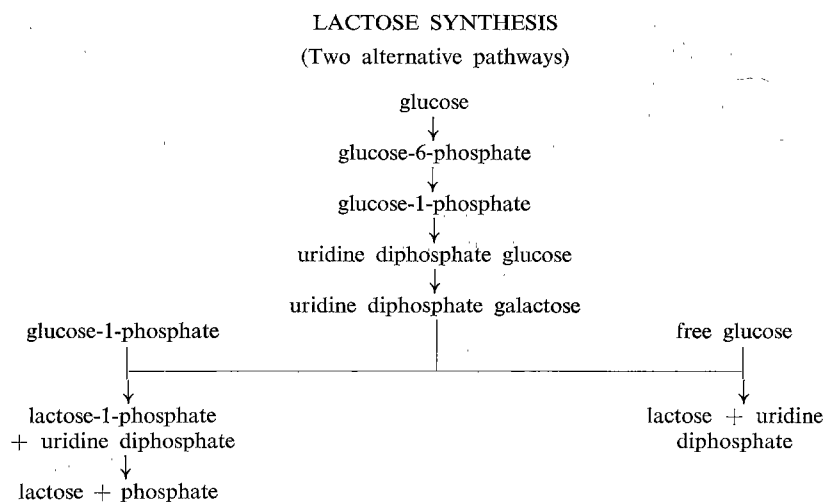
### 4.1 Biosynthesis of milk proteins

The synthesis of  $\alpha$ - and  $\beta$ -caseins and of  $\beta$ -lactoglobulin (totalling 90 % of milk protein in the cow) takes place in the mammary gland, while immunoglobulin, milk serum albumin, and  $\gamma$ -casein probably come from the circulating blood. The globulin present in colostrum may come from the plasma cells of the mammary gland. The experimental evidence suggests that the milk proteins are synthesized in the mammary gland from a pool of free amino acids derived from the free plasma amino acids, and some of the steps involved in this protein biosynthesis have been elucidated. Some amino acids are synthesized in the mammary gland from glucose and other substances, but it is not known what products serve as sources of nitrogen for their synthesis. Inorganic phosphates in the blood act as precursors of the phosphorus in casein, but at what stage the phosphorus is incorporated is not precisely known.

### 4.2 Biosynthesis of lactose

Blood glucose is the most important precursor in the synthesis of the glucose and galactose moieties of lactose in the mammary gland, a much less important role being played by substances such as acetate and pro-

pionate. There still exists some doubt regarding the precise pathway of lactose biosynthesis. It has been thought that both the glucose and galactose moieties come from glucose-1-phosphate, but more recent studies suggest that the glucose moiety is derived from free glucose in equilibrium with blood glucose while the galactose moiety comes from the hexose phosphate, as shown below.



### 4.3 Biosynthesis of milk fats

Milk fats consist essentially of triglycerides. The fatty acids are partly synthesized in the mammary gland, in rats from glucose and in ruminants from acetate. In the ruminant these fatty acids are of the short-chain type ( $C_4 - C_{14}$ ). This synthetic process is under hormonal control, but the nature of the control varies in different species. It now seems likely that the malonyl co-enzyme A pathway is a major route of fatty acid synthesis in the mammary gland. This envisages the carboxylation of acetyl co-enzyme A to give malonyl co-enzyme A, a process involving an enzyme which is biotin-dependent (acetyl co-enzyme A carboxylase). Acetyl co-enzyme A reacts successfully with several malonyl co-enzyme A molecules to give rise to fatty acids.

In ruminants, the long-chain fatty acids (stearate, oleate) are taken up from the blood stream as triglycerides. The glycerol moiety of the milk triglycerides is derived partly from blood glycerides and partly from synthesis from glucose in the gland. The blood glycerides are contained in chylomicrons and low-density lipoprotein fractions. It is possible that lipoprotein lipase, which is found in the mammary gland, may be involved in absorption of the triglycerides by the mammary gland.

In the ruminant the degree of milk fatty acid saturation is largely independent of the nature of the dietary fat, but in the woman it is dependent on the nature of the dietary fat.

