BREAST FEEDING AND VIRUS INFECTIONS

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Every student of medicine and biology is told that the compo-
sition of milk is perfectly adapted to the nutritional requirements
of the young mammal and a well fed animal is in many ways no doubt
well able to deal with infections including those due to viruses.
Indeed malnutrition is believed to be an important reason for the
high mortality from measles and herpes simplex virus infections which
occur in certain areas of the world, although this effect is not
independent of immune processes since it is probably due in part to
the lack of immune response in the undernourished infant. Never-
theless good nutrition does not confer immunity against viruses.
In animal husbandry it is well known that animals that are well fed
artificially, especially those deprived of colostrum, are prone to
scours, that is to gastroenteritis, which we now know is often due
to infection with viruses, such as coronaviruses, for example trans-
missible gastroenteritis (TGE) virus of piglets, and rotaviruses of
piglets, calves and lambs. In such cases it seems that the colostrum
contains antiviral antibodies because the mother has been infected
earlier in life, and these confer resistance to infection with these
viruses[1]. Secretory antibodies are also produced by the respiratory
and gastrointestinal tract and clearly have an important role in
protecting them against infection, but the infant produces these
only later in life and after it has received an antigenic stimulus.

It is unwise however to argue for the value of human milk by
analogy with domestic animals since the anatomy and physiology of
placentation and lactation differ greatly from species to species,
and the pathogenesis of virus infections also varies from virus to
virus. It seems best therefore to review firstly the evidence that
milk, and particularly human milk, has antiviral activity and to
what this may be due. Secondly, we need to review the evidence that

breast feeding actually influences the occurrence of virus infections, for the mere fact that a milk has an antiviral effect against a particular organism in the laboratory does not prove that taking that milk protects the infant to any useful extent against intection with it.

ANTIVIRAL ACTIVITY OF MILK

Antibodies

It is well known that milk contains secretory IgA antibodies, and there is much evidence[2,3] to show that such antibodies directed against the surface antigens of viruses neutralise the infectivity of the virus particle, without the presence of complement or other accessory factors. Although locally administered antigens stimulate particularly high titres of secretory antibodies, human breast milk contains antibody against many viruses to which the mother has been previously exposed, including some which produce localised infections of the respiratory or gastrointestinal tract (Table 1). It is assumed that immunocytes migrate into the mammary gland from other parts of the body where they have encountered antigens[4]. These antibodies are detected most easily in colostrum and decline in concentration as this is succeeded by milk. Thus it seems likely that most children receive maternal antiviral antibody not only via the placenta before birth but also after birth in the milk. Most of these antibodies are believed not to be absorbed but to remain in the intestinal tract after being swallowed, until they are eventually digested. They could therefore be expected to be most effective in preventing infections of the gastrointestinal tract, and it would be unreasonable to expect antibodies against respiratory viruses to be protective even if small amounts of milk were inhaled during suckling.

Table 1. Antiviral antibodies found in human colostrum or milk

Virus	Reference
Polio virus type 1, 2, 3	15
Coxsackie virus types A9, B3, B5	15
Echo virus types 6 and 9	15
Rota virus	7, 16, 17
Respiratory syncytial virus	18
Certain alpha viruses	19

