154. Bifidus Factor in Carrot. I

Bifidobacterium bifidum and Bifidus Factor

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Since 1952 the authors conducted studies on carrot treatment in infantile diarrhea originated by Moro and recognized the good effect. In 1955 it was discovered that in the infant Bifidobacterium bifidum in the feces increases by giving carrot. Since it was confirmed later that a very active bifidus factor is present in the carrot a joint study was conducted since 1959 with Prof. Zenzo Tamura of the Faculty of Pharmaceutical Sciences of the University of Tokyo on the isolation and identification of this factor.

In 1966 it was surmised that this bifidus factor is composed of several closely related substances of 4'-phosphopantetheine, a precursor of coenzyme A, and in 1970 Tamura et al. ascertained that this bifidus factor is composed of the following 5 substances; pantetheine, 4'-phosphopantetheine, 4'-phosphopantethine, 4'-phosphopantetheine-S-sulfonic acid and 3'-dephospho-coenzyme A-S-sulfonic acid. Of these, it was found that the former three are known substances but the latter two are completely unknown substances.

Many previous studies on the difference between breast feeding and bottle feeding showed that breast feeding is superior, and according to Robinson the mortality and morbidity of the breast-fed infants are far less than those of the bottle-fed infants. According to the results of the survey done in Tokyo it was also found that the ratio of mortality among the breast-fed, mixed-fed and bottle-fed infants was 1:2:3 in the mature infants and 1:2:4 in the premature infants.

What differences appear in the body of the infants between breast feeding and bottle feeding? One of the principal differences is in the intestinal flora. Since the intestine of the embryo is sterile there are no microorganisms in the meconium of the newborn but microorganisms begin to inhabit the intestine shortly after the infection during the passage through the birth canal. After this the intestinal flora of the infant shows a characteristic finding according to the
method of nutrition; *B. bifidum* composing 80 to 90% of the flora in the bread-fed infants, *E. coli* and *Str. faecalis* composing 70 to 80% in the bottle-fed infants.\(^5\)

What advantage is there when the number of *B. bifidum* in the intestine is large? *B. bifidum* produces lactic acid and acetic acid\(^6\) and it was presumed that by this the growth of *E. coli* and other pathogenic microorganisms is inhibited, and when the demand for nutrition by *B. bifidum* is great and the growth of *B. bifidum* is predominant, there is a lack of nutriment necessary for the growth of microorganisms having pathogenicity.

Recently Homma\(^7\) showed that *B. bifidum* prevents the invasion of pathogenic coli into villi of the germ free mice.

There is a classical theory that the amine produced by the *E. coli* in the intestine is the cause of severe diarrhea in the infant but Negishi and Billy\(^8\) reported that although β-phenylethylamine, putrescine and cadaverine are demonstrated in the medium in which *E. coli* is cultured, the amount of amine produced, when *E. coli* is cultured in the medium in which *B. bifidum* is cultured beforehand, is very small, stating that the increase of *E. coli* is inhibited in the environment permitting the survival of *B. bifidum*. According to Adam\(^9\) and the authors,\(^10\) it is said that *B. bifidum* produces more vitamin B\(_1\) than *E. coli*.

It is said that the number of *B. bifidum* in the intestine of the infant is an index in judging the condition of the health of the infant. The authors\(^11\) studied the relation of the Kaup index to the intestinal flora in a large number of infants and found that the number of *B. bifidum* in the feces was large in those infants who were either breast-fed, bottle-fed or mixed-fed and were in a good state of nutrition and with a Kaup index of 1.5 to 1.9.

It is a well-known fact that in infantile diarrhea *B. bifidum* in the intestine decreases and *E. coli* increases. The authors\(^13,14\) also demonstrated that, compared to the normal value in the healthy infant, in the infant with diarrhea *B. bifidum* in the feces decreases and *E. coli* increases distinctly. The authors\(^15\) studied the intestinal flora in the infant with conditions other than diarrhea, finding that in most cases *B. bifidum* decreases during illness as compared to when healthy. When the intestinal flora of an infant was studied for several months the change in the flora was small when the general condition of the body was not disturbed as in cold, varicella and bronchitis but in the case where the general condition was bad as in pneumonia *B. bifidum* decreased and *E. coli* increased. In the case of what is considered as a kind of an artificial invasion like in plastic surgery for harelip in the infant or fever induced by the injection of
bacterial pyrogenic substance in fever therapy of the infant for cerebral palsy there was observed also a change in the intestinal flora, \( B. \text{bifidum} \) decreasing and \( E. \text{coli} \) increasing temporarily.\(^{15}\) As stated above, that a large number of \( B. \text{bifidum} \) inhabits the intestine of the infant is indeed a desirable condition for the infant but \( B. \text{bifidum} \) readily decreases by the various kinds of invasion from within the intestine and outside of the intestine of the infant.

What is the bifidus factor? \( B. \text{bifidum} \) was discovered by Tissier in 1899 and at that time attention was paid to the fact that \( B. \text{bifidum} \) is observed in a large number in the feces of breast-fed infants, and the relation between the human milk and \( B. \text{bifidum} \) was studied. From the fact that lactose is contained in the human milk at the rate of 7% and in the cow milk at the rate of 4%, it was found that lactose is used by \( B. \text{bifidum} \) as a nutriment. However, there are various theories and one of them is that besides lactose there is a minute quantity of substance contained in the human milk which promotes the growth of \( B. \text{bifidum} \). In 1949 Petuely\(^{16}\) discovered a substance which when given to a bottle-fed infant changes the intestinal flora similar to that of the breast-fed infant and called it a bifidus factor. After this Kristen,\(^{17}\) Petuely\(^{18,19}\) stated that this bifidus factor was lactulose, and when 1 to 2 grams of this was given for every 70 calories taken by the infant the intestinal flora changes so that there was a pure growth of \( B. \text{bifidum} \) within 24 to 96 hours. However, although lactulose shows effect \textit{in vivo} but has no effect \textit{in vitro}.

György and Kuhn \textit{et al.}\(^{20-24}\) isolated from the feces of the breast-fed infant \( B. \text{bifidum} \) which grew only in the medium to which human milk was added. The \( B. \text{bifidum} \) was called \textit{Lactobacillus bifidum var. Pennsylvanicus} (abbreviated var. \textit{Penn.} strain). As a result of studying the bifidus factor in the human milk using this microorganism, it was found that it was oligosaccharide containing N-acetyl-glucosamine, and that among the related substances to glucosamine the most active compound was alkyl-N-acetyl-D-glucosamine.

Tomarelli\(^{25}\) and Zillinken\(^{26}\) also isolated a bifidus factor from the gastric mucosa of pig and reported that it was an oligosaccharide containing glucosamine. However, according to the conclusion by György \textit{et al.}\(^{27}\) the oligosaccharide may be a precursor of \( B. \text{bifidum} \)-proliferating substance, and Petuely\(^{19}\) stated that \( B. \text{bifidum} \) does not increase at all even if the oligosaccharide is given to an infant, and in addition, since the isolation of var. \textit{Penn.} strain from the feces of the breast-fed infant is very rare the oligosaccharide in the human milk is not the bifidus factor, and if it had any influence it may be a
secondary one. Later, Raynaud and Levesque reported that there is a polypeptide in the enzymolytic product of casein which makes the Tissier strain proliferate markedly and called the bifidus factor of György et al. factor I and this substance factor II. Later, Rose et al. stated that for the growth of the var. Penn. strain, besides factor I, a polypeptide different from factor II is necessary and this polypeptide is contained in the pancreatin which markedly promotes the growth of B. bifidum. They called this a supplementary factor.

References