Lactating mammary tissue in some species, in addition to the Embden-Meyerhof pathway of carbohydrate breakdown, exhibits an active pentose phosphate cycle of carbohydrate metabolism. The latter provides reduced triphosphopyridine nucleotide (TPNH), which is necessary for the synthesis of milk fatty acids. This active lipogenesis regenerates TPN<sup>+</sup>, which in turn stimulates the pentose phosphate cycle. There is thus an intimate coupling between carbohydrate breakdown by the pentose phosphate pathway and the biosynthesis of fatty acids in mammary tissue. It is here that insulin probably exerts its stimulating action on mammary gland lipogenesis.

#### 4.4 Problems requiring investigation

(1) Little is known of the sites and modes of action of hormones, including prolactin, STH, and glucocorticoids, on the mammary gland. This is a field where further systematic research is required.

(2) More information is required on species differences in mammary gland metabolism. In particular, studies on the primate gland are needed.

(3) The occurrence and biological significance of minor constituents of human milk such as fucose-containing oligosaccharides, enzymes, and possibly hormones should be investigated.

(4) The excretion in milk of drugs, including antibiotics, requires systematic study.

### 5. PHYSIOLOGY OF SUCKLING

The milk-ejection reflex normally occurs in response to putting the child to the breast. It consists essentially of a reflex contraction of the myoepithelial cells surrounding the alveoli, which squeezes the alveoli and so ejects the milk from the alveoli into the duct system and into the sinuses where it is immediately available to the suckling. This reflex, under the name of the "draught" or "let-down", has been recognized for centuries both in man and in animals, but only in recent years has its true nature been appreciated. The sudden increase in milk pressure within the gland was long thought to be caused by a very active secretion of milk in response to suckling, but this has been entirely disproved. As already stated, it is the active ejection of milk from the alveoli into the larger ducts and sinuses. This reflex has a nervous afferent and a hormonal efferent pathway, i.e., it is a neurohormonal reflex. In response to the suckling stimulus oxytocin is released from the posterior pituitary

gland into the blood stream and, on reaching the mammary gland, causes contraction of the myoepithelial cells surrounding the alveoli (Fig. 3).

Recent studies on ruminants have provided evidence that purely nervous reflexes may also be concerned in the transfer of milk along the ducts both between milkings (when the transfer occurs in response to baroreceptor stimulation in the duct system) and immediately after the milking stimulus. These transfers of milk probably facilitate the major movement of milk that takes place when the myoepithelial cells contract. On the application of the milking stimulus this purely nervous reflex occurs before alveolar contraction, the latter being delayed owing to the time required for the oxytocin to be carried in the blood from the posterior pituitary to the mammary gland.

In many species, including man, unless milk ejection occurs the suckling will obtain only a fraction of the milk contained within the mammary gland. In the sheep and goat substantial emptying of the udder of milk can be achieved in the complete absence of the milk-ejection reflex. This finding is perhaps associated with the architecture of the gland in these species, which permits ready drainage of the milk from the alveoli into the cisterns; or it may be that the myoepithelial cells are unusually sensitive to local sensory stimulation.

The afferent pathways of the milk-ejection reflex are still not well defined, despite numerous studies both on the effects of lesions and of electrical stimulation experiments on the mammary nerves, spinal cord, mesencephalon, limbic system, and hypothalamus. There is evidence that the cells of the supraoptic and paraventricular nuclei of the hypothalamus are concerned in the synthesis of oxytocin, but nothing is known of the mechanism regulating the rate of synthesis. From these nuclei the hormone passes down the axones of the cells into the posterior pituitary, where it is released into the blood stream in response to the suckling stimulus. Only recently has a sufficiently sensitive and specific assay method been available for detecting oxytocin in blood. Oxytocin has been detected in the jugular blood of the cow and ewe at milking, but as yet no information is available on oxytocin levels in the blood of nursing women.

Failure to remove the milk from the actively secreting gland at regular intervals rapidly leads to an inhibition of the secretory processes. Thus repeated failure of the milk-ejection reflex quickly results in complete cessation of lactation.