Other antiviral substances

    It has been found that milk also has antiviral activity which
is not due to antibodies. For instance, a lipid factor or factors
may have an inhibitory effect on certain arbo viruses[5]. However
we have found that milk can have an antiviral effect on a wide range
of other viruses[6]. The effect is clearly of a different kind from
that produced by antibody and this was recognised as we were
developing a method of assay. To detect antiviral neutralising
antibody it is mixed with a virus and after a delay for reaction the
mixture is added, possibly after dilution, to a system which detects
free virus -- a sensitive tissue culture, for example. If neutralisa-
tion has occurred the virus does not infect, and therefore fails to
grow, to damage cells and to cause a cytopathic effect, which is
often detected as a focus or plaque in a cell sheet. This is the
basis of the standard plaque reduction test. Breast milk or fractions
obtained from it can reduce plaque counts of virus even if no specific
antibody is present (Fig. 1), but in this case the virus, the anti-
viral substance and the cells have all to be present in the same
system and remain together. This suggests that the antiviral sub-
stance binds rather weakly to the virus or possibly to the cell.
The antiviral effect is found against a virus such as vesicular
stomatitis virus (VSV) which does not infect man -- nor does any
antigenically related virus -- so an antibody is not likely to be
the explanation (Fig. 1). Furthermore the properties of the activity
do not correspond to those of antibody; for instance it is found
in milk treated with phenol or chloroform-butanol. However it has
not been possible to find a particularly active fraction of human
milk among many provided by Dr G. Spik, and it is difficult to account
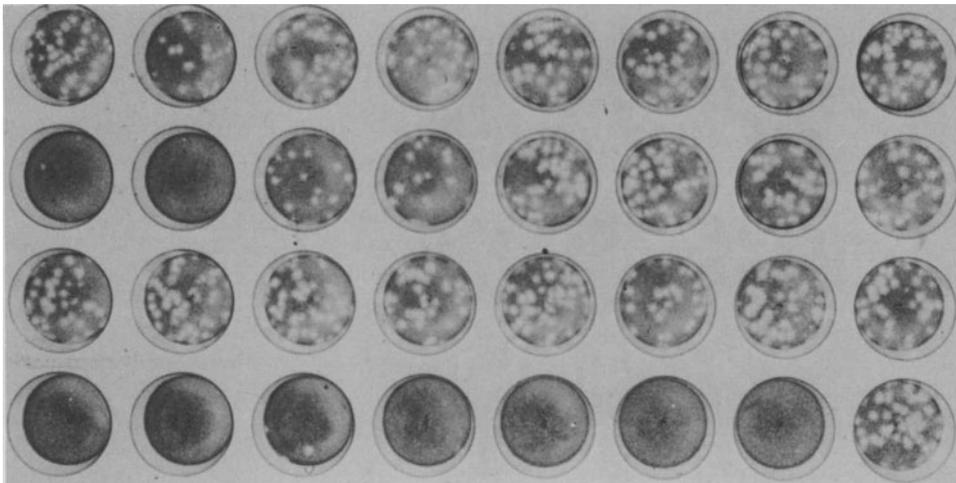

Fig. 1

for all the activity in the original milk from the sum of the
activity of the fractions (K.G. Nicholson, personal communication).
Our present concept is that the effect may be produced by certain
polysaccharides which are found on a number of different molecular
constituents of milk.

Dr Nicholson has also examined samples of breast milk collected
from women in rural Gambia by Dr M. Rowlands and his colleagues.
Some of the results are shown in Table 2 and indicate that although
the activity declines somewhat earlier in lactation it is generally
well maintained thereafter. It may still be present when antiviral
antibody can no longer be detected. Indeed anti rota virus activity
in human milk is probably due to this substrate, particularly later
in lactation[7]. Similar activity is found in cow's milk.

We also studied the effect on breast milk and cow's milk of
various treatments. It was clear that the drying of cow's milk to
produce baby food destroyed much of its antiviral activity, although
pasteurised milk was still antiviral.

Lymphocytes

I include these not because there is much firm knowledge but
because it seems to me to be a subject worthy of exploration.
Lymphocytes sensitised by exposure of the host can be activated and
become transformed by contact with viral antigens. Indeed lymphocyte
transformation is presumably an integral part of the delayed hyper-
sensitivity reaction which seems to make such an important contri-
bution to immunity against viruses such as vaccinia and herpes
viruses[8]. However the question here is whether maternal lymphocytes
contained in colostrum and milk[9] can prevent infection with
respiratory or gastrointestinal viruses. For instance, it has been
suggested that circulating lymphocytes that have not been sensitised
or activated can inactivate viruses if mixed with them. However
further study suggests that the rate of decay of infectivity may not
be reduced in the presence of lymphocytes. Polymorphonuclear cells
can ingest influenza virus particles but are not then infected by
them[9]; they could thus prevent virus particles from attaching to
susceptible epithelial cells.