The milk-ejection reflex may become conditioned to occur in response to events which the nursing woman or animal has come to associate with suckling. The reflex is readily inhibited by such factors as fear, pain, or stress, the inhibition being brought about either by stimulation of the sympathetico-adrenal system or by central inhibition of oxytocin release. The importance of a quiet regular routine at milking times in the cow-

shed has long been recognized as essential for efficient milking, but the necessity for ensuring for a mother, as far as possible, freedom from pain, fear, and embarrassment at the times when she is nursing her baby is still not widely understood. For many years the importance of the milk-ejection reflex in women was overlooked, and even now its precise pattern requires to be determined. The reflex is essential for the maintenance of lactation in woman, and since it takes some time before a regular milk-ejection reflex is established after parturition it is clear that this period is critical in human lactation.

### **5.1 Problems requiring investigation**

(1) Studies on oxytocin levels in the blood of nursing women are required.

(2) The mechanisms controlling the formation of hypothalamic neurohormones, particularly oxytocin, are quite unknown and need to be studied.

## **6. ASPECTS OF HUMAN LACTATION AND BREAST-FEEDING**

### **6.1 Lactation**

The chain of events leading to milk secretion and milk ejection has been less intensively studied in man than in other animals, but what evidence there is suggests no important difference. As in the animal, both milk secretion and ejection are in part controlled by the hypothalamus and are, through it, subject to influence from higher centres; but in man higher centres of nervous activity play a much larger role and, as a result, psychological influences on lactation are conspicuous. The wide variety of interrelated factors that can effect human lactation is indicated in Fig. 4.

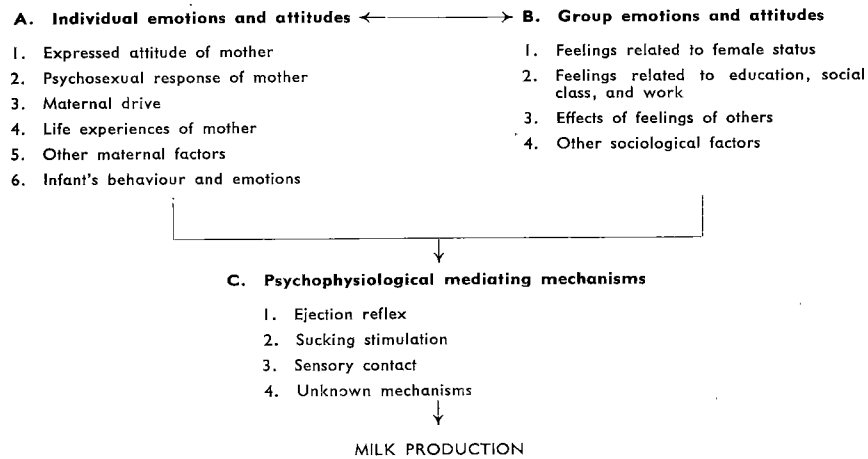
### **6.2 Breast-feeding**

The behaviour pattern of breast-feeding is to some extent dependent on the ability to lactate, but many women, particularly in affluent societies, never attempt breast-feeding or abandon it early. Reasons for this are indicated on Fig. 4.

Women who exhibit positive maternal behaviour and who express enthusiasm for breast-feeding are usually more successful at it. Experiences in pregnancy, labour, and previous lactations may play an important role in determining a woman's attitude towards breast-feeding and are thus related to its success or failure. Breast-feeding is a co-operative

process between two people, and its smooth course depends on the behaviour of the infant as much as on the behaviour of the mother. Encouragement by the mother's attendants during the early stage of lactation favours a satisfactory outcome to lactation. So does proper handling of the infant.

FIG. 4. PSYCHOLOGICAL FACTORS IN HUMAN LACTATION



In cultures where the baby is fed more frequently and there is less rigidity in breast-feeding routines, breast-feeding appears to be more successful.

### 6.3 Particular problems of developing countries

In many developing countries where substitute foodstuffs are not easily available the infant is practically dependent on human milk for its dietary protein, and failure of breast-feeding may lead rapidly to malnutrition, particularly protein malnutrition. In these countries successful breast-feeding has been almost universal, but there is now a drift of population from rural areas to the towns, with a concomitant trend towards abandoning breast-feeding. This serious situation deserves study in the context of the already high incidence of protein malnutrition in children in these communities.

Because of the shortage of suitable protein foods for infants, breast-feeding for periods of up to two years is usually encouraged. While there is evidence that adequate lactation may be supported for a remarkably long time on inadequate maternal diets by drawing on maternal tissues, such prolonged lactation might well be expected to have serious effects on the nutrition and health of the mother. This paradox of poorly

nourished mothers producing adequate yields of milk requires investigation. Further careful studies of the effects of prolonged lactation on maternal health and nutritional status are essential, since existing studies on nursing mothers designed to determine the nutritional requirements during lactation are surprisingly few.

Studies of the chemical composition of milk in undernourished mothers reveal that, while the concentration of vitamins is considerably reduced, the concentration of the proximate principles, particularly protein, is well maintained. Preliminary studies of the effects of dietary supplementation upon different nutrients on the chemical composition of milk have revealed some interesting and paradoxical features which merit further investigation.

During lactation there exists a phase of amenorrhoea and non-ovulation, the duration of which varies greatly. The exact mechanism of this ovarian inhibition is unknown. It may prove possible to reinforce this physiological mechanism and so protect lactation against premature conception by the administration of suitable ovarian inhibitors.

Many herbal concoctions have had a reputation in various localities as galactogues, and some of the examples of successful breast-feeding by virgins and old women have been attributed to their use. While no effective galactagogue has yet been isolated from such plant sources, it may be worth continuing the search.

#### **6.4 Problems requiring investigation**

(1) More information is needed on the reciprocal relation between ovarian function and lactation and on the effect of prolonged treatment with ovarian inhibitors on lactational performance.

(2) Studies on the chemical composition of milk with particular reference to the effects thereon of maternal dietary deficiencies and duration of lactation require to be further pursued.

(3) The effects of continued lactation on the health and nutritional status of the mother require further careful study, and experiments on nursing mothers designed to determine requirements of different nutrients in lactation are an urgent necessity.

(4) The effects of socio-economic conditions on the breast-feeding pattern of different population groups merit attention. Field studies should be undertaken to investigate the effects of industrialization and urbanization on the breast-feeding patterns of different population groups.

(5) Psychophysiological mechanisms that link the emotions of the mother with milk secretion and milk ejection deserve study, as does the relation of human lactation to the personality of the mother and to her previous experiences, particularly in regard to pregnancy, labour, and breast-feeding.

## 7. RECOMMENDATIONS

The Group, having made a wide survey of the physiology of lactation and considered areas in which knowledge, facilities, or support are at present inadequate, puts forward the following recommendations, which are *not* arranged in any particular order.

It is recommended that WHO should :

(1) Provide grants and research fellowships to enable research workers in the field of lactation to extend their experience by working for a time in other appropriate research centres, especially in relation to the problems listed at the end of each section of this report. Priority should be given to research on the primates, especially man.

(2) Support the establishment of laboratories in certain countries for the titration of hormones in cases of normal and abnormal lactation.

(3) Make contact with organizations already engaged in the collection of primate (human and monkey) pituitary tissues, to obtain their advice and help in organizing the extension of the collection to other parts of the world and in arranging for the preparation of extracts, especially of human prolactin and somatotrophin, for international use. A study group of those immediately concerned should be set up to supervise the project.

(4) Make contact with individuals and organizations engaged in the collection of hypothalamic tissue, with the object of improving facilities both for the collection of tissue and for the extraction of the hypothalamic factors, especially those concerned in the release of pituitary hormones concerned in lactation. A study group of those immediately concerned should be set up to supervise this project also.

(5) Encourage studies on human lactation in relation to malnutrition and undernutrition in developing countries. They should include field studies of breast-feeding patterns in different socio-economic groups, metabolic and endocrinological studies of undernourished nursing mothers, and investigation of the nutritional requirements of the nursing mother. Studies on these lines are already under way in some developing countries and should receive support and encouragement from WHO.