We also know that lymphocytes in the presence of antibody will
attack cells infected with virus and destroy them (ADCC) and this
may be a means of getting rid of a focus of infected cells. This
antibody dependent cytolysis might take place on the surface of a
baby's mucosa with maternal antibodies and lymphocytes. Most of this
represents nothing more than speculation but it does indicate that
it might be worthwhile trying to develop techniques to separate
functionally active white cells from milk and test them to determine
whether they have antiviral activity. Preliminary evidence shows
that breast milk lymphocytes from 5 of 17 mothers were specifically
transformed by RS virus (Toms G.I., Hey F., Gardner P.S., Pulton C.R.
and Scott R., personal communication).

Table 2. Antiviral activity of Gambian breast milk samples at 20% and 50% concentrations assayed by plaque reduction against vesicular stomatitis virus

Time post-partum	20% milk			5% milk		
	No. of samples	Mean protection	Range	No. of samples	Mean protection	Range
0-2 days	8	85.3	57.1-97.2	8	70.7	48.1-90.5
2-30 days	18	77.7	55.5-97.2	18	47.6	25.3-86.4
1-2 months	14	74.6	55.1-95.1	14	44.6	14.1-80.5
2-4 months	9	71.5	51.8-89.9	9	32.4	19.1-50.4
4-6 months	6	75.1	56.7-83.1	8	36.4	16.6-61.1
6-12 months	4	73.8	52.0-92.9	7	47.8	17.6-68.5
12-18 months	4	63.1	59.5-68.1	7	38.7	9.7-73.3

EVIDENCE THAT BREAST FEEDING PREVENTS VIRUS INFECTIONS

We cannot review here all the evidence that breast feeding reduces the incidence of infections in general in the infant, but apparently the practice reduces the incidence of both gastro-intestinal and respiratory infections[10].

As mentioned earlier it is a most plausible idea that breast feeding may prevent rota virus infections and gastroenteritis. We found in a recent study that rota virus infections were occurring in our area in older children than had been reported by others in previous years in other areas of London[11]. It was known that more mothers in our area were breast feeding their children and for longer than before and it was therefore an attractive hypothesis that this was why the peak age of attack had moved to an older age group. It has been suggested that difficulties in vaccinating successfully with oral polio vaccine are due to prolonged breast feeding as practiced in many tropical countries[12,13]. However the evidence is not con-clusive, and other factors such as infection with other entero-viruses may be more important.

However respiratory disease may also be prevented by breast feeding and recent work in Newcastle has shown that bronchiolitis of infants due to respiratory syncytial virus is less frequent in breast fed than in artificially fed infants[14] (Table 3). The difference remains even when one takes account of the possibility that the effect may be indirect via some secondary association between attitudes to breast feeding and socio-economic status, smoking habits

Table 3. Frequency per cent of breast feeding in patients admitted to hospital in Newcastle with respiratory syncytial virus infections

	R.S. infection		Matched uninfected controls
	all cases	severe cases (tube fed)	
	127	67	497
Not breast fed	30%	28%	49%
Breast fed at time of admission or equivalent age	13%	15%	20%

Adapted from[14].

and so on. The mean relative risk of being in the virus infected
group if the child is not breast fed is 2.2 : 1, although clearly
other factors besides breast feeding probably have some role.

SUMMARY

     Breast milk may contain specific neutralising antibodies against
any virus to which the mother has been exposed. It also contains
substances with weak antiviral activity against many viruses. It is
possible that cells present may also have antiviral effects but this
has not been proved. There is some evidence that breast feeding
protects against intestinal infections, for instance with rota
viruses, and also a respiratory virus, namely respiratory syncytial
viruses.